Risk Factors Comparison 2025-03-31 to 2024-02-16 Form: 10-K

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In addition to the other information in this Annual Report on Form 10- K, any of the factors described below could significantly and negatively affect our business, financial condition, results of operations or prospects. The trading price of our Class A Common Stock may decline due to these risks. Risks Related to LINZESS, Apraglutide and Other Product Candidates We are highly dependent on the commercial success of LINZESS (linaclotide) in the U. S. for the foreseeable future. We and our partner, AbbVie, began selling LINZESS in the U. S. in December 2012. Revenues from our LINZESS collaboration constitute a significant portion of our total revenue, and we believe they will continue to do so for the foreseeable future. The commercial success of LINZESS depends on a number of factors, including: ● the effectiveness of LINZESS as a treatment for adult patients with IBS- C, or CIC, and as a treatment for pediatric patients aged 6- 17 years- old with FC; ● the size of the treatable patient population; ● the effectiveness of the sales, managed markets and marketing efforts ~~by us and AbbVie~~ , including ~~our~~ **the** ability to adapt ~~our~~ **a** commercial model and market strategy to the evolving landscape; ● the coverage and reimbursement levels set by governmental authorities, private health insurers and other third- party payors **; ● the status of government regulation in the life sciences industry, particularly with respect to healthcare reform and drug pricing** ; ● the adoption of LINZESS by physicians, which depends on whether physicians view it as **a** safe and effective treatment for adult patients with IBS- C and CIC and ~~for~~ pediatric patients ages 6- 17 years- old with FC; ● our success in educating and activating adult IBS- C and CIC patients, and children and adolescents ages 6- 17 years- old FC patients and their caregivers, to seek physician care for their symptoms; ● our ability to both secure and maintain adequate reimbursement for, and optimize patient access to, LINZESS and our ability to demonstrate that LINZESS is safer, more efficacious and / or more cost- effective than alternative therapies; ● the effectiveness of our partners' distribution networks; ● the occurrence of any side effects, adverse reactions or misuse, or any unfavorable publicity in these or other areas, associated with linaclotide; and ● the development or commercialization of products or therapies that compete with LINZESS. Our revenues from the commercialization of LINZESS are subject to these and other factors, and therefore **has been and** may be unpredictable from quarter- to- quarter **and year- to- year** . We are subject to uncertainty relating to pricing and reimbursement policies in the U. S. **, including recent and future healthcare reform measures,** which, if not favorable for our products, could hinder or prevent our products' commercial success. Our and our partner' s ability to commercialize our products successfully depends in part on the coverage and reimbursement levels set by governmental authorities, private health insurers and other third- party payors. In determining whether to approve reimbursement for our products and at what level, we expect that third- party payors will consider factors that include the efficacy, cost effectiveness and safety of our products, as well as the availability of other treatments **,** including generic prescription drugs and OTC alternatives. Further, in order to obtain and maintain acceptable reimbursement levels and access for patients at copay levels that are reasonable and customary, we have offered, and expect to continue to face increasing pressure to offer, discounts or rebates from list prices or discounts to third- party payors or other unfavorable pricing modifications. Obtaining and maintaining favorable reimbursement can be a time consuming and expensive process, and there is no guarantee that we or AbbVie, with respect to ~~linaclotide~~ **LINZESS** in the U. S., will be able to negotiate or continue to negotiate pricing terms with third- party payors at levels that are profitable to us, or at all. Certain third- party payors also require prior authorization for, or ~~even~~ **have** ~~refuse~~ **refused** to provide, reimbursement for our products, and others may do so in the future. Our business would be materially adversely affected if we and our partners are not able to receive approval for reimbursement of our products from third- party payors on a broad, timely or satisfactory basis; **or** if reimbursement is subject to overly broad or restrictive prior authorization requirements; or if reimbursement is not maintained at satisfactory levels or becomes subject to prior authorization. In addition, our business could be adversely affected if government healthcare programs, private health insurers, including managed care organizations, or other reimbursing bodies or payors limit or reduce the indications for or conditions under which our products may be reimbursed. Moreover, as discussed further below **and above in Part I, Item 1, under the heading Pricing and Reimbursement** , changes in insurance coverage or reimbursement levels by governmental authorities, private health insurers and other third- party payors, or in the type of such coverage held by patients may materially harm our business and commercialization efforts. We **have experienced and** may experience **additional** pricing pressures in connection with the sale of our current and future products due to the healthcare reforms discussed below **and above in Part I, Item 1, under the heading Pricing and Reimbursement** , as well as the trend toward initiatives aimed at reducing healthcare costs, the increasing influence of managed care, the scrutiny of pharmaceutical pricing, the ongoing debates on reducing government spending and additional legislative proposals. There has been significant scrutiny of pharmaceutical pricing and the resulting costs of pharmaceutical products that could cause significant operational and reimbursement changes for the pharmaceutical industry. There have been a number of federal and state efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices, price increases or other related costs. Certain of these efforts have resulted in legislative and regulatory reforms. For example, and as discussed further below **and above in Part I, Item 1, under the heading Pricing and Reimbursement** , the IRA ~~, which~~ could have the effect of reducing the **net** prices ~~we can charge and increasing the discounts we provide~~ for our products and product candidates. As another example, legislation enacted in 2021 revised the Medicaid drug rebate program in which we and other manufacturers participate so that Medicaid rebates were no longer capped at 100 % of the quarterly average manufacturer price **effective January 1** , **2024** ~~or AMP~~ . We anticipate that ~~our ability to increase prices on our products, including LINZESS, and our revenues, may be adversely affected by~~ legislative and regulatory reforms ~~such as~~ **, including** the Medicaid drug rebate program revisions **, may adversely affect**

our revenues and our ability to maintain satisfactory net prices on our products, including LINZESS . ~~27Healthcare -- 45Healthcare --~~ **Healthcare** reform and other governmental and private payor initiatives may have an adverse effect upon,and could prevent,our products' or product candidates' commercial success.The U.S.government and individual states have been aggressively pursuing healthcare reform designed to impact delivery of,and / or payment for,healthcare,which ~~include~~ **includes** initiatives intended to reduce the cost of healthcare.For example,in March 2010,the U.S.Congress enacted the PPACA,as modified by the Health Care and Education Reconciliation Act,or the ACA,which,among other things,expanded healthcare coverage through Medicaid expansion and the implementation of the individual health insurance mandate;included changes to the coverage and reimbursement of drug products under government healthcare programs;imposed an annual fee on manufacturers of branded drugs;and expanded government enforcement authority.Beyond the ACA,there have been ongoing legislative and administrative and other health care reform efforts ~~been aggressively pursuing healthcare reform designed to impact delivery of,and / or payment for,healthcare,which include initiatives intended to reduce the cost of healthcare.For example,in March 2010,the U.S.Congress enacted the PPACA,as modified by the Health Care and Education Reconciliation Act,or the ACA,which,among other things,expanded healthcare coverage through Medicaid expansion and the implementation of the individual health insurance mandate;included changes to the coverage and reimbursement of drug products under government healthcare programs;imposed an annual fee on manufacturers of branded drugs;and expanded government enforcement authority.Beyond the ACA,there have been ongoing legislative and administrative and other health care reform efforts~~ ,which could have an adverse effect on our products' or product candidates' commercial success.Some healthcare reform ~~efforts~~ **27efforts** affect pricing or payment for drug products or the healthcare industry more generally.Drug pricing and payment reform was a focus of the **former Biden Administration and is likely to continue to be a focus of the current** Trump Administration ~~and has been a focus of the Biden Administration~~ .For example, ~~under the Trump Administration,~~ federal legislation ~~increased~~ **enacted in 2021 eliminated the statutory cap on Medicaid drug rebate program effective January 1,2024.Most significantly,in August 2022,President Biden signed the IRA into law.This statute marks the most significant action by Congress with respect to the pharmaceutical industry since the adoption of the ACA in 2010.The IRA contains various drug pricing and payment provisions.Among other provisions,the IRA imposes a yearly cap ($ 2,000 in 2025) on out- of- pocket prescription drug prices in Medicare Part D.Additionally,the IRA,through a newly established Manufacturer Discount Program,eliminated,effective January 1,2025,** the size of the discount on brand- name drugs that pharmaceutical manufacturers are required to offer Medicare beneficiaries who are in the Medicare Part D coverage gap,or " donut hole," **by significantly lowering** ~~from 50 percent to 70 percent.As another example,under the Biden Administration,federal legislation enacted in 2021 eliminates a statutory cap on Medicaid drug rebate program rebates effective January 1,2024.As another example,the IRA contains various drug pricing and payment provisions.Among other --~~ **the beneficiary maximum** ~~provisions,the IRA imposes a yearly cap ($ 2,000 in 2025) on~~ out- of- pocket ~~prescription~~ **cost and requiring pharmaceutical manufacturers to provide a 10 % discount in the initial coverage phase of the plan and 20 % discount in the catastrophic coverage phase of the plan on brand- name** ~~drug~~ **drugs** ~~prices in Medicare Parts B and D~~ .In addition,the IRA requires Medicare to negotiate prices for certain high- cost drugs and biologicals,including both physician- administered products covered under Medicare Part B benefit and self- administered drugs covered under the Medicare Part D benefit.CMS annually selects a specified number of negotiation- eligible drugs from those drugs with the highest total Medicare Part B or D expenditures over a preceding 12- month period.Eligible drugs generally include single ~~-~~ source brand- name drugs or biological products that have been on the market without therapeutically- equivalent generic or biosimilar alternatives for a specified number of years with certain exceptions (e.g.,orphan drugs indicated for only one rare disease or condition and drugs with less than $ 200 million in annual Medicare expenditures).CMS will publish the negotiated price,known as the MFP for each of the selected products.Manufacturers of selected drugs would be required to offer the drug for Medicare recipients at the MFP.Manufacturers who fail to negotiate or offer the MFP can face significant civil money penalties or excise tax liability on sales of that drug. ~~The~~ **In 2024,HHS published the results of the** first **Medicare** ~~drugs --~~ **drug** ~~were~~ **price negotiations for ten** selected ~~in 2023~~ **drugs that treat a range of conditions,including diabetes,chronic kidney disease,** and ~~the MFP for~~ **rheumatoid arthritis,and** ~~those --~~ **the prices of the selected** drugs will ~~take~~ **become** ~~effect~~ **effective** ~~in~~ **on January 1,** 2026. ~~Only~~ **On January 17,2025,HHS announced the selection of 15 additional drugs,which included LINZESS,covered by** Medicare Part D ~~drugs are selected for the first two years of the program (i.e., MFPs that take~~ **for the second cycle of price negotiations.The negotiated price for LINZESS will be** ~~effect~~ **effective** ~~in 2026 and~~ **starting January 1,** 2027 ~~)~~ .Depending on the share of Medicare spending each year that is attributed to LINZESS ~~or~~ or any ~~) on out- of- pocket prescription drug prices in Medicare Parts B and D.In addition,the IRA requires Medicare to negotiate prices for certain high- cost drugs and biologicals,including both physician- administered products covered under Medicare Part B benefit and self- administered drugs covered under the Medicare Part D benefit.CMS annually selects a specified number of negotiation- eligible drugs from those drugs with the highest total Medicare Part B or D expenditures over a preceding 12- month period.Eligible drugs generally include single source brand- name drugs or biological products that have been on the market without therapeutically- equivalent generic or biosimilar alternatives for a specified number of years with certain exceptions (e.g.,orphan drugs indicated for only one rare disease or condition and drugs with less than $ 200 million in annual Medicare expenditures).CMS will publish the negotiated price,known as the MFP for each of the selected products.Manufacturers of selected drugs would be required to offer the drug for Medicare recipients at the MFP.Manufacturers who fail to negotiate or offer the MFP can face significant civil money penalties or excise tax liability on sales of that drug.The first drugs were selected in 2023 and the MFP for those drugs will take effect in 2026.Only Medicare Part D drugs are selected for the first two years of the program (i.e.,MFPs that take effect in 2026 and 2027).Depending on the share of Medicare spending each year that is attributed to LINZESS or any~~ other product candidate that we develop and whether or not those drugs become eligible for Medicare negotiation,those drugs and our revenue may be adversely impacted by this provision. ~~Health~~ **It is unclear how the IRA will be implemented.While there**

had been some questions about the Trump Administration' s position on this program,CMS issued a public statement on January 29,2025,declaring that lowering the cost of prescription drugs is a top priority of the new administration and CMS is committed to considering opportunities to bring greater transparency in the negotiation program.On June 6,2023,Merck & Co.filed a lawsuit against the HHS and CMS asserting that,among other things,the IRA' s Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution.Subsequently,a number of other parties,including the U.S.Chamber of Commerce,also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS.HHS has generally won the substantive disputes in these cases,and various federal district court judges have expressed skepticism regarding the merits of the legal arguments being pursued by the pharmaceutical industry.Certain of these cases ~~care -~~ are now on appeal and the Court of Appeals for the Third Circuit heard oral argument in three of these cases.We expect that litigation involving these and other provisions of the IRA will continue,with unpredictable and uncertain results.Healthcare reform efforts have been and may continue to be subject to scrutiny and legal challenge.For example,with respect to the ACA,tax reform legislation was enacted that eliminated the tax penalty established for individuals who do not maintain mandated health insurance coverage beginning in 2019 and,in 2021,the U.S.Supreme Court dismissed the latest judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA.As another example,revisions to regulations under the federal anti- kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans.The revisions were challenged in court and,pursuant to court order,the removal was delayed,and recent legislation imposed a moratorium on implementation of the rule until January 2032.Certain pharmaceutical manufacturers and organizations have filed lawsuits challenging the IRA drug price negotiation program. ~~Adoption~~ 28Adoption of new healthcare reform legislation at the federal or state level could negatively affect demand for,or pricing of,our products or product candidates if approved for sale.In addition,other legislative changes have been adopted that could have an adverse effect upon,and could prevent,our products' or product candidates' commercial success.For example,the Budget Control Act of 2011,as amended,or the Budget Control Act,includes provisions intended to reduce the federal deficit,including reductions in Medicare payments to providers through 2032 (except May 1,2020 to March 31,2022).Any significant spending reductions affecting Medicare,Medicaid or other publicly funded or subsidized health programs,or any significant taxes or fees imposed as part of any broader deficit reduction effort or legislative replacement to the Budget Control Act,or otherwise,could have an adverse impact on our anticipated product revenues. ~~46In~~ Additionally,in its 2024 decision in Loper Bright Enterprises v.Raimondo,the U.S.Supreme Court overruled the " Chevron doctrine," which gives deference to regulatory agencies' statutory interpretations in litigation against federal government agencies,such as the U.S.FDA,CMS and other federal agencies where the law is ambiguous.This Supreme Court decision may lead to challenges of long standing decisions and policies of these agencies,which could lead to uncertainties in the industry and disrupt the federal agency' s operations.In addition to governmental efforts in the U.S.,foreign jurisdictions as well as private health insurers and managed care plans are likely to continue challenging manufacturers' ability to obtain reimbursement,as well as the level of reimbursement,for pharmaceuticals and other healthcare- related products and services. ~~These cost~~ We are unable to predict what additional legislation,regulations or policies,if any,relating to the healthcare industry or third - party ~~control initiatives could significantly decrease the available~~ coverage and reimbursement may be ~~the price we might establish for our products,which would have an adverse effect on our financial results.The Food and Drug Administration Amendments Act of 2007 also provides the U.S.FDA enhanced --~~ enacted in ~~post- marketing authority,including~~ the ~~authority to require post- marketing studies and clinical trials,labeling changes based on new safety information,and compliance with~~ future or what effect such legislation , regulations or policies would have on ~~or~~ our ~~regulatory actions~~ business. Any cost- control initiatives, legislative and administrative or other healthcare system reforms aimed at controlling and reducing healthcare costs, including through measures designed to limit reimbursement, restrict access or impose unfavorable pricing modifications on pharmaceutical products, could impact our and our partners' ability to obtain or maintain reimbursement for our products at satisfactory levels ~~,~~ and could significantly decrease the available coverage and the price we have or might establish ~~or~~ for ~~at all~~ our products and product candidates , which ~~could~~ would ~~materially harm~~ have an adverse effect on our business and financial results. We must work effectively and collaboratively with AbbVie to market and sell LINZESS in the U. S., and we must adapt our ~~linaclotide partners~~ commercial model and market strategy to the evolving landscape for LINZESS to achieve its maximum commercial potential. We are ~~subject~~ working closely with AbbVie to execute ~~uncertainty relating to pricing and reimbursement policies outside the U. S., as well as risks relating to the improper importation of linaclotide and sale of counterfeit versions of linaclotide. If such policies are not favorable, or~~ our joint commercialization plan ~~if linaclotide is improperly imported or~~ for ~~is counterfeited, our business~~ LINZESS. The commercialization plan includes ~~and --~~ an ~~financial results~~ agreed upon marketing campaign that targets the physicians who see patients who could ~~be adversely affected~~ benefit from LINZESS treatment . LINZESS In some foreign countries, particularly Canada..... unsatisfactory levels, our and our partners ' s consumer marketing campaign targets ~~ability to successfully commercialize linaclotide in such country would be impacted negatively. Furthermore, if these --~~ the adult men and women who suffer ~~measures prevent us or any of our partners~~ from ~~selling linaclotide on a profitable basis in a particular country, they could prevent the commercial launch or continued sale of linaclotide in that country. CONSTELLA was first launched in certain European countries for the symptomatic treatment of moderate to severe~~ IBS- C or CIC. In order to optimize the commercial potential of LINZESS, we and AbbVie must execute upon this commercialization plan effectively and efficiently. In addition, we and AbbVie must continually assess, modify and adapt our commercialization plan in a coordinated and integrated fashion, including evaluating and adjusting as necessary the level and mix of marketing and promotion efforts, in response to changing business, market or other factors in order to advance the commercial potential of LINZESS. Further, we and AbbVie must continue to focus the sales and marketing efforts for

the brand on educating customers about the relevant data and information for LINZESS in treating adults **with** ~~in the second quarter of 2013 and our partner, AbbVie, is currently commercializing CONSTELLA in a number of European countries. LINZESS was first launched in Japan for the treatment of~~ IBS- C ~~in adults in the first quarter of 2017,~~ and **CIC, and taking a measured approach to educating and raising awareness on the FC indication** for **pediatric patients ages 6- 17 years- old. We** ~~the treatment of chronic constipation in adults in the third quarter of 2018,~~ and ~~our partner Astellas is currently commercializing~~ **AbbVie must ensure a highly targeted and efficient promotional mix combined to continue effectively promoting** LINZESS ~~in Japan~~ **to key healthcare professionals** . ~~In addition~~ **If we and AbbVie fail to evolve with the changing commercial landscape successfully and perform these commercial functions in the highest quality manner and in accordance with our joint commercialization plan and related agreements** , LINZESS ~~was first launched in China for the treatment of~~ **will not achieve its maximum commercial potential and we may suffer financial harm. Our commercial efforts to further target and engage adult patients with** IBS- C ~~in adults in November 2019, and our~~ **or** ~~partner AstraZeneca, is currently commercializing~~ **CIC may not effectively increase appropriate patient awareness or patient / physician dialogue and may not increase the revenues that we generate from** LINZESS in China (including Hong Kong and..... our reputation, financial results and business . We cannot give any assurance that apraglutide will ~~be successful in clinical trials, and if successful, will~~ receive regulatory approval, which is necessary before it can be commercialized. ~~28Upon~~ **29Upon** the closing of the VectivBio Acquisition, we added apraglutide ~~, VectivBio' s lead investigational asset~~ , a next generation, long- acting GLP- 2 analog in development for **SBS** ~~the treatment of~~ patients **who are dependent on PS** ~~with SBS- IF and aGvHD~~ , to our pipeline. Apraglutide will require extensive clinical development, management of nonclinical, clinical and manufacturing activities, regulatory approval ~~,~~ **and** adequate manufacturing supply, and if approved, fully integrating apraglutide into ~~the~~ **our** commercial infrastructure to support ~~with~~ the appropriate sales, marketing, and market access efforts to generate sales in pursuit of revenue. **In February 2024, we announced positive topline results from our pivotal Phase III clinical trial, STARS, which evaluated the efficacy and safety of once- weekly subcutaneous apraglutide in reducing PS dependency in adult patients with SBS- IF.** We **are also conducting an open- label extension study, STARS Extend, to further assess safety of apraglutide in adult patients with SBS- IF. Based on these results, we** have **initiated** ~~not yet completed~~ a ~~pivotal trial~~ **rolling NDA submission to the U. S. FDA** for ~~this product candidate~~ **apraglutide for the treatment of adult patients with SBS who are dependent on PS** . We are not permitted to market or promote this product candidate before we receive regulatory approval from the U. S. FDA, the EMA, or comparable foreign regulatory authorities in the applicable jurisdiction, and we may never receive any such regulatory approval for apraglutide. To obtain regulatory approvals for apraglutide, we must demonstrate with substantial evidence from adequate and well- controlled clinical trials, and to the satisfaction of the U. S. FDA, EMA or comparable foreign regulatory authorities, that such product ~~candidates~~ **candidate** ~~are~~ **is** safe and effective for ~~their~~ **its** intended uses. **We may** ~~However, we cannot~~ be ~~certain that apraglutide will be successful in~~ **required by the U. S. FDA, EMA or comparable foreign regulatory authorities to perform additional or unanticipated** clinical trials **to obtain** ~~. Further, results from clinical trials can be interpreted in different ways, and apraglutide may not receive~~ regulatory approval **. In the** ~~even~~ **event the U. S. FDA were to determine that the data from our pivotal Phase III clinical trial, STARS, combined with the data from our open- label extension study, STARS Extend, is insufficient for acceptance of our NDA, or** if we ~~believe it~~ **need to conduct any other U. S. FDA- required studies, approval of our any NDA may be delayed or may require us to expend more resources than we have available. It** is ~~successful~~ **also possible that additional studies, if performed and completed, may not be considered sufficient by the U. S. FDA to approve our NDA. Any delay** in ~~clinical trials~~ **obtaining, or an inability to obtain, any marketing approvals would prevent us from commercializing our product candidates, including apraglutide, generating revenues on such product candidates and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly and materially harm our business** . Even if we do receive such regulatory approval, we may be unable to successfully commercialize apraglutide within any approved indications or develop apraglutide for the treatment of additional indications, which would materially adversely impact our business and prospects. The regulatory approval processes in the U. S., in the E. U. and in other foreign jurisdictions are **onerous,** lengthy, time consuming **, expensive** and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for apraglutide or our other product candidates, our business will be harmed. The time required to **complete drug development and to** obtain regulatory approval from the U. S. FDA, EMA and other comparable **foreign** regulatory authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors. In addition, regulatory approval policies, regulations, or the type and amount of clinical data necessary to gain regulatory approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions, which may cause delays in the regulatory approval of or may result in the decision not to approve apraglutide or other product candidates. Regulatory approval is never guaranteed. Data obtained from nonclinical studies and clinical trials are susceptible to varying interpretations, and regulatory authorities may not interpret our data as favorably as we do, which may further delay, limit or prevent development efforts, clinical trials, or regulatory approval. Even if we believe the nonclinical or clinical data for our product candidates are sufficient to support approval, such data may not be considered sufficient to support approval by the U. S. FDA, EMA and other comparable **foreign** regulatory authorities **. As an example, in December 2024, the U. S. FDA issued Zealand, which is developing glepaglutide, a long- acting GLP- 2 analog, for the potential treatment of SBS for patients who are dependent on PS, a Complete Response Letter concluding that glepaglutide did not meet the full requirements for substantial evidence to establish efficacy and safety and recommended conducting an additional clinical trial to provide further data. Consequently, Zealand now is expecting to initiate an additional Phase III clinical trial in 2025** . Of the large number of drugs in development, only a small percentage successfully complete the U. S. FDA, EMA or comparable **foreign** regulatory approval processes and are commercialized. Accordingly, it is possible that we will never obtain regulatory

approval **, or that regulatory approval may be substantially delayed,** for apraglutide or our other product candidates. The U. S. FDA, EMA or other **foreign** comparable regulatory authorities may delay, limit, or deny approval of our product candidates, including apraglutide, for many reasons, including the following: ● the U. S. FDA, EMA or other comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials or with our interpretation of data from preclinical studies or clinical ~~trials~~ **30trials** ; ● the population studied in the clinical program may not be sufficiently broad or representative to assure safety or efficacy in the full population for which we seek approval; ● the data collected from our clinical trials may not be sufficient to support the submission of ~~a~~ **an** NDA, MMA, or other submission or to obtain regulatory approval in the U. S., Europe or elsewhere; ● participants in our clinical trials or individuals using drugs similar to our product candidates may experience serious and unexpected drug- related side effects; ● we may be unable to demonstrate to the U. S. FDA, EMA or other comparable foreign regulatory authorities that a product candidate' s risk- to- benefit ratio for its proposed indications is acceptable; ● the U. S. FDA, EMA or ~~the~~ **other** ~~applicable~~ **comparable** foreign regulatory ~~authority~~ **authorities** may disagree regarding the formulation, labeling and / or the specifications of a product candidate; ● the U. S. FDA, EMA or other comparable foreign regulatory authorities may fail to approve the ~~29manufacturing~~ **manufacturing** processes, test procedures and specifications, or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and ● the regulatory approval policies or regulations of the U. S. FDA, EMA, or other applicable comparable foreign regulations in the E. U. and other jurisdictions may significantly change in a manner rendering our clinical data insufficient for approval. In addition, apraglutide may **also** be ~~also~~ regulated as a drug and device combination product by the U. S. FDA, EMA and comparable foreign regulatory authorities. Developing and obtaining regulatory approval for combination products can pose unique challenges because they involve components that are regulated under different types of regulatory requirements and potentially by different U. S. FDA centers or regulatory authorities. As a result, combination product candidates may raise regulatory, policy and review challenges. Differences in regulatory pathways for each component of a combination product can impact the regulatory processes for all aspects of product development and management, including clinical investigations, marketing applications, manufacturing and quality control, adverse event reporting, promotion and advertising, user fees and post- approval modifications. Although the U. S. FDA, EMA, and comparable foreign authorities have systems in place for the review and approval of combination products, we may experience additional delays in the development and commercialization of apraglutide due to regulatory timing constraints and uncertainties in the product development and approval process. Moreover, although we expect that the device component would be reviewed in connection with the review of the drug marketing application for apraglutide, if and when submitted, and that no separate marketing authorization or certification for the device component will be required, the U. S. FDA, EMA or comparable regulatory authorities may disagree and require that we obtain a separate marketing authorization or certification for the device component, which could further delay or prevent regulatory approval of apraglutide. This lengthy **drug development and** regulatory approval process, as well as the unpredictability of the results of clinical trials, may result in our failure to obtain regulatory approval to potentially market apraglutide or our other product candidates, which would significantly harm our business, results of operations, ~~fail or may not increase the revenues that we generate from LINZESS~~ .Furthermore,they may result in adverse events,or perceived adverse events,in certain patient populations that are then attributed to the currently approved patient population,which may result in adverse regulatory action at the ~~31U~~ **U** .S.FDA or in other countries or harm linaclotide' s reputation in the marketplace,each of which could materially harm our revenues from linaclotide.The strength of our company' s pipeline will depend in large part on the outcomes of studies ~~and regulatory approvals~~ of assets in our pipeline,such as apraglutide **,CNP- 104,IW- 3300** ,and any other assets that we may acquire or license from third parties.Through the VectivBio Acquisition ~~,~~ we added apraglutide to our pipeline. **We are conducting a** ~~In February 2024,we announced positive topline results from our pivotal~~ Phase III clinical trial,STARS, ~~which evaluated~~ **to assess** the **safety and** efficacy ~~and safety~~ of ~~once- weekly subcutaneous~~ apraglutide ~~in reducing PS dependency~~ in adult patients with SBS- IF **,and expect to report topline results in March 2024.In October 2023,we presented positive final data from the STARS Nutrition Phase II study of apraglutide in patients with SBS- IF and colon- in- continuity** .We are also conducting open ~~-~~ label extension studies to further evaluate the efficacy,safety and tolerability of apraglutide in SBS- IF and to support potential submissions of marketing applications for apraglutide in the U.S.,European Union,or E.U.,and Japan. ~~Based on the STARS~~ **We are also conducting a** Phase ~~III~~ **II exploratory study** ~~clinical trial results and data analyzed from the open- label extension studies~~ , **STARGAZE,** ~~we initiated a rolling NDA submission~~ to **evaluate** ~~the U.S.FDA for~~ apraglutide **in** ~~for the treatment of adult~~ patients with ~~SBS who~~ **steroid- refractory gastrointestinal aGvHD,and expect data in** and prospects. Delays in the completion of clinical testing of any of our products or product candidates could result in increased costs and delay or limit our ability to generate revenues. Delays in the completion of clinical testing could significantly affect our product development costs and timing of data readouts and regulatory submissions and potential approvals. We do not know whether planned clinical trials will be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to: ● obtaining regulatory authorization to commence a clinical trial; ● reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; **32** ● manufacturing sufficient quantities of a product candidate for use in clinical trials; ● obtaining institutional review board or ethics committee approval to conduct a clinical trial at a prospective site; ● recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for the treatment of similar conditions; and ● maintaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow- up. Additionally, changes in regulatory requirements and guidance may occur, and we may need or otherwise determine to amend clinical trial protocols to reflect these changes. Each protocol amendment would require institutional review board or ethics committee review and approval, which may adversely impact the costs, timing or successful completion of the associated

clinical trials. If we or our partners terminate or experience delays in the completion of any clinical trials, the commercial prospects for our products or product candidates may be harmed, and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval. ~~30Our failure~~ **The pricing of apraglutide and our other product candidates, if and when approved for marketing, will depend in part on pricing and reimbursement strategies adopted by our competitors. The pricing of apraglutide and our other product candidates, if and when approved for marketing, will depend, in part, on the pricing and reimbursement strategies adopted by our competitors. For example, with respect** to **apraglutide, a marketed GLP- 2 product already exists in the U. S., E. U. and other international markets, which may or may not be genericized within the coming years. Additionally, it is possible that another investigational GLP- 2 may be approved and launched in advance of the potential approval of apraglutide in the U. S., EMA and Japan. Order of market entry and reimbursement decisions could place apraglutide at a competitive disadvantage, possibly deny market exclusivity rights, and / or elevate the need for significant clinical differentiation to support certain pricing decisions. If these or other factors impact the price we can charge for apraglutide, we may reduce our revenue and results of operations could be affected. Similar competitive factors could apply to pricing and reimbursement decisions for our other product candidates, if approved, in the future. We face competition and new products may emerge that provide different or better alternatives for treatment of the conditions that our products are approved to treat. The pharmaceutical industry and the markets in which we operate are intensely competitive. We compete in the marketing and sale of our products, the development of new products or product candidates and the acquisition of rights to new products with commercial potential. Certain of our competitors have substantially greater financial, technical and human resources than us. Mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors and enable them to compete more effectively. Competition may also increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Additionally, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render our products obsolete or noncompetitive. Linaclotide competes with certain prescription therapies and OTC products, some of which have attained significant levels of market acceptance. The availability of prescription competitors and OTC products could limit the demand, and the price we are able to charge, for LINZESS unless we are able to maintain market acceptance among the medical community and patients and differentiate LINZESS on the basis of actual or perceived clinical benefits supported by broad payer access. For example, Takeda' s AMITIZA (lubiprostone) is approved by the U. S. FDA for sale in the U. S. for the treatment of IBS- C, CIC and opioid- induced constipation; Bausch' s TRULANCE (plecanatide) is approved by the U. S. FDA for sale in the U. S. for the treatment of adults with IBS- C and CIC; Takeda' s MOTEGRITY (prucalopride) is approved by the U. S. FDA for the treatment of CIC in adults; Ardelyx' s IBSRELA ™ (tenapanor) is approved by the U. S. FDA for the treatment for IBS- C in adults; and Vibrant Gastro Inc.' s Vibrant, a drug- free capsule, is approved by the U. S. FDA for the treatment of CIC in adults who have not experienced relief of their bowel symptoms by using laxative therapies at the recommended dosage for at least one month. OTC laxatives such as MiraLAX ® and DULCOLAX ®, and lactulose, a prescription laxative treatment, are also available for the treatment of constipation. Additionally, we believe other companies are developing products that could compete with linaclotide, should they be 33approved by the U. S. FDA or comparable foreign regulatory authorities and become commercially available. In addition, there are other compounds in late- stage development and other potential competitors that are in earlier stages of development that, if approved, may compete with linaclotide. If our current or potential competitors are successful in completing drug development for their drug candidates and obtain approval from the U. S. FDA or comparable foreign regulatory authorities, they could limit the demand for linaclotide. In addition to competition from such prescription and OTC products, we may also face competition from multiple low- cost generic versions of such products when available in the U. S. For example, an authorized generic version of AMITIZA was first launched in the U. S. in January of 2021 and multiple versions are now available. It is possible that additional generic versions may become available in the future. In addition, any product candidates that we** successfully develop and commercialize ~~that we successfully develop and commercialize~~ will compete with existing drugs and new drugs that may become available in the future.Apraglutide,if successfully developed and approved,will compete with companies that are commercializing or developing drugs for SBS,such as Takeda,which currently distributes the GLP- 2 analog teduglutide,marketed as GATTEX ® (teduglutide) in the U.S.and REVESTIVE ® (teduglutide for injection) in Europe,and Zealand ~~Pharma A / S~~ ,which is developing ~~the~~ **glepaglutide,a long- acting** GLP- 2 analog ~~glepaglutide~~ **,** for the treatment of SBS **for patients who are dependent on PS** and ~~which submitted~~ **is expecting to initiate** an ~~NDA to the U~~ additional **Phase III clinical trial in 2025. Hanmi Pharmaceutical is also developing a GLP- 2 analog, to be administered once a month, and which is in a Phase II clinical trial. Products with other mechanisms of action may emerge as future competition. Our products or** product candidates **may cause undesirable side effects or have other properties that could delay or prevent their development, create unpredictable clinical trial results, impact its regulatory approval or limit their commercial potential. Undesirable side effects caused by** ~~or~~ **our products or product candidates, including adverse events associated with our product candidates, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the U. S. FDA, EMA or other comparable foreign regulatory authorities. Additionally, with respect to our** approved products ~~would impair~~ **, as patient experience increases and expands,** ~~our~~ **or** ~~ability~~ **if one or more of our product candidates receives marketing approval, we, our partners, or others may later identify previously unknown side effects, known side effects may be found** to ~~grow~~ **be more frequent** and / or ~~adversely affect~~ **severe than in the past,** ~~our~~ **or** ~~business. As part of~~ **detect**

unexpected safety signals for our products ~~our~~ **or any products perceived** ~~growth strategy, we intend~~ to ~~explore further linaclotide~~ be similar to our products.The foregoing,or the perception of the foregoing,may have the following effects,among others:● sales of our products may be impaired;● regulatory approvals for our products may be delayed,denied,restricted or withdrawn;● we or our partners may decide to,or be required to,change the products' labeling or send product warning letters or field alerts to physicians,pharmacists or hospitals;● reformulation of the products,additional nonclinical **studies** or clinical ~~studies~~ **trials** ,changes in labeling or changes to or re- approvals of manufacturing facilities may be required; ~~33~~ ● we or our partners may be precluded from pursuing approval of our products in new territories or from studying additional development opportunities **to enhance our products' clinical profiles, including within new or existing indications, populations or formulations,** as well as **in potential combination products; ● we may be required** to ~~advance~~ **create a Risk Evaluation and Mitigation Strategy, or REMS, plan, or similar actions in other jurisdictions which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers or other elements to assure safe use; ● our or our products' reputation in the marketplace may suffer; and ● government investigations or lawsuits, including class action suits, may be brought against us or our partners. 34Any of the above occurrences could prevent us from achieving or maintaining market acceptance of our product candidates, if** ~~the~~ **they or formulations,as well as in potential combination products;● we may be required to create a Risk Evaluation and Mitigation Strategy,or REMS,plan,or similar actions in other jurisdictions which could include a medication guide outlining the risks of such side effects for distribution to patients,a communication plan for healthcare providers or other elements to assure safe use;● our or our products' reputation in the marketplace may suffer;and ● government investigations or lawsuits,including class action suits,may be brought against us or our partners.Any of the above occurrences could prevent us from achieving or maintaining market acceptance of our product candidates,if they** are approved,and could significantly harm our business,results of operations,and prospects,prevent sales of our products,increase expenses and impair our and our partners' ability to successfully commercialize our products.Linaclotide has been prescribed to millions of patients since its launch in the U.S.and other territories beginning in December 2012.The number and type of patients treated with linaclotide could continue to grow if physicians prescribe linaclotide to more patients and as we and our partners conduct clinical trials,including in new indications,populations or formulations,as well as explore potential combination products,in existing and new territories.As the patient experience with linaclotide increases and expands,we and others may identify previously unknown side effects,known side effects may be found to be more frequent or severe than in the past,and others may detect unexpected safety signals for linaclotide or any products perceived to be similar to linaclotide.The most commonly reported adverse reaction since linaclotide became commercially available,as well as in the clinical trials for linaclotide in IBS- C and CIC,has been diarrhea.In the linaclotide Phase III IBS- C and CIC trials in adults,severe diarrhea was reported in 2 % or less of the linaclotide- treated patients and its incidence was similar between the IBS- C and CIC populations.In the linaclotide Phase III FC trial in pediatric patients ages 6- 17 years- old,severe diarrhea was reported in one linaclotide- treated patient.In addition,the U.S.FDA- approved labeling for LINZESS contains a boxed warning describing the risk of serious dehydration in pediatric patients less than two years of age and a contraindication against its use in these patients ~~.These and other restrictions could limit the commercial potential of LINZESS.We and AbbVie have established a nonclinical and clinical post- marketing plan with the U.S.FDA to understand the safety and efficacy of LINZESS in pediatric patients.In June 2023,the U.S.FDA approved LINZESS as a once- daily oral treatment for pediatric patients ages 6- 17 years- old with FC,making LINZESS the first and only FDA- approved prescription therapy for FC in this patient population.The safety and effectiveness of LINZESS in patients with FC less than 6 years of age or in patients with IBS- C less than 18 years of~~ development ~~of~~ **and regulatory requirements still remain, which may present additional challenges, and we may not be successful in obtaining approval for additional indications for LINZESS that we are seeking** ~~our~~ **or may seek in the future. In August 2012, the U. S. FDA approved LINZESS as a once- daily treatment for adult men and women suffering from IBS- C or CIC. Although we and AbbVie completed additional nonclinical studies and clinical trials in adults that were required by the U. S. FDA in connection with the approval of LINZESS, LINZESS remains subject to ongoing U. S. FDA requirements, including those governing the testing, manufacturing, labeling, packaging, storage, advertising, promotion, sale, distribution, recordkeeping and submission of safety and** other **post- market** ~~pipeline programs through internal or external opportunities. We and AbbVie are exploring development opportunities to enhance the clinical profile of LINZESS by studying linaclotide in new or existing indications, populations and formulations~~ --- **information** ~~to assess its potential to treat various conditions~~ . For example, ~~we~~ **the U. S. FDA has the authority to require post- marketing studies and clinical trials, labeling changes based on new safety information, and compliance with REMS approved by the U. S. FDA. The U. S. FDA- approved labeling for LINZESS contains a boxed warning describing the risk of serious dehydration in pediatric patients less than two years of age and a contraindication against its use in these patients. We** and AbbVie have established a nonclinical and clinical post- marketing plan with the U. S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In June 2023, the U. S. FDA approved LINZESS as a once- daily treatment for pediatric patients ages 6- 17 years- old with FC **, making** ~~. Additional clinical pediatric programs in IBS- C and FC are ongoing. These development efforts may fail or may not increase the revenues that we generate from~~ LINZESS . Furthermore, they may result in..... gastrointestinal aGvHD, and expect data in the first ~~quarter of 2024. Through the COUR Collaboration Agreement, we and COUR are developing CNP- 104 for the treatment of PBC. COUR is currently conducting a clinical study to evaluate the safety, tolerability, pharmacodynamic effects and efficacy of CNP- 104 in PBC patients, with topline data expected in the third quarter of 2024. We are also advancing IW- 3300, a GC- C agonist, for the potential treatment of visceral pain conditions, such as IC / BPS, and endometriosis. We may spend several years and make significant investments in developing any current or future product candidate, and failure may occur at any point. Our product candidates must satisfy rigorous standards of safety and efficacy before they can be approved for sale by the U. S. FDA, EMA or comparable foreign authorities. To satisfy these~~

standards, we must allocate resources among development programs and we must engage in costly and lengthy research and development efforts, which are subject to unanticipated delays and other significant uncertainties. Despite our efforts, our product candidates may not offer therapeutic or other improvement over existing competitive drugs, be proven safe and effective in clinical trials, or meet applicable regulatory standards. It is possible that none of the product candidates we develop will be approved for commercial sale, which would impair our ability to grow. We have ongoing or planned nonclinical and clinical trials, including for linaclotide, apraglutide, and our other product candidates. Many companies in the pharmaceutical industry have suffered significant setbacks in clinical trials even after achieving promising results in earlier nonclinical or clinical trials. Findings from completed nonclinical studies may not be replicated in later clinical trials, and clinical trials may not be predictive of the results we may obtain in later- stage clinical trials or of the likelihood of regulatory approval. Results from clinical trials and findings from nonclinical studies could lead to abrupt changes in development activities, including the possible limitation or cessation of development activities associated with a particular product candidate or program. We cannot be certain that apraglutide or our other product candidates will be successful in clinical trials. Furthermore, our analysis of data obtained from nonclinical and clinical activities is subject to confirmation and interpretation by the U. S. FDA, EMA and other applicable regulatory authorities, which could delay, limit or prevent regulatory approval. The U. S. FDA, EMA or other regulatory authorities also may require additional clinical trials, which may be costly or delay, limit, prevent or otherwise impact regulatory submission or approval. Satisfaction of U. S. FDA, EMA or other applicable regulatory requirements is costly, time- consuming, uncertain and subject to unanticipated delays. We cannot give any assurance that apraglutide or our other product candidates will receive regulatory approval. Even if we do receive such regulatory approval, we may be unable to successfully commercialize apraglutide or our other product candidates in any approved 31indications or develop such product candidates for the treatment of additional indications, which would materially adversely impact our business and prospects. The pricing of apraglutide and our other product candidates, if and when approved for marketing, will depend in part on pricing and reimbursement strategies adopted by our competitors. The pricing of apraglutide and our other product candidates, if and when approved for marketing, will depend, in part, on the pricing and reimbursement strategies adopted by our competitors. For example, with respect to apraglutide, a marketed GLP- 2 product already exists in the U. S., E. U. and other international markets, which may or may not be genericized within the coming years. Additionally, another investigational GLP- 2 may be launched in advance of the potential approval of apraglutide in the U. S. and EMA. Order of market entry and reimbursement decisions could place apraglutide at a competitive disadvantage, possibly deny market exclusivity rights, and / or elevate the need for significant clinical differentiation to support certain pricing decisions. If these or other factors impact the price we can charge for apraglutide, we may reduce our revenue and results of operations could be affected. Similar competitive factors could apply to pricing and reimbursement decisions for our other product candidates, if approved, in the future. We must work effectively and collaboratively with AbbVie to market and sell LINZESS in the U. S., and we must adapt our commercial model and market strategy to the evolving landscape for LINZESS to achieve its maximum commercial potential. We are working closely with AbbVie to execute our joint commercialization plan for LINZESS. The commercialization plan includes an **and only** agreed upon marketing campaign that targets the physicians who see patients who could benefit from LINZESS treatment. Our consumer marketing campaign targets the adult men and women who suffer from IBS- C or CIC. Our commercialization plan also includes an integrated call plan for our sales forces in an effort to optimize the education of key healthcare professionals on whom our and AbbVie' s sales representatives call, and the frequency with which the representatives meet with them. In order to optimize the commercial potential of LINZESS, we and AbbVie must execute upon this commercialization plan effectively and efficiently. In addition, we and AbbVie must continually assess, modify and adapt our commercialization plan in a coordinated and integrated fashion, including evaluating and adjusting as necessary the level and mix of marketing and promotion efforts, in response to changing business, market or other factors in order to advance the commercial potential of LINZESS, such as the U. S. FDA approval of LINZESS in pediatric patients ages 6- 17 years- old for FC. Further, we and AbbVie must continue to focus our combined sales and marketing efforts on educating customers about the relevant data and information for LINZESS in treating adults with IBS- C and CIC, and taking a measured approach to educating and raising awareness on the FC indication for pediatric patients ages 6- 17 years- old. We and AbbVie must ensure a highly targeted and efficient promotional mix combined with providing our sales forces with the highest quality support, guidance, and oversight for them to continue effectively promoting LINZESS to key healthcare professionals. If we and AbbVie fail to evolve with the changing commercial landscape successfully and perform these commercial functions in the highest quality manner and in accordance with our joint commercialization plan and related agreements, LINZESS will not achieve its maximum commercial potential and we may suffer financial harm. Our commercial efforts to further target and engage adult patients with IBS- C or CIC may not effectively increase appropriate patient awareness or patient / physician dialogue and may not increase the revenues that we generate from LINZESS. We face competition and new products may emerge that provide different or better alternatives for treatment of the conditions that our products are approved to treat. The pharmaceutical industry and the markets in which we operate are intensely competitive. We compete in the marketing and sale of our products, the development of new products or product candidates and the acquisition of rights to new products with commercial potential. Certain of our competitors have substantially greater financial, technical and human resources than us. Mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in our competitors and enable them to compete more effectively. Competition may also increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Additionally, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical and medical technology industries at a rapid pace. These developments may render our products obsolete or noncompetitive. 32Linaclotide competes with certain prescription therapies and OTC products, some of which have attained significant levels of market acceptance. The availability of prescription competitors and OTC products could limit the demand, and the price we are able to charge, for LINZESS unless we

~~are able to maintain market acceptance among the medical community and patients and differentiate LINZESS on the basis of its cost and / or actual or perceived benefits. For example, Takeda' s AMITIZA (lubiprostone) is approved by the U. S. FDA for sale in the U. S. for the treatment of IBS- C, CIC and opioid- induced constipation; Bausch' s TRULANCE (plecanatide) is approved by the U. S. FDA for sale in the U. S. for the treatment of adults with IBS- C and CIC; Takeda' s MOTEGRITY (prucalopride) is approved by the U. S. FDA for sale in the U. S. for the treatment of CIC in adults; in April 2022, Ardelyx launched in the U. S. IBSRELA ™ (tenapanor), a U. S.~~ FDA- approved ~~treatment~~ **prescription therapy** for **FC** ~~IBS- C~~ in **this** adults; and in August 2022,..... respect to our approved products, as patient experience increases and expands, or if..... within new or existing indications, populations - **population** or formulations, as well as in..... contraindication against its use in these patients . The safety and effectiveness of LINZESS in patients with FC less than 6 years of age or in patients with IBS- C less than 18 years of age have not been established. ~~These and other restrictions could limit the commercial potential of LINZESS. We and AbbVie have established a nonclinical and clinical post- marketing plan with the U. S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In June 2023, the U. S. FDA approved LINZESS as a once- daily treatment for pediatric patients ages 6- 17 years- old with FC, making LINZESS the first and only FDA- approved prescription therapy for FC in this patient population. Additional clinical pediatric programs in IBS- C and FC are ongoing. There can be no assurances, however, whether there may be any significant unknown side effects that could limit the commercial potential of LINZESS in this pediatric population. Patients treated with apraglutide may experience well known class- specific adverse events, including, but not limited to, abdominal pain, injection site reactions, nausea, headaches, abdominal distension, upper respiratory tract infection, vomiting and fluid overload. There may be additional mechanistic side effects that only reveal themselves upon the completion of larger studies. Additionally, apraglutide has been designed to have a long half- life, creating uncertainty about its long- term safety profile. For example, the increased pleiotropic activity of apraglutide will need to be assessed in longer- term non- clinical safety studies. 34Even though LINZESS is approved by the U. S. FDA for use in adult and certain pediatric patients, post- approval development and regulatory requirements still remain, which may present additional challenges, and we may not be successful in obtaining approval for additional indications for LINZESS that we are seeking or may seek in the future. In August 2012, the U. S. FDA approved LINZESS as a once- daily treatment for adult men and women suffering from IBS- C or CIC. Although we and AbbVie completed additional nonclinical and clinical studies in adults that were required by the U. S. FDA in connection with the approval of LINZESS, LINZESS remains subject to ongoingU. S. FDA requirements, including those governing the testing, manufacturing, labeling, packaging, storage, advertising, promotion, sale, distribution, recordkeeping and submission of safety and other post- market information. The U. S. FDA- approved labeling for LINZESS contains a boxed warning describing the risk of serious dehydration in pediatric patients less than two years of age and a contraindication against its use in these patients. We and AbbVie have established a nonclinical and clinical post- marketing plan with the U. S. FDA to understand the safety and efficacy of LINZESS in pediatric patients. In June 2023, the U. S. FDA approved LINZESS as a once- daily treatment for pediatric patients ages 6- 17 years- old with FC, making LINZESS the first and only FDA- approved prescription therapy for FC in this patient population. The safety and effectiveness of LINZESS in patients with FC less than 6 years of age or in patients with IBS- C less than 18 years of age have not been established.~~ Additional clinical pediatric programs in IBS- C and FC are ongoing in support of post- approval requirements. Our ability to expand the indication or labeling information for LINZESS will depend on, among other things, our successful completion of pediatric clinical programs. ~~These~~ **35These** post- approval requirements impose resource and cost burdens on us. Failure to effectively, appropriately and timely conduct and complete the required studies relating to our products, monitor and report adverse events and meet our other post- approval commitments would lead to negative regulatory action at the U. S. FDA, which could include **restrictions on the sale of our products or** withdrawal of regulatory approval of our products for their currently approved indications and patient populations. **in China** (including Hong Kong and Macau).The pricing and reimbursement strategy is a key component of our partners' commercialization plans for CONSTELLA in Europe and ~~Canada and~~ LINZESS in Japan and China.Our revenues may suffer if our partners are unable to successfully and timely conclude reimbursement,price approval or funding processes and market CONSTELLA in key member states of the E.U. ~~and Canada~~ or LINZESS in Japan or China,or if coverage and reimbursement for either CONSTELLA or LINZESS is limited or reduced.If our partners are not able to obtain or maintain coverage,pricing or reimbursement on acceptable terms or at all,or if such terms change in any countries in its territory,our partners may not be able to,or may decide not to,sell either CONSTELLA or LINZESS in such countries.We and our partners also face the risk that linaclotide is imported or reimported into markets with relatively higher prices from markets with relatively lower prices,which would result in a decrease of sales and any payments we receive from the affected market.Additionally,third parties may illegally produce,distribute and / or sell counterfeit or otherwise unfit or adulterated versions of linaclotide.In either case,we and our partners may not be able to detect or,if detected,prevent or prohibit the sale of such products,which could result in dangerous health consequences for patients,loss of confidence in us,our partners and our products,and adverse regulatory or legal consequences.Any of the foregoing or other consequences could adversely impact our reputation,financial results **and business** ~~Even~~ **36Even** though linaclotide is approved for marketing in the U. S. and in a number of other countries, we or our partners may never receive approval to commercialize linaclotide in additional parts of the world. In order to market any products outside of the countries where linaclotide is currently approved, we or our partners must comply with numerous and varying regulatory requirements of other jurisdictions regarding, among other things, safety and efficacy. Approval procedures vary among jurisdictions and can involve product testing and administrative review periods different from, and greater than, those in the U. S. and the other countries where linaclotide is approved. Potential risks include that the regulatory authorities: ● may not deem linaclotide safe and effective; ● may not find the data from nonclinical studies and clinical trials sufficient to support approval; ● may not approve of manufacturing processes and facilities; ● may not approve linaclotide for any or all indications or patient populations for which approval is sought; ● may require significant warnings or restrictions on use to the product labeling for linaclotide; or ● may change their approval

policies or adopt new regulations. If any of the foregoing were to occur, our or our partners' receipt of regulatory approval in the applicable jurisdiction could be delayed or we or our partners may never receive approval at all. Further, regulatory approval in one jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory processes in others. If linaclotide is not approved for all indications or patient populations or with the labeling requested, this would limit the uses of linaclotide and have an adverse effect on its commercial potential or require costly post- marketing studies. ~~35Risks~~ -- **Risks** Related to Our Growth StrategyIf we are unable to execute on our strategy to in- license or acquire externally developed products or product candidates, or engage in other transactions with value creation potential, our business and prospects would be materially adversely affected. Our future success is largely dependent on our ability to successfully execute on our growth strategy, which includes in- licensing or otherwise acquiring the rights to externally developed ~~gastrointestinal~~ **GI or rare diseases** products or product candidates or engaging in other transactions with value creation potential. The success of this strategy depends upon our ability to identify, select and acquire promising assets, platforms or other opportunities. For example, through the VectivBio Acquisition, we added apraglutide to our pipeline. There is no assurance that apraglutide will ~~be successful in clinical trials, and if successful, that it will receive regulatory approval. For another example, through the COUR Collaboration Agreement, we and COUR are developing CNP- 104 for the treatment of PBC, and we have been granted an option to acquire an exclusive license to research, develop, manufacture and commercialize products containing CNP- 104 in the U. S. for the treatment of PBC after reviewing the data from this study. There is no assurance that we will exercise the option for CNP- 104, and if exercised, that we will complete subsequent clinical trials and~~ receive regulatory approval. In addition, the process of proposing, negotiating and implementing a license or acquisition is lengthy and complex and there is no assurance we will be able to enter into similar transactions in the future. Pursuit of external opportunities is also a highly competitive area and a number of other companies, including some with substantially greater financial, development, marketing and sales resources, may compete with us for license or acquisition opportunities. We have limited resources to identify and execute the acquisition or in- licensing of third- party products, product candidates, businesses or technologies and integrate them into our current infrastructure. Moreover, we expect to incur a variety of costs and devote resources to potential acquisitions or in- licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. If we are unable to successfully acquire the rights to additional products or product candidates on terms that we find acceptable, or at all, or execute other value creating transactions, we will remain smaller, less diversified and highly dependent on the commercial success of LINZESS **and apraglutide, if approved** , and our business and prospects would be materially and adversely affected. In addition, such in- licenses, acquisitions or other transactions may entail numerous operational and financial risks, including: ● development, regulatory and commercialization challenges; **37** ● exposure to unknown liabilities; ● disruption of our business and diversion of our management' s time and attention to develop acquired products, product candidates, businesses or technologies; ● incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions; ● higher than expected acquisition and integration costs; ● difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel; ● increased amortization expenses; ● impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and ● inability to motivate key employees of any acquired businesses. The development of product candidates in particular is a highly uncertain process ~~, as we discuss further below~~ . Any product candidate that we in- license or acquire may require additional development efforts prior to **and after** commercial sale, including extensive clinical testing and approval by the U. S. FDA, EMA and ~~applicable~~ **other comparable** foreign regulatory authorities. We may also rely on our licensors and collaboration partners to conduct development activities for certain of our product ~~36candidates~~ -- **candidates** , and while we may have oversight of such development activities, such licensees or collaboration partners may not effectively develop any such product candidates. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities or competitors may develop alternatives that render our potential product candidates obsolete or less attractive. It is possible that none of the product candidates we may in- license or acquire will be approved for commercial sale or be otherwise commercially viable, which would impair our ability to grow. Furthermore, we may have little or no insight or control over the development and commercialization of any product that we in- license outside the licensed territory. If other licensees do not effectively develop or commercialize any such product outside the licensed territory, our reputation or the reputation of any such product may be impacted. We may be unable to maintain the..... the regulatory review or approval process. If we are unable to successfully partner with other companies to develop and commercialize products and / or product candidates, our ability to grow would be impaired and our business would be adversely affected. As part of our business strategy, we may partner with pharmaceutical, biotechnology or other companies to develop and commercialize products or product candidates. Although we have entered into such arrangements with respect to the development and commercialization of linaclotide worldwide and of apraglutide in Japan, there can be no assurance that we will be able to do so in the future with respect to other products or product candidates that we either ~~37develop~~ -- **develop** internally or in- license or that we will be able to gain the interest of potential partners; establish and maintain development, manufacturing, marketing, sales or distribution relationships on acceptable terms; that such relationships, if established, will be successful or on favorable terms; or that we will gain market acceptance for such products or product candidates. The process of proposing, negotiating and implementing a partnership arrangement is lengthy and complex. If we enter into any partnering arrangements with third parties, any revenues we receive will depend upon the efforts of such third parties. If we are unable to establish successful partnering arrangements when advantageous, we may not gain access to the financial resources and industry experience necessary to develop, commercialize or successfully market our products or product candidates, may be forced to curtail, delay or stop a development program or one or more of our other development programs, delay commercialization, reduce the scope of our planned sales or marketing activities or undertake development or commercialization activities at our

own expense, and therefore may be unable to generate revenue from products or product candidates or do so to their full potential. Risks Related to the VectivBio Acquisition We may be unable to successfully integrate the business and personnel of VectivBio, and may not realize the expected benefits and anticipated synergies of such acquisition. ~~In~~ **38In** December 2023, we completed the VectivBio Acquisition. We may not realize the expected benefits from such acquisition because of integration difficulties or other challenges. The success of the VectivBio Acquisition will depend, in part, on our ability to realize all or some of the expected benefits from the acquisition and anticipated synergies from integrating its business with our existing business. The integration process may be complex, costly and time- consuming and we may not ultimately realize the return on our investment. Risks we may face in connection with the VectivBio Acquisition include, among others: ● failure to successfully implement our business plans for the combined business, including the development of apraglutide for SBS ~~- IF~~ **patients who are dependent on PS** ; ● failure of the VectivBio Acquisition to further our business strategy as we expected, including the ~~development and~~ **commercialization of apraglutide** , if approved, ~~the commercialization of apraglutide~~ for SBS ~~- IF~~ **patients who are dependent on PS** ; ● unexpected losses of key employees, customers or suppliers, and the complexities associated with integrating personnel from another company; ● unanticipated issues in conforming VectivBio' s standards, processes, procedures and controls with our operations; ● coordinating product candidate and process development; ● increasing the scope, geographic diversity and complexity of our operations; ● diversion of management' s attention from other business concerns; ● adverse effects on our or VectivBio' s existing business relationships; ● unanticipated changes in applicable laws and regulations; ● unanticipated expenses and liabilities associated with the VectivBio Acquisition; and ● other difficulties in the assimilation of VectivBio operations, technologies, product candidates and systems. We may have unanticipated or larger than anticipated liabilities for patent and trademark infringement claims, violations of laws, commercial disputes, taxes and other known and unknown types of liabilities. There may be liabilities that we underestimated or did not discover in the course of performing our due diligence investigation. ~~38If~~ **If** we experience difficulties with the integration process or if the business of VectivBio deteriorates, the anticipated benefits, cost savings, growth opportunities and other synergies of the VectivBio Acquisition may not be realized fully or at all, or may take longer to realize than expected. If any of the above risks occur, our business, financial condition, results of operations and cash flows may be materially and adversely impacted, we may fail to meet the expectations of investors or analysts, and our stock price may decline as a result. Risks Related to Our Dependence on Third PartiesBecause we work with partners to develop, manufacture and commercialize linaclotide, we and our partners are dependent upon third parties, and our and our partners' relationships with those third parties, in our and our partners' efforts to obtain regulatory approval for, and to commercialize, linaclotide, as well as to comply with regulatory and other obligations with respect to linaclotide. AbbVie played a significant role in the conduct of the clinical trials for linaclotide and in the subsequent collection and analysis of data, and AbbVie holds the ~~new drug application, or~~ NDA ~~,~~ for LINZESS. AbbVie **also** ~~alsocontinues ----~~ **continues** to play a significant role in the conduct of our pediatric program for linaclotide. In addition, we are commercializing LINZESS in the U. S. with AbbVie. AbbVie is also responsible for the development, regulatory approval and commercialization of linaclotide in countries worldwide other than Japan and China (including Hong Kong and Macau). AbbVie is commercializing ~~LINZESS~~ **39LINZESS** in Mexico ~~, and Saudi Arabia~~ and CONSTELLA in Canada as well as in certain countries including in Europe. Astellas and AstraZeneca are responsible for development and commercialization of LINZESS in Japan and China (including Hong Kong and Macau), respectively. Each of our partners for linaclotide also is responsible for active pharmaceutical ingredient, or API, finished drug product and finished goods manufacturing (including bottling and packaging) for its respective territories and distributing the finished goods to wholesalers. We and / or our partners have commercial supply agreements with independent third parties to manufacture the linaclotide API. The integration of our efforts with our partners' efforts is subject to the uncertainty of the markets for pharmaceutical products in each partner' s respective territories, and accordingly, these relationships must evolve to meet any new challenges that arise in those regions. These integrated functions may not be carried out effectively and efficiently if we fail to communicate and coordinate with our linaclotide partners, and vice versa. Our linaclotide partnering strategy imposes obligations, risks and operational requirements on us as the central node in our global network of partners. If we do not effectively communicate with each partner and ensure that the entire network is making integrated and cohesive decisions focused on the global brand for linaclotide, linaclotide will not achieve its maximum commercial potential. Further, we have limited ability to control the amount or timing of resources that our partners devote to linaclotide. If any of our partners fails to devote sufficient time and resources to linaclotide, or if its performance is substandard or otherwise hindered, it will delay the potential submission or approval of regulatory applications for linaclotide, as well as the manufacturing and commercialization of linaclotide in the particular territory. A material breach by any of our partners of our collaboration or license agreement with such partner, or a significant disagreement between us and a partner, could also delay the regulatory approval and commercialization of linaclotide, potentially lead to costly litigation, and could have a material adverse impact on our financial condition. Moreover, although we have non- compete restrictions in place with each of our linaclotide partners, they may have competitive products or relationships with other commercial entities, some of which may compete with us. If any of our partners competes with us or assists our competitors, it could harm our competitive position. In addition, adverse event reporting requires significant coordination with our partners and third parties. We are the holder of the global safety database for linaclotide responsible for coordinating the safety surveillance and adverse event reporting efforts worldwide with respect to linaclotide; each of Astellas, AstraZeneca and AbbVie is responsible for reporting adverse event information from its territory to us. If we fail to perform such activities and maintain the global safety database for linaclotide or if our partners do not report adverse events related to linaclotide, or fail to do so in a timely manner, we may not receive the information that we or our partners are required to report to the U. S. FDA or a **comparable** foreign regulatory authority regarding such products. Furthermore, we or our partners may fail to adequately monitor, identify or investigate adverse events, or to report adverse events to the U. S. FDA or **a comparable** foreign regulatory authority accurately and within the prescribed timeframe. If we or our partners are

unsuccessful in any of the foregoing due to poor process, execution, systems, oversight, communication, adjudication or otherwise, then we may suffer any number of consequences, including the imposition of additional restrictions on the use of linaclotide, removal of linaclotide from the market, criminal prosecution, the imposition of civil monetary penalties, seizure of such products, or delay in approval of future products. ~~39We~~ **We** rely entirely on contract manufacturers, our partners and other third parties to manufacture linaclotide, apraglutide, and our other product candidates and to distribute linaclotide. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties, or are otherwise unable to manufacture and distribute sufficient quantities to meet demand, our development and commercialization efforts may be materially harmed. We have no internal manufacturing or distribution capabilities. Instead, we rely on a combination of contract manufacturers and our partners to manufacture API, finished drug product and finished goods for linaclotide, apraglutide, and our other product candidates. For linaclotide, each of our partners is responsible for API, finished drug product and finished goods manufacturing (including bottling and packaging) for its respective territories and distributing the finished goods to wholesalers. We and / or our partners have commercial supply agreements with independent third parties to manufacture linaclotide API. For apraglutide, we design and develop the manufacturing process together with CDMOs **, and we rely on these CDMOs and other third- party suppliers** for the manufacture **and supply, including filling and packaging of all the components of the finished product** for human use. Should we, or any of our partners or any third- party manufacturers we or our partners engage, experience setbacks or challenges in our manufacturing efforts, our development and commercialization efforts may be materially harmed. ~~Each~~ **40Each** of our partners and the third- party manufacturers we or our partners engage, must comply with GMP and other stringent regulatory requirements enforced by the U. S. FDA, EMA and other **comparable** foreign regulatory authorities in other jurisdictions. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our and our partners' own quality assurance releases. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with a facility where the product is manufactured, a regulatory agency may impose restrictions on that product or the manufacturer, including withdrawal of the product from the market or suspension of manufacturing. If we, our partners or the manufacturing facilities for our products fail to comply with applicable regulatory requirements, a regulatory agency may take the following actions, among others: ● issue warning letters or untitled letters; ● impose civil or criminal penalties; ● suspend or withdraw regulatory approval; ● suspend any ongoing clinical trials; ● refuse to approve pending applications or supplements to applications submitted by us or our partners; ● impose restrictions on operations, including costly new manufacturing requirements; or ● seize or detain products or require us to initiate a product recall. Manufacturers of our products may be unable to comply with these GMP requirements and with other regulatory requirements. We have little control over compliance with these regulations and standards by our partners and the third- party manufacturers we or our partners engage. In addition, we expect that apraglutide may be regulated by the U. S. FDA as a drug- device combination product. Our third- party manufacturers may not be able to comply with GMP regulations applicable to drug- device combination products, including applicable provisions of the U. S. FDA' s drug GMP regulations and device GMP requirements embodied in the Quality System Regulation, or similar regulatory requirements outside the U. S. Our partners and the third- party manufacturers we or our partners engage may experience problems with their respective manufacturing and distribution operations and processes, including, for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination, natural disasters and public health epidemics. In addition, the raw materials necessary to make API for our products and product candidates are acquired from a limited number of sources. Any delay or disruption in ~~40the~~ -- **the** availability of raw materials or a change in raw material suppliers could result in production disruptions, delays or higher costs with consequent adverse effects on us. The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in commercial production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, and shortages of qualified personnel, as well as compliance with federal, state and foreign regulations and the challenges associated with complex supply chain management. Even if our partners or the third- party manufacturers we or our partners engage do not experience problems and commercial manufacturing is achieved, their maximum or available manufacturing capacities may be insufficient to meet commercial demand. Finding alternative manufacturers or adding additional manufacturers requires a significant amount of time and involves significant expense. New manufacturers would need to develop and implement the necessary production techniques and processes, which along with their facilities, would need to be inspected and approved by the regulatory authorities in each applicable territory. If our partners or the third- party manufacturers we or our partners engage fail to adhere to applicable GMP or other regulatory requirements, experience delays or disruptions in the availability of raw materials or experience ~~manufacturing~~ **41manufacturing** or distribution problems, we will suffer significant consequences, including product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, shipment delays, inventory shortages, inventory write- offs and other product- related charges and increased manufacturing costs. If we experience any of these results, or if maximum or available manufacturing capacities are insufficient to meet demand, our and our partners' development or commercialization efforts may be materially harmed. If any of our linaclotide partners undergoes a change of control or in management, this may adversely affect our collaborative relationship or the success of the commercialization of linaclotide in the U. S. or in the other countries where it is approved, or the ability to achieve regulatory approval, launch and commercialize linaclotide in other territories. We work jointly and collaboratively with partners on many aspects of the development, manufacturing and / or commercialization of linaclotide. In doing so, we have established relationships with several key members of the management teams of our linaclotide partners in functional areas such as development, quality, regulatory, drug safety and pharmacovigilance, operations, marketing, sales, field operations and

medical science. Further, the success of our collaborations is highly dependent on the resources, efforts and skills of our partners and their key employees. As we and our partners develop and commercialize linaclotide in the U. S. and the other countries where it is approved, and develop, launch and commercialize linaclotide in other parts of the world, the drug' s success becomes more dependent on us maintaining highly collaborative and well aligned partnerships. ~~In May 2020, AbbVie announced the completion of its acquisition of Allergan plc. Our collaboration, now with AbbVie, for the development and commercialization of linaclotide in North America, and our license, now to AbbVie, to develop and commercialize linaclotide in all countries worldwide other than China (including Hong Kong and Macau) and Japan, remain in effect. In connection with this transaction, we continue to engage with AbbVie to reestablish relationships and confirm alignment, including on our development and commercialization strategy for linaclotide. Any failure to do so could adversely affect the development and commercialization of linaclotide.~~ If any of our linaclotide partners undergoes a change of control or in management, we would similarly need to reestablish many relationships and confirm alignment, including on our development and commercialization strategy for linaclotide. Further, in connection with any change of control or change in management, there is inherent uncertainty and disruption in operations, which could result in distraction, inefficiencies, and misalignment of priorities. As a result, in the event of a change of control or in management at one of our linaclotide partners, we cannot be sure that we will be able to successfully execute on our development and commercialization strategy for linaclotide in an effective and efficient manner and without disruption or reduced performance. Finally, any change of control or in management may result in a reprioritization of linaclotide within a partner' s portfolio, or such partner may fail to maintain the financial or other resources necessary to continue supporting its portion of the development, manufacturing or commercialization of linaclotide. If any of our linaclotide partners undergoes a change of control and the acquirer either (i) is unable to perform such partner' s obligations under its collaboration or license agreement with us or (ii) does not comply with the divestiture or certain other provisions of the applicable agreement, we have the right to terminate the collaboration or license agreement and **re-** ~~reacquire~~ -- **acquire** that partner' s rights with respect to linaclotide. If we elect to exercise these rights in such circumstances, we will need to either establish the capability to develop, manufacture and commercialize ~~41linaclotide~~ -- **linaclotide** in that partnered territory on our own or we will need to establish a relationship with a new partner. We have assembled a team that represents the functional areas necessary to support the commercialization of LINZESS in the U. S. If AbbVie was subject to a change of control that allowed us to further commercialize LINZESS in the U. S. on our own, and we chose to do so, we would need to enhance each of these functional aspects, as well as develop others, to replace the capabilities that AbbVie was previously providing to the collaboration. Any such transition might result in a period of reduced efficiency or performance by our operations and commercialization teams, which could adversely affect our ability to commercialize LINZESS. We do not have certain operational capabilities outside of the U. S. If AbbVie, Astellas or AstraZeneca was subject to a change of control that allowed us to continue linaclotide' s development or commercialization anywhere outside of the U. S. on our own, and we chose to do so rather than establishing a relationship with a new partner, we would need to build operational capabilities in the relevant territory. In any of these situations, the development and commercialization of linaclotide could be negatively impacted. Risks Related to Regulatory, Legal and Compliance MattersWe face potential product liability exposure, and, if claims brought against us are successful, we could incur substantial liabilities. The use of our product candidates in clinical trials and the sale of our approved products, including the sale of linaclotide, expose us to product liability claims. If we do not successfully defend ourselves against product liability ~~claims~~ **42claims**, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in: ● decreased demand for approved products; ● impairment of our business reputation; ● withdrawal of clinical trial participants; ● initiation of investigations by regulators; ● litigation costs; ● distraction of management' s attention from our primary business; ● substantial monetary awards to patients or other claimants; ● loss of revenues; and ● the inability to commercialize our product candidates. We currently have product liability insurance coverage for the commercial sale of our products and for the clinical trials of our product candidates which is subject to industry- standard terms, conditions and exclusions. Our insurance coverage may not be sufficient to reimburse us for expenses or losses associated with claims. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. On occasion, large judgments have been awarded in lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business. We will incur significant liability if it is determined that we are promoting any " off- label " uses of our products. Physicians are permitted to prescribe drug products and medical devices for uses that are not described in the product' s labeling and that differ from those approved by the U. S. FDA or other applicable regulatory agencies. Such " off- label " uses are common across medical specialties. Although the U. S. FDA and other regulatory agencies do not regulate ~~42a~~ **a** physician' s choice of treatments, the U. S. FDA and other regulatory agencies do restrict manufacturer communications on off- label use. Companies are not permitted to promote drugs or medical devices for off- label uses or to promote unapproved drugs or medical devices. Accordingly, we do not permit promotion of any product that we develop, license, commercialize, promote, co- promote or otherwise partner prior to approval or for any indication, population or use not described in or consistent with such product' s labeling. The U. S. FDA and other regulatory and enforcement authorities actively enforce laws and regulations prohibiting promotion of off- label uses and the promotion of products for which marketing approval has not been obtained. A company that is found to have promoted off- label uses or have engaged in improper pre- approval promotion will be subject to significant liability, including civil and administrative remedies as well as criminal sanctions. Even if it is later determined that we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions and have to divert significant management resources from other matters. Notwithstanding the regulatory restrictions on off- label promotion, the U. S. FDA and other regulatory authorities allow companies to engage in truthful, non- misleading, and non- promotional disease awareness and scientific exchange

concerning their products, investigational assets and therapeutic areas of interest. We intend to engage in disease awareness and medical and scientific exchange and education activities and communicate with healthcare providers in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program, which is designed to ensure that all such activities are performed in a legal and compliant manner, we cannot be certain that our program will address all areas of potential exposure and the risks in this area cannot be entirely eliminated. ~~If~~ **43If** we fail to comply with healthcare and other regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected. The marketing of pharmaceutical and biopharmaceutical products and related arrangements with healthcare providers, third- party payors, patients and other third parties in the healthcare industry are subject to a wide range of healthcare laws and regulations within the U. S. and in foreign jurisdictions in which we operate. These laws and regulations may constrain our business and / or financial arrangements. Within the U. S., federal laws and regulations include: ● federal healthcare program anti- kickback laws, which prohibit, among other things, persons from offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for, or the purchasing or ordering of, a good or service for which payment may be made under federal healthcare programs such as Medicare and Medicaid; ● federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, information or claims for payment from Medicare, Medicaid, or other third- party payors that are false or fraudulent, and which may apply to manufacturers for reasons including providing coding and billing advice to customers or engaging in prohibited off- label promotional activities; ● federal Health Insurance Portability and Accountability Act of 1996, **or HIPAA,** which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on certain types of entities, which include many healthcare providers with whom we interact and health plans with which we may interact; ● the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products prior to approval or for off- label use and regulates the distribution of samples; ● the 21st Century Cures Act, which amends Section 114 of the Food and Drug Administration Modernization Act of 1997 to define healthcare economic information and the circumstances under which healthcare economic information may be disseminated; ● federal laws, including the Medicaid Drug Rebate Program, that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to ~~43government~~ **government** authorities or private entities, often as a condition of reimbursement under government healthcare programs; and ● the so- called " federal sunshine " law, which requires pharmaceutical and medical device companies to monitor and report certain financial interactions with physicians, certain non- physician practitioners and teaching hospitals to the federal government for re- disclosure to the public ~~;~~ **.** ~~andThere~~ **There** are also state law equivalents of certain of the above federal laws, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts, which laws include anti- kickback and false claims laws **,** which may apply to items or services reimbursed by any third- party payor, including commercial insurers, state transparency laws, state laws limiting interactions between pharmaceutical manufacturers and members of the healthcare industry, and state laws governing the privacy and security of health information in certain circumstances. Other laws and regulations have also been enacted by various states to regulate the sales and marketing practices of pharmaceutical or biopharmaceutical manufacturers. The laws and regulations generally limit financial interactions between manufacturers and health care providers; require manufacturers to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the U. S. federal government; and / or require disclosure to the government and / or public of financial interactions (so- called " sunshine laws "). State laws may also require disclosure of pharmaceutical pricing information and marketing expenditures. Certain state and local laws require the registration of pharmaceutical sales representatives. **Additionally, some 44individual states have begun establishing Prescription Drug Affordability Boards (or similar entities) to review high- cost drugs and, in some cases, set upper payment limits.** Many of these laws and regulations contain ambiguous requirements or require administrative guidance for implementation. Outside the U. S., our activities may be subject to healthcare 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 E. U. The provision of benefits or advantages to physicians is also governed by the national anti- bribery laws of E. U. Member States, and by Bribery Act 2010 in the United Kingdom **.** Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain E. U. Member States must be publicly disclosed, and in the United Kingdom a public consultation on the introduction of equivalent transparency requirements is currently underway. 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 E. U. Member States and the United Kingdom. These requirements are provided in the national laws, self- regulatory industry codes, or professional codes of conduct applicable in the E. U. Member States and the United Kingdom. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment. We also are subject to the FCPA which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity, related to any ex- U. S. activities, as well as other similar anti- bribery laws in any other country in which we may do business. **It is possible that governmental authorities will conclude that our business practices, or the business practices of third parties with whom we collaborate, 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, or those of third party partners, are found to be in violation of any of these laws or any other governmental regulations, we may be subject to lawsuits, significant civil,**

criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. We are subject to stringent and changing U. S. and foreign laws, regulations, rules, contractual obligations, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; disruptions of our operating results and business; and other adverse business consequences. We may be subject to privacy and security laws in the various jurisdictions, both inside and outside the U. S., in which we operate and / or obtain or store personally identifiable information, such as the E. U. GDPR, the United Kingdom' s GDPR and the Swiss Federal Act on Data Protection, or FADP. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. For example, the GDPR, which took effect in May 2018, applies to the processing of personal data in the EEA. The GDPR increases obligations with respect to clinical trials **and non- clinical studies** conducted in the EEA, by certain companies that process data in relation to (i) offering goods or services to, or (ii) monitoring the behavior of, individuals located in the EEA. As such, we **are** ~~would be~~ subject to the GDPR for data processing associated, ~~44for --~~ **for** example, with conducting clinical trials in the EEA or entering into research collaborations in the EEA. The GDPR imposes stringent obligations for processing of personal data, such as setting high standards for consent, requiring the provision of detailed processing notices, facilitating the exercise of data subject rights and requiring reporting certain data breaches to regulators and affected individuals, as well as establishing standards for how we document our relationships with third parties that process GDPR- covered personal data on our behalf. The FADP also applies to the collection and processing of personal data by companies located in Switzerland, or in certain circumstances, by companies located outside of Switzerland. The FADP has been revised and adopted by the Swiss Parliament and took effect on September 1, 2023. The revisions to the FADP may result in increased costs of compliance, risks of noncompliance and penalties for noncompliance. ~~The~~ **45The** GDPR, United Kingdom' s GDPR and FADP also increase the scrutiny applied to transfers of personal data from the EEA, UK, and Switzerland, respectively (including from clinical trial sites in the EEA) to countries that are considered by the European Commission, United Kingdom or Switzerland, respectively, to lack an adequate level of data protection, such as the U. S. In July 2020 the Court of Justice of the E. U. (CJEU) invalidated the E. U.- U. S. Privacy Shield Framework, under which personal data could be transferred from the EEA to U. S. entities that had self- certified under the Privacy Shield scheme. The framework has been replaced by the E. U.- U. S. Data Privacy Framework for which the European Commission adopted ~~am~~ **an** adequacy decision in July 2023. While we do not currently rely upon this framework, we expect there to be legal challenges to this framework in the future, which could draw into question the legitimacy of other cross- border transfer mechanism, including the standard contractual clauses on which we rely to transfer personal data from the EEA to the U. S. and other jurisdictions. As supervisory authorities issue further guidance on personal data export mechanisms or where the standard contractual clauses cannot be used, we could incur additional compliance costs, complaints, and / or regulatory investigations and, if we are unable to otherwise transfer personal data among jurisdictions in which we operate, our services and geographical location or segregation of our relevant systems and operations could be affected. In addition, in the U. S., we are subject to the ~~California Consumer Privacy Act, or~~ CCPA, as amended by the CPRA, which became effective on January 1, 2023 (the CPRA, together with CCPA, the California Privacy Law). The California Privacy Law gives California consumers (defined to include all California residents) certain rights regarding personal information collected about them; the California Privacy Law also imposes certain obligations and limitations on companies regarding the collection, use, selling or sharing (as defined in the California Privacy Law) of personal information collected from or about California consumers. **Other states have passed comprehensive privacy laws specifically regulating health information that may affect our business. For example, Washington state recently passed the My Health My Data Act to which we are subject, which regulates the collection and sharing of health information, and provides a right of action for violation of the statute.** The compliance obligations imposed by the GDPR, United Kingdom' s GDPR, FADP, the California Privacy Law **, Washington' s My Health My Data Act** , and other applicable privacy laws, have required us to revise our operations. Breaches of applicable data protection requirements may result in substantial fines and other regulatory penalties, as well as confer a private right of action on data subjects **or** ~~(in the case of the GDPR, UK GDPR and FADP) and~~ consumers ~~(in the case of the California Privacy Law)~~ and their representatives for breaches of certain data protection requirements. We expect to be subject to additional privacy laws at both the U. S. state level and abroad as many jurisdictions either recently have data privacy legislation or are considering enacting such legislation to which we may become subject. Achieving and sustaining compliance with applicable international, federal and state privacy, security, fraud and reporting laws may prove time- consuming and costly. If our operations, or the operations of third parties upon which we rely, are found to be in violation of any of the laws described above or any other laws, rules or regulations that apply to us, we will be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. For example, under the GDPR and the United Kingdom' s GDPR, penalties for noncompliance could be up to 20 million Euros or 4 % of our total worldwide annual revenue of the preceding financial year, whichever is greater. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, rules or regulations, we cannot be certain that our program will address all areas of potential exposure and the risks in this area cannot be entirely eliminated, particularly because the requirements and government interpretations of the requirements in this space are constantly evolving. Any action against us for violation of these laws, rules or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management' s attention from the operation of our business, as well as damage our business or reputation. 45Healthcare reform and other governmental and private.....' approved indications and patient populations. The VectivBio Acquisition increases our exposure to doing business in foreign jurisdictions. ~~Following~~ **46Following** the VectivBio Acquisition, we retained VectivBio' s

legacy headquarters in Basel, Switzerland and, as a result, we now have employees and operations in foreign jurisdictions. Operating in foreign jurisdictions exposes us to additional risks such as ~~:~~ fluctuations in currency exchange rates; compliance with different legal and regulatory environments; foreign regulatory regimes applicable to clinical trials and obtaining approvals for product candidates; compliance with applicable data privacy laws and regimes such as the E. U. GDPR, the United Kingdom' s GDPR and the Swiss **FADP** ~~Federal Act on Data Protection~~ ; risk relating to the political and economic status of foreign governments; differences in the manner in which different cultures do business; difficulties in staffing and managing foreign operations; differences in financial reporting; and operating difficulties; among other factors. The realization of any of these risks, if severe enough, could have an adverse effect on our consolidated financial position, results of operations and cash flows. Risks Related to Intellectual PropertyLimitations on our ability to obtain patent protection and / or the patent rights relating to our products and our product candidates may limit our ability to prevent third parties from competing against us. Our success depends on our ability to obtain and maintain sufficient patent protection for our products and product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. The strength of patents in the pharmaceutical industry involves complex legal and scientific questions and can be uncertain. Patent applications in the U. S. and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we were the first to conceive inventions covered by our patents and pending patent applications or that we were the first to file patent applications for such inventions. In addition, we cannot be certain that our patent applications will be granted, that any issued patents will adequately protect our intellectual property, or that such patents will not be challenged, narrowed, invalidated or circumvented. We have several issued patents in the U. S. related to LINZESS, including a LINZESS composition of matter and methods of use patent (U. S. Patent 7, 304, 036) expiring in 2026. Additional U. S. patents related to LINZESS include multiple patents relating to our commercial, room temperature stable formulations of the 72 mcg, 145 mcg and 290 mcg doses of linaclotide and methods of using these formulations, the latest of which expires in the early 2030s, as well as other patents **and patent applications** covering ~~processes for making LINZESS,~~ formulations ~~thereof~~ **of linaclotide** , and molecules related to ~~LINZESS~~ **linaclotide** . In addition, we have exclusive rights to apraglutide including issued composition of matter and method of use patents in the U. S. in lead indications. We aim to maintain a strong and broad estate of patents in the U. S. and other geographic areas. To this end, we have exclusively licensed 57 patents and 3 pending patent applications in the U. S., E. U., Japan, China and other jurisdictions protecting apraglutide. We also own one **U. S. granted** patent and ~~36~~ **one granted Japanese patent as well as approximately 38** pending patent applications worldwide that cover apraglutide, including ultrapure compositions, methods of manufacture and methods of use in various diseases ~~including aGvHD~~ . ~~47Although~~ -- **Although** none of these issued patents currently is subject to a patent reexamination or review, we cannot guarantee that they will not be subject to reexamination or review by the USPTO in the future. We believe in the strength of our LINZESS and apraglutide patent portfolio and that we have sufficient freedom to operate; however, if any of our present or future patents is challenged, narrowed, invalidated or circumvented, or our pending patent applications are not granted, our ability to prevent third parties from competing with LINZESS or apraglutide could be limited and our business and financial results may be materially harmed. Furthermore, the America Invents Act, which was signed into law in 2011, has made several major changes in the U. S. patent statutes. These changes permit third parties to challenge our patents more easily and create uncertainty with respect to the interpretation and practice of U. S. patent law. Moreover, the U. S. Supreme Court has ruled on several patent cases that narrow the scope of patent protection available and weakening the rights of patent owners in certain circumstances. Depending on the impact of these decisions and other actions by the U. S. Congress, the federal courts, the USPTO, and their foreign counterparts, the laws and regulations governing patents may change, or their interpretation or implementation may change, in unpredictable ways that could impact, potentially adversely, our ability to obtain new patents or to enforce and defend patents that we have already obtained or that we might obtain in the ~~future~~ **47future** . For example, such changes may increase the costs and complexity associated with obtaining, enforcing or defending our patents, including in ANDA litigation. We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our partners and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. It is possible, however, that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies, and we could lose our trade secrets through such breaches or violations. Additionally, our trade secrets could otherwise become known or be independently discovered by our competitors. In addition, the laws of certain foreign countries do not protect proprietary rights to the same extent or in the same manner as the U. S., and, therefore, we or our partners may encounter problems in protecting and defending our intellectual property in certain foreign jurisdictions. If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in such litigation could have a material adverse effect on our business. Our commercial success depends on our ability, and the ability of our partners, to develop, manufacture, market and sell our products and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our partners are developing products. As the biotechnology and pharmaceutical industry expands and more patents are issued, the risk increases that our potential products may give rise to claims of infringement of the patent rights of others. There may be issued patents of third parties of which we are currently unaware that may be infringed by LINZESS, apraglutide, or our product candidates. Because patent applications can take many years to issue, there may be currently pending applications which may later result in issued patents that LINZESS, apraglutide, or our product candidates may infringe. We may be exposed to, or threatened with, litigation by third parties alleging that

LINZESS, apraglutide, or our product candidates infringe their intellectual property rights. If LINZESS, apraglutide, or one of our product candidates is found to infringe the intellectual property rights of a third party, we or our partners could be enjoined by a court and required to pay damages and could be unable to develop or commercialize LINZESS, apraglutide, or the applicable product candidate unless we obtain a license to the intellectual property rights. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the counterparty could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our products, pending a trial on the merits, which may not occur for several years. ~~48There~~ -- **There** is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. If a third party claims that we or our partners infringe its intellectual property rights, we may face a number of issues, including, but not limited to: ● infringement and other intellectual property claims which, regardless of merit, may be expensive and time- consuming to litigate and may divert our management' s attention from our core business; ● substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party' s rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner' s attorneys' fees; ● a court prohibiting us from selling our product unless the third party licenses its rights to us, which it is not required to do; ● if a license is available from a third party, we may have to pay substantial royalties, fees or grant cross- licenses to our intellectual property rights; and ● redesigning our products so they do not infringe, which may not be possible or may require substantial monetary expenditures and time. ~~If~~ **48If** we fail to comply with our obligations or have disagreements over contract interpretation in agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationship with our licensor, the scope of our intellectual property or technology rights could be narrowed and we could lose license rights that are important to our business. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to: ● the scope of rights granted under the license agreement and other interpretation- related issues; ● the extent to which our technology and processes infringe intellectual property of the licensor that is not subject to the licensing agreement; ● the sublicensing of patent and other rights; ● our diligence obligations under the license agreement and what activities satisfy those diligence obligations; ● the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors, our collaborators and us; ● the priority of invention of patented technology; and ● the fulfilment of our obligations under the license. In addition, certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could harm our business, financial condition, results of operations and prospects. If our licenses or material relationships or any in- licenses upon which our licenses are based are terminated or breached, we may: ● lose our rights to develop and market product candidates; ● lose patent protection for product candidates; ~~49~~ ● experience significant delays in the development or commercialization of product candidates; ● not be able to obtain any other licenses on acceptable terms, if at all; or ● incur liability for damages. **We are currently a party to and may in the future be party to license agreements.** Apraglutide is among the assets that are subject to licensing agreements with third parties ~~. If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize apraglutide. We are currently a party to and may in the future be party to license agreements~~. For example, we are a party to an amended and restated intellectual property license agreement with Ferring pursuant to which we have exclusive rights to apraglutide including **an** issued composition of matter and method of use ~~patents~~ **patent** in the U. S. in lead indications, or the Ferring Agreement. The Ferring Agreement imposes, and other current or future license agreements may impose, various diligence, milestone payment, royalty, and other obligations on us. These milestone, royalty, and other payments associated with the license, will make it less profitable for us to develop apraglutide or other product candidates that are the subject of current or future licenses. If we fail to comply with our obligations under the Ferring Agreement, or we are subject to a bankruptcy, we may be required to make certain payments to Ferring, we may lose the exclusivity of our license, or Ferring may have the right to terminate the license. If the Ferring Agreement is terminated, we could lose intellectual property rights that are important to our business, be liable for damages to the licensor or be prevented from developing and ~~commercializing~~ **49commercializing** our apraglutide. Termination of the agreement or reduction or elimination of our rights under the agreement may also result in us being required to negotiate a new or reinstated agreement with less favorable terms, and it is possible that we may be unable to obtain any such additional license at a reasonable cost or on reasonable terms and will be unable to develop and commercialize apraglutide. These or similar risks may apply to other license agreements, including future license agreements. **If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize apraglutide.** In some cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensor fails to obtain or maintain a patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. We **may be unable to** maintain the benefits associated with orphan drug designation,including market exclusivity,which may harm our business.In the U.S.,orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs,tax advantages,and user- fee waivers.In addition,if a product receives the first U.S.FDA approval for the indication for which it has orphan designation,the product is entitled to orphan drug exclusivity,which means the U.S.FDA may not approve any other application to market the same drug for the same indication for a period of seven

years,except in limited circumstances,such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity.In the E.U.,orphan drug designation entitles a company to financial incentives such as reduction of fees or fee waivers and ten years of data and market exclusivity for the approved therapeutic indication following marketing authorization of a medicinal product,including biological medicinal products.This period may be reduced to six years if,at the end of the fifth year,the medicinal product no longer fulfills the orphan designation criteria,including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.Because the extent and scope of patent protection for our products may in some cases be limited,orphan drug designation is especially important for our product candidates for which orphan drug designation may be available.For eligible drugs,we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position.If we do not obtain orphan drug exclusivity for our drug product candidates that does not have a broad patent protection,our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity and our revenue will be reduced.Even though we have orphan drug designation for apraglutide in the U.S.and in the E.U.,we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products.Based on available preclinical and clinical data,both the U. ~~D~~ **S** .FDA and the EMA have granted apraglutide orphan drug designation for the treatment of SBS ~~.The U.S.FDA also granted orphan drug designation for apraglutide for the prevention of aGvHD~~ .Orphan drug applicability will be reassessed by health authorities upon completion of clinical studies and submission of our marketing application.In the E.U.,the orphan designation for apraglutide may not be maintained at the time of grant of the marketing authorization if the EMA and COMP do not consider that there is sufficient confirmatory evidence to support that the **orphan designation** criteria ~~orphan designation~~ continue to be met.Even if we obtain orphan drug exclusivity for a product,that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition.Even after an orphan drug is approved,the U.S.FDA or **EMA** ~~European Commission~~ can subsequently approve the same drug with the same active moiety for the same condition if the U.S.FDA or EMA concludes that the later drug is safer,more effective,or makes a major contribution to patient care.Orphan drug designation neither shortens the development time or regulatory review time of a **drug nor gives the drug any advantage in the regulatory review or approval process.50We** have received notices of Paragraph IV certifications related to LINZESS in conjunction with ANDAs filed by generic drug manufacturers, and we may receive additional notices from others in the future. We have, and may continue to, become involved in legal proceedings to protect or enforce intellectual property rights relating to our products and our product candidates, which could be expensive and time consuming, and unfavorable outcomes in such proceedings could have a material adverse effect on our business. Competitors may infringe the patents relating to our products and our product candidates or may assert that such patents are invalid. To counter ongoing or potential infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. Litigation with generic manufacturers has become increasingly common in the biotechnology and pharmaceutical industries. In addition, in an infringement or invalidity proceeding, a court or patent administrative body may determine that a patent of ours is not valid or is unenforceable, 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. Generic drug manufacturers were first able to file ANDAs for generic versions of LINZESS in August 2016. When filing an ANDA for one of our products, a generic drug manufacturer may choose to challenge one or more of the patents that cover such product and seek to commercialize generic versions of one or more LINZESS doses. As such, we have brought, and may bring in the future, legal proceedings against generic drug manufacturers. We and AbbVie have received Paragraph IV certification notice letters regarding ANDAs submitted to the U. S. FDA by generic drug manufacturers requesting approval to engage in commercial manufacture, use, sale and offer for sale of linaclotide capsules (72 mcg, 145 mcg and 290 mcg), proposed generic versions of our U. S. FDA- approved drug ~~50LINZESS~~ -- **LINZESS** . We filed patent infringement lawsuits against five companies making such ANDA filings and subsequently entered into settlement agreements with each of these filers. Frequently, innovators receive multiple ANDA filings. Consequently, we may receive additional notice letters regarding ANDAs submitted to the U. S. FDA (and we may receive amendments to those notice letters), but we may not become aware of these filings for several months after any such submission due to procedures specified under applicable U. S. FDA regulations. After evaluation, we have in the past filed, and may, in the future, file patent infringement lawsuits or take other action against companies making ANDA filings. If a patent infringement suit has been filed within 45 days of receipt of a notice letter, the U. S. FDA is not permitted to approve any ANDA that is the subject of such lawsuit for 30 months from the date of the NDA holder' s and patent owner' s receipt of the ANDA filer' s notice letter, or until a court decides that the relevant patents are invalid, unenforceable and / or not infringed. Additionally, the validity of the patents relating to our products and our product candidates may be challenged by third parties pursuant to administrative procedures introduced by the America Invents Act, specifically inter partes review, or IPR, and / or post grant review, or PGR, before the USPTO. Generic drug manufacturers may challenge our patents through IPRs or PGRs instead of or in addition to ANDA legal proceedings. Patent litigation (including any lawsuits that we file against generic drug manufacturers in connection with the receipt of a notice letter), IPRs and PGRs involve complex legal and factual questions and we may need to devote significant resources to such legal proceedings. We can provide no assurance concerning the duration or the outcome of any such patent- related lawsuits or administrative proceedings, including any settlements or other resolutions thereof which could, in addition to other risks, result in a shortening of exclusivity periods. An adverse result in any litigation or defense proceedings could put one or more of the patents relating to our products and our product candidates at risk of being invalidated or interpreted narrowly, or could otherwise result in a loss of patent protection for the product or product candidate at issue, and could put our patent applications at risk of not issuing, which would materially harm our business. Upon any loss of patent protection for one of our products, or upon an " at- risk " launch (despite pending patent infringement litigation, before any court decision or while an appeal of a lower court decision is pending) by a manufacturer of a generic version of one of our patented products, our revenues for that

product could be significantly reduced in a short period of time, which would materially and adversely affect our business. Interference or derivation proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to the patents relating to our products and our product candidates and patent applications or those of our partners. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distraction of our management and other employees. In addition, we may not be able to prevent, alone or with ~~our~~ **51our** partners, misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the U. S. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, as well as the potential for public announcements of the results of hearings, motions or other interim proceeding or developments, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. Risks Related to Our Finances and Capital RequirementsWe incurred significant losses from our inception in 1998 through the year ended December 31, 2018, and we may incur losses in future periods. In recent years, we have focused primarily on developing, manufacturing and commercializing linaclotide, as well as developing our other product candidates. For example, in June 2023, we acquired VectivBio and added apraglutide, a next generation long- acting GLP- 2 analog, in development for the treatment of patients with SBS ~~- IF~~ **who are dependent on PS** , to our pipeline. We have financed our business to date primarily through the issuance of equity, our collaboration and license arrangements, and debt issuances, including our ~~August 2019 issuance of the~~ $ 200. 0 million aggregate principal amount of Convertible Senior Notes, bearing an interest of ~~0~~ **1** . ~~75~~ **50** % and due in ~~2024~~ **2026** , or the ~~2024 Convertible Notes, the $ 200. 0 million aggregate principal amount of~~ Convertible Senior Notes, ~~bearing an~~ **and** ~~interest of 1. 50 % and due in 2026, or the 2026 Convertible Notes (together with the 2024 Convertible Notes, the Convertible Senior Notes), and our four -~~ **our** ~~- year~~ $ ~~500~~ **550** . 0 million secured revolving credit facility, or the Revolving Credit Facility. We currently derive a significant ~~51portion --~~ **portion** of our revenue from our LINZESS collaboration with AbbVie for the U. S. We believe that the revenues from the LINZESS collaboration will continue to constitute a significant portion of our total revenue for the foreseeable future. Such revenue is highly dependent on LINZESS demand and other factors such as fluctuations in retail chains' and wholesalers' buying patterns and inventory levels, pricing and reimbursement. Our collaborative arrangements revenue outside of the U. S. has and may continue to fluctuate as a result of the timing and amount of royalties from sales of linaclotide in the markets in which it is currently approved, or any other markets where linaclotide receives approval, as well as clinical and commercial milestones received and recognized under our current and future strategic partnerships outside of the U. S. **For** ~~Prior to~~ the year ended December 31, **2023, we incurred a net loss in connection with the VectivBio Acquisition. Prior to the year ended December 31,** 2019, we incurred net losses in each year since our inception in 1998. As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of approximately $ 1. 7 billion. We cannot be certain that sales of our products, and the revenue from our other commercial activities **,** will not fall short of our projections or be delayed. Further, we expect to continue to incur substantial expenses in connection with our efforts to commercialize linaclotide **and, if approved, apraglutide** , research and develop our product candidates, and access externally developed products or product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing pharmaceutical products, as well as those related to our expectations for our products and our other activities, we are unable to predict the extent of any future losses. Failure to achieve sustainable net income and maintain positive cash flows would have an adverse effect on stockholders' equity and working capital. We may need additional funding and may be unable to raise capital when needed, which could cause us to delay, reduce or eliminate our corporate or product development or commercialization efforts. We have previously raised funds to finance our operations through capital raising activities, including the sale of shares of our Class A Common Stock in public offerings and convertible and other debt issuances. However, marketing and selling gastrointestinal drugs, purchasing commercial quantities of pharmaceutical products, developing product candidates, conducting clinical trials and accessing externally developed products or product candidates are expensive and uncertain. Circumstances, our strategic imperatives, or opportunities to create or acquire new programs, as well as maturities, redemptions or repurchases of our outstanding debt securities, could require us to, or we may choose to, seek to raise additional funds. The amount and timing of our future funding requirements will depend on many factors, including, but not limited to: ● the level of underlying demand **and price we are able to charge** for our products ~~by prescribers and patients~~ in the countries in which they are approved; ● the costs associated with commercializing our products in the U. S.; **52** ● the costs of establishing, maintaining and / or expanding sales, marketing, distribution, and market access capabilities for our products; ● the regulatory approval of linaclotide within new indications, populations and formulations, as well as the associated development and commercial milestones and royalties **; ● the regulatory approvals of apraglutide** ; ● the rate of progress, the cost of our clinical trials and the other costs associated with our development programs, including our clinical trial of apraglutide in adult patients with SBS- IF, post- approval nonclinical and clinical studies of linaclotide in pediatrics and our investment to enhance the clinical profile of LINZESS within IBS- C and CIC, as well as to study linaclotide in additional indications, populations and formulations to assess its potential to treat various conditions; ● the costs and timing of in- licensing additional products or product candidates or acquiring other complementary companies or assets; ● the ~~achievement and timing of milestone payments and royalties due or payable under our collaboration and license agreements; ● the~~ status, terms and timing of any collaboration, licensing, co- commercialization or other arrangements; ~~● the timing of any regulatory approvals of apraglutide and our other product candidates; 52~~ ● whether the holders of our Convertible Senior Notes hold the notes to maturity without conversion into our Class A Common Stock or cash and whether we are required to repurchase any of our Convertible Senior Notes prior to maturity upon a fundamental change, as defined in each of the indentures governing the Convertible Senior Notes; and ● whether we seek to redeem, repurchase or retire all or part of our outstanding debt through cash purchases and / or exchanges, in open market purchases, privately negotiated transactions, by tender offer or otherwise. Additional funding may not be available

on acceptable terms or at all. If adequate funds are not available, we may be required to delay or reduce the scope of our commercialization efforts, delay, reduce or eliminate one or more of our development programs or delay or abandon potential strategic opportunities. Our ability to pay principal of and interest on our outstanding debt will depend in part on the receipt of payments from AbbVie under our collaboration agreement for North America. Semi- annual payments on our Convertible Senior Notes began in December 2019. In addition, in ~~May~~ 2023, we entered into the Revolving Credit Facility. As of December 31, ~~2023~~ **2024** , the outstanding principal balance on the Revolving Credit Facility was $ ~~300~~ **385** . 0 million. We expect that for the next few years, at a minimum, the net quarterly payments from AbbVie will be a significant source of cash flows from operations. If the cash flows derived from the net quarterly payments that we receive from AbbVie under the collaboration agreement for North America are insufficient on any particular payment date to fund the interest payment on our outstanding indebtedness, at a minimum, we will be obligated to pay the amounts of such shortfall out of our general funds. The determination of whether AbbVie will be obligated to make a net quarterly payment to us in respect of a particular quarterly period is a function of the revenue generated by LINZESS in the U. S. as well as the development, manufacturing and commercialization expenses incurred by each of us and AbbVie under the collaboration agreement for North America. Accordingly, since we cannot guarantee that our company will maintain net income or positive cash flows, we cannot provide assurances for any particular quarterly period that (i) we will have the available funds to fund the interest payment on our outstanding indebtedness, at a minimum, in the event that there is a deficiency in the net quarterly payment received from AbbVie, (ii) there will be a net quarterly payment from AbbVie at all or (iii) we will not also be required to make a true- up payment to AbbVie under the collaboration agreement for North America. Our indebtedness could adversely affect our financial condition or restrict our future operations. As of December 31, ~~2023~~ **2024** , we had total indebtedness of $ ~~700~~ **585** . 0 million and available cash and cash equivalents of $ ~~92~~ **88** . ~~3~~ **6** million. We incurred significant new indebtedness in connection with the VectivBio Acquisition. In May 2023, we entered into the Revolving Credit Facility, which includes a $ 10. 0 million letter of credit subfacility. In June 2023, we ~~borrowed~~ **53borrowed** $ 400. 0 million to fund a portion of the consideration paid to purchase VectivBio' s outstanding ordinary shares in connection with the VectivBio Acquisition. ~~As of December 31, 2023, we have repaid $ 100. 0 million of the outstanding principal balance.~~ The agreement governing the Revolving Credit Facility, or the Revolving Credit Agreement **, as amended in September 2024** , contains certain covenants applicable to us and certain of our subsidiaries that may, under certain circumstances, impose significant operating and financial restrictions on us, including, without limitation, limitations on additional indebtedness, liens, various fundamental changes, dividends and distributions, investments (including acquisitions), transactions with affiliates, asset sales, prepayment of junior financing, changes in business and other limitations customary in senior secured credit facilities. The Revolving Credit Agreement also includes cross- default features providing that defaults under certain other indebtedness would result in a default under the Revolving Credit Agreement. In addition, the Revolving Credit Agreement requires us to maintain a maximum consolidated secured net leverage ratio of 3. **50 to 1.** 00 **until the end of the final quarter of 2025, or the Initial Period, (ii) 3. 25** to 1. 00 **until the end of the first quarter of 2026, or the Interim Period, and (iii) 3. 00 to 1. 00 thereafter,** and a minimum interest coverage ratio of 3. 00 to 1. 00, in each case at the end of each fiscal quarter. The Revolving Credit Agreement allows us to elect to increase the permitted maximum consolidated secured net leverage ratio to **(i) 4. 00 to 1. 00 during the Initial Period, (ii)** 3. **75 to 1. 00 during the Interim Period, and (iii) 3.** 50 to 1. 00 **thereafter, in each case for up to** for four fiscal quarters in the event ~~we~~ **it** ~~consummate~~ **consummates** an acquisition for consideration in excess of $ 50 **. 0** million, subject to certain limitations on how often this election can be made. Additionally, the lenders under the Revolving ~~53Credit~~ -- **Credit** Agreement will be permitted to accelerate all outstanding borrowings and other obligations, terminate outstanding commitments and exercise other specified remedies upon the occurrence of customary events of default. In addition, while ~~none of~~ the ~~indentures~~ **indenture** governing our Convertible Senior Notes **does not** include covenants restricting the operation of our business except in certain limited circumstances, in the event of a default under ~~any of~~ the Convertible Senior Notes, the ~~applicable~~ noteholders or the trustee under the indenture governing the ~~applicable~~ Convertible Senior Notes may accelerate our payment obligations under ~~such~~ **the** Convertible Senior Notes, which could have a material adverse effect on our business, financial condition and results of operations. We are also required to offer to repurchase the Convertible Senior Notes upon the occurrence of a fundamental change, which could include, among other things, any acquisition of our company (other than an acquisition in which at least 90 % of the consideration is Class A Common Stock listed on The Nasdaq Global Select Market or The New York Stock Exchange), subject to the terms of ~~each of~~ the indenture governing the Convertible Senior Notes. The repurchase price must be paid in cash, and this obligation may have the effect of discouraging, delaying or preventing an acquisition of our company that would otherwise be beneficial to our security holders. **The** ~~Each of the indentures~~ **indenture** governing our Convertible Senior Notes also includes cross- default features providing that certain failures to pay for outstanding indebtedness would result in a default under the ~~indentures~~ **indenture** governing our Convertible Senior Notes. In the event of such default, the trustee or noteholders could elect to declare all amounts outstanding to be immediately due and payable under the ~~applicable~~ indenture, which could have a material adverse effect on our business, financial condition and results of operations. To the extent we become subject to such covenants, our ability to comply with such covenants in future periods will depend on our ongoing financial and operating performance, which in turn will be subject to economic conditions and to financial, market and competitive factors, many of which are beyond our control. ~~The ability to comply with these covenants in future periods will also depend on our ability to successfully implement our overall business strategy and realize the anticipated benefits of the VectivBio Acquisition, including synergies, cost savings, innovation and operational efficiencies.~~ Our significant indebtedness, combined with our other financial obligations and contractual commitments, could have important consequences on our business, including: ● limiting our ability to obtain additional financing to fund future working capital, capital expenditures or other general corporate purposes, including product development, commercialization efforts, research and development activities, strategic arrangements, acquisitions and refinancing of our outstanding debt; ● requiring a substantial portion of our

cash flows to be dedicated to debt service payments instead of other purposes, thereby reducing the amount of cash flows available for working capital, capital expenditures, corporate transactions and other general corporate purposes; ● increasing our vulnerability to adverse changes in general economic, industry and competitive conditions; ● limiting our flexibility in planning for and reacting to changes in the industry in which we compete; **54** ● placing us at a disadvantage compared to other, less leveraged competitors or competitors with comparable debt at more favorable interest rates; and ● increasing our cost of borrowing. If we do not generate sufficient cash flows from operations or if future borrowings are not available to us in an amount sufficient to service our indebtedness, including payments of principal when due on our outstanding indebtedness or, in the case of our Convertible Senior Notes, in connection with a transaction involving us that constitutes a fundamental change under the indentures governing the Convertible Senior Notes, or under our Revolving Credit Facility, or to fund our liquidity needs, we may be forced to refinance all or a portion of our indebtedness on or before the maturity dates thereof, sell assets, reduce or delay currently planned activities or curtail operations, seek to raise additional capital or take other actions. We may not be able to execute any of these actions on commercially reasonable terms or at all. This, together with any of the factors described above, could materially and adversely affect our business, financial condition and results of operations. ~~54The~~ -- **The** capped call transactions entered into in connection with our ~~2024~~ Convertible **Senior** ~~Notes and our 2026 Convertible~~ Notes may affect the value of our Class A Common Stock. In connection with the issuance of our ~~2024~~ Convertible **Senior** ~~Notes and our 2026 Convertible~~ Notes, we entered into capped call transactions, or the Capped Calls, with certain financial institutions. These transactions are expected generally to reduce the potential dilution upon any conversion of our ~~2024~~ Convertible **Senior** ~~Notes or our 2026 Convertible~~ Notes, as applicable, or offset any cash payments we are required to make in excess of the principal amount of converted Convertible Senior Notes, as the case may be. In connection with these transactions, the financial institutions likely purchased our Class A Common Stock in secondary market transactions and entered into various OTC derivative transactions with respect to our Class A Common Stock. These entities or their affiliates are likely to modify their hedge positions from time to time prior to conversion or maturity of the ~~2024~~ Convertible **Senior** Notes ~~and the 2026 Convertible Notes, as applicable,~~ by purchasing and selling shares of our Class A Common Stock or other instruments they may wish to use in connection with such hedging. Any of these activities could adversely affect the value of our Class A Common Stock and, as a result, the number of shares and the value of the Class A Common Stock noteholders will receive upon conversion of the ~~2024~~ Convertible **Senior** Notes ~~, or the 2026 Convertible Notes, as applicable~~ . In addition, under certain circumstances the counterparties have the right to terminate the Capped Calls on terms set forth in the applicable confirmations, which may result in us not receiving all or any portion of the anticipated benefit of the Capped Calls. If the price of our Class A Common Stock increases such that the hedge transactions settle in our favor, we could also be exposed to credit risk related to the counterparties to the Capped Calls, which would limit or eliminate the benefit of such transactions to us. Our quarterly and annual operating results may fluctuate significantly. **Our** ~~We expect our~~ operating results **have been, and we expect they will continue** to be **,** subject to frequent fluctuations. Our net income (loss) and other operating results will be affected by numerous factors, including: ● the level of underlying demand and price for our products in the countries in which they are approved; ● retail chains' and wholesalers' buying patterns, pricing and reimbursement and inventory levels with respect to our products; ● the costs associated with commercializing our products in the U. S.; ● the achievement and timing of milestone payments and royalties due or payable under our collaboration and license agreements; ● our execution of any collaboration, partnership, licensing or other strategic arrangements, and the timing of payments we may make or receive under these arrangements; ● any impairments of assets or goodwill, and associated write- downs; **55** ● any variations in the level of expenses related to our development programs; ● addition or termination of clinical trials **; ● results of or developments in nonclinical studies and clinical trials of our product candidates or those of our competitors or potential collaborators** ; ● any impact on taxes or changes in tax rules; ● regulatory developments affecting our products and product candidates; ● **the success of competitive products or technologies; ●** any material lawsuit in which we may become involved; **● general economic, industry, and market conditions;** and ● the impact of public health emergencies, including containment or mitigation measures, or natural disasters. ~~55If~~ **If** our operating results fall below the expectations of investors or securities analysts for any of the foregoing reasons or otherwise, the price of our Class A Common Stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. Our ability to use net operating loss and tax credit carryforwards and certain built- in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and it is possible that our net operating loss and tax credit carryforwards may expire before we generate sufficient taxable income to use such carryforwards, or that certain transactions or a combination of certain transactions may result in material additional limitations on our ability to use our net operating loss and tax credit carryforwards **. For the year ended December 31, 2023, we incurred a net loss in connection with the VectivBio Acquisition** . Prior to the year ended December 31, 2019, we incurred significant net losses since our inception. To the extent that we do not generate federal and state taxable income in the future, unused net operating loss and tax credit carryforwards will carry forward to offset future taxable income, if any, until the date, if any, on which such unused carryforwards expire. Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, contain rules that limit the ability of a company that undergoes an ownership change, which is generally any change in ownership of more than 50 % of its stock over a three- year period, to utilize its net operating loss and tax credit carryforwards and certain built- in losses recognized in years after the ownership change. These rules generally operate by focusing on ownership changes involving stockholders owning directly or indirectly 5 % or more of the stock of a company and any change in ownership arising from a new issuance of stock by the company. Generally, if an ownership change occurs, the yearly taxable income limitation on the use of net operating loss and tax credit carryforwards and certain built- in losses is equal to the product of the applicable long- term tax exempt rate and the value of the company' s stock immediately before the ownership change. Certain future equity offerings or strategic transactions, if any, could potentially result in a 50 % or greater change of control. If we do not generate sufficient taxable income prior to the expiration, if any, of the

applicable carryforwards or if the carryforwards are subject to the limitations described above, we may be unable to offset our taxable income with losses, or our tax liability with credits, before such losses and credits expire and therefore would incur larger federal or state income tax liability. We have completed several financings since our inception which may have resulted in a change in control as defined by Section 382, or could result in a change in control in the future. Our ability to use foreign tax loss carryforwards acquired in the VectivBio Acquisition may be limited. Prior to our acquisition of VectivBio, VectivBio incurred significant net losses since its inception. In Switzerland, tax loss carryforwards may, with certain limitations, be used to offset future taxable income. However, if not utilized, the tax loss carryforwards, under Swiss laws, expire seven years after the tax year in which they were incurred. Due to our current limited income in Switzerland, there is a high risk that the tax loss carryforwards will expire ~~in~~ **56in** part or in their entirety and will not be used to offset future taxable income. Any limitations in our ability to use tax loss carryforwards to offset taxable income could adversely affect our financial condition. If the distribution of the shares of Cyclerion Therapeutics, Inc., or Cyclerion, common stock in connection with the Separation is not generally tax- free for U. S. federal income tax purposes, we and our stockholders could be subject to significant tax liabilities. The distribution **of the shares of Cyclerion common stock in connection with the Separation** , together with certain related transactions, is intended to qualify for tax- free treatment to us and our stockholders for U. S. federal income tax purposes. We received a favorable private letter ruling from the Internal Revenue Service, or IRS, under the pilot program established in Revenue Procedure 2017- 52 relating to the U. S. federal income tax treatment of the distribution. Consistent with the guidelines set forth in Revenue Procedure 2017- 52, the IRS private letter ruling does not cover all of the issues that are relevant to determining whether the distribution is generally tax free for U. S. federal income tax purposes. Accordingly, completion of the distribution was conditioned upon, among other things, our receipt of an opinion from an outside tax advisor that the distribution will qualify as a transaction that is generally tax- free to both us and our stockholders for U. S. federal income tax purposes under Sections 355 and 368 (a) (1) (D) of the Internal Revenue Code. The private letter ruling and opinion were based on and relied on, among other things, certain facts and assumptions, as well as certain representations, statements and undertakings from us and Cyclerion (including those relating to the past and future conduct of us and Cyclerion). If any of these facts, assumptions, representations, statements or undertakings is, or becomes, inaccurate or incomplete, or if we or Cyclerion breach any of our respective covenants relating to the distribution, the IRS private letter ruling and any tax opinion may be invalid. Moreover, the opinion is not binding on the IRS or any courts. Accordingly, notwithstanding receipt of the ~~56IRS~~ -- **IRS** private letter ruling and the opinion, the IRS could determine that the distribution and certain related transactions should be treated as taxable transactions for U. S. federal income tax purposes. If the distribution, together with certain related transactions, fails to qualify as a transaction that is generally tax- free under Sections 355 and 368 (a) (1) (D) of the Internal Revenue Code, in general, for U. S. federal income tax purposes, we would recognize taxable gain with respect to Cyclerion' s distributed common stock and our stockholders who received shares of Cyclerion common stock in the distribution would be subject to tax as if they had received a taxable distribution equal to the fair market value of such shares. General Risk FactorsWe may not be able to manage our business effectively if we lose any of our current management team or if we are unable to attract, motivate and retain key personnel. We may not be able to attract, motivate or retain qualified management and scientific, clinical, operations and commercial personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the greater- Boston area. If we are not able to attract, motivate and retain necessary personnel to accomplish our business objectives, we will experience constraints that will significantly impede the achievement of our objectives. We are highly dependent on the drug research, development, regulatory, commercial, financial and other expertise of our management, particularly Thomas McCourt, our chief executive officer; ~~Sravan Emany~~ **Gregory Martini** , our senior vice president, chief financial ~~officer; Andrew Davis, our senior vice president, chief business~~ officer; John Minardo, our senior vice president, chief legal officer and secretary; and Michael Shetzline, our senior vice president, chief medical officer and head of research and drug development. Transitions in our senior management team or other key employees, or the unavailability of any such persons for any reason, can be inherently difficult to manage and may disrupt our operations or business or otherwise harm our business, for example **,** due to the diversion of our board and management' s time and attention and a decline in employee morale. In addition to the competition for personnel, the Boston area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment efforts, which may or may not be successful. We also have scientific and clinical advisors who assist us in formulating our product development, clinical strategies and our global supply chain plans, as well as sales and marketing advisors who have assisted us in our commercialization strategy and brand plan for our products. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may ~~have~~ **57have** arrangements with other companies to assist in the development and commercialization of products that may compete with ours. Security breaches and other disruptions to our information technology structure could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer. In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, our proprietary business information and that of our suppliers and business partners, as well as personally identifiable information of our patients, clinical trial participants and employees. We also rely to a large extent on information technology systems to operate our business, including to deliver our products. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third- party providers possess certain of our sensitive data. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our large and complex information technology and infrastructure (and those of our partners, vendors and third- party providers) **are** ~~may be~~ vulnerable to attacks by hackers ~~or~~ **and may be** breached due to employee, partner, vendor or third- party error, malfeasance or other disruptions. We, our partners,

vendors and other third- party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever- increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. While we have invested in information technology and security and the protection of confidential information, there can be no assurance that our efforts will prevent service interruptions or ~~57security~~ -- **security** breaches. Further, while some or all of our workforce, and those of our partners, vendors and other third- party providers, work remotely, we may have greater vulnerability to cyberattacks or other losses of confidential information, as well as interruptions in information technology systems. Any such interruptions, losses or breaches would substantially impair our ability to operate our business and would compromise our, or our partners, vendors and other third- party providers, networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, negatively impact our financial condition and damage our reputation, any of which could adversely affect our business. While we maintain cyber liability insurance, this insurance may not be sufficient to cover the financial or other losses that may result from an interruption or breach of our (or our partners', vendors' and third- party providers') systems. Anti- takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could negatively impact the market price of our Class A Common Stock. Provisions in our certificate of incorporation and bylaws may have the effect of delaying or preventing a change of control. These provisions include the following: ● Our board of directors has the right to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors. ● Our board of directors may issue, without stockholder approval, shares of preferred stock. The ability to authorize preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us. ● Stockholders must provide advance notice to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders' meeting. These provisions may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect such acquirer' s own slate of directors or otherwise attempting to obtain control of our company. ● Our stockholders may not act by written consent. As a result, a holder, or holders, controlling a majority of our capital stock are not able to take certain actions outside of a stockholders' meeting. ● Special meetings of stockholders may be called only by the chairman of our board of directors, our chief executive officer or a majority of our board of directors. As a result, a holder, or holders, controlling a majority of our capital stock are not able to call a special meeting. **58** ● A super- majority (80 %) of the outstanding shares of Class A Common Stock are required to amend our bylaws, which make it more difficult to change the provisions described above. In addition, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may prohibit certain business combinations with stockholders owning 15 % or more of our outstanding voting stock. These and other provisions in our certificate of incorporation and our bylaws and in the Delaware General Corporation Law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then- current board of directors. ~~If we~~ **We have** ~~identify~~ **identified** ~~a~~ material ~~weakness~~ **weaknesses** in our internal control over financial reporting **. If we are not able to remediate these material weaknesses, or if we identify additional material weaknesses in the future** , it could have an adverse effect on our business and financial results **,** and our ability to meet our reporting obligations could be negatively affected, each of which could negatively affect the trading price of our Class A Common Stock **. In connection with the audit of our consolidated financial statements for the year ended December 31, 2024, we and our independent registered public accounting firm have identified material weaknesses in our internal control over financial reporting and we determined that our internal control over financial reporting was not effective as of December 31, 2024** . A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Accordingly, a material weakness increases the risk that the financial information we report contains material errors. ~~We regularly review~~ **For further discussion of the material weaknesses we have identified** and ~~update~~ our ~~internal~~ **remediation plan, see Part II, Item 9A, under the heading "** ~~controls~~ **Controls** ~~, disclosure controls~~ and ~~procedures~~ **Procedures** ~~, and corporate governance policies~~ **" in this Annual Report on Form 10- K** . **While** ~~In addition,~~ we **have designed and** are ~~required under~~ **implementing a remediation plan to remediate these material weaknesses, we cannot assure that the measures we have taken to date, together with any measures we may take in the future, will be sufficient to remediate the material weaknesses we have identified or avoid the identification of additional material weaknesses in the future. If the steps we take do not remediate the material weaknesses in a timely manner, there could continue to be a reasonable possibility that these control deficiencies or others could result in a material misstatement of our annual or interim financial statements that would not be prevented or detected on a timely basis. If we are not able to remediate these material weaknesses in a timely manner or otherwise comply with the requirements of Section 404 of** the Sarbanes- Oxley Act **in a timely manner, our ability to record, process, summarize and report financial information accurately and within applicable time periods may be adversely affected. If we are not able to remediate these material weaknesses in a timely manner, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in our stock price. In addition, our conclusion that we have material weaknesses could give rise to increased scrutiny, review, audit and investigation over our accounting controls and procedures. We regularly review and update our internal controls, disclosure controls and procedures, and corporate governance policies. In addition, we are required under the Sarbanes- Oxley Act** of 2002 to report annually on our ~~58internal~~ -- **internal** control over financial reporting. Our system of internal controls, however well- designed and operated, is based in part on certain assumptions and includes elements that rely on information from third parties, including our partners. Our system can provide only reasonable, not absolute, assurances that the objectives of the system are met. ~~If we, or our~~

~~independent registered public accounting firm, determine that our internal controls over financial reporting are not effective, or we discover areas that need improvement in the future, these shortcomings could have an adverse effect on our business and financial results, and the price of our Class A Common Stock could be negatively affected.~~ Further, we are dependent on our partners for information related to our results of operations. Our net profit or net loss generated from the sales of LINZESS in the U. S. is partially determined based on amounts provided by AbbVie and involves the use of estimates and judgments, which could be modified in the future. **For example, during 2024, we recorded adjustments to our collaborative arrangement revenues to reflect changes in estimates of certain LINZESS gross- to- net reserves, as reported by AbbVie.** We are highly dependent on our linaclotide partners for timely and accurate information regarding any revenues realized from sales of linaclotide in their respective territories, and in the case of AbbVie for the U. S., the costs incurred in developing and commercializing it in order to accurately report our results of operations. Our results of operations are also dependent on the timeliness and accuracy of information from any other licensing, collaboration or other partners we may have, as well as our and our partners' use of estimates and judgments. If we do not receive timely and accurate information or if estimated activity levels associated with the relevant collaboration or partnership at a given point in time are incorrect, whether the result of a material weakness or not, we could be required to record adjustments in future periods. Such adjustments could have an adverse effect on our financial results, which could lead to a decline in our Class A Common Stock price. ~~If~~ **59If in the future** we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could lead to a decline in our stock price. Failure to comply with reporting requirements could also subject us to sanctions and / or investigations by the SEC, The Nasdaq Stock Market or other regulatory authorities. We expect that the price of our Class A Common Stock will fluctuate substantially. The market price of our Class A Common Stock may be highly volatile due to many factors, including: ● the commercial performance of our products in the countries in which they are approved, as well as the costs associated with such activities; ● any third- party coverage and reimbursement policies for our products; ● market conditions in the pharmaceutical and biotechnology sectors; ● developments, litigation or public concern about the safety of our products or our potential products; ● announcements of the introduction of new products by us or our competitors; ● announcements concerning product development, including clinical trial results or timelines, or intellectual property rights of us or others; ● actual and anticipated fluctuations in our quarterly and annual operating results; ● deviations in our operating results from any guidance we may provide or the estimates of securities analysts; ● sales of additional shares of our Class A Common Stock or sales of securities convertible into Class A Common Stock or the perception that these sales might occur; ● any conversions of our Convertible Senior Notes into Class A Common Stock or activities undertaken by the counterparties to the Capped Calls; ● additions or departures of key personnel; ~~59~~ **● developments concerning current or future collaboration, partnership, licensing or other strategic arrangements; ● discussion of us or our stock price in the financial or scientific press or in online investor communities; ● general economic, industry, and market conditions; and ● the impact of public health epidemics, including containment or mitigation measures, or natural disasters. Our business could be negatively affected as a result of a proxy contest or certain other stockholder actions. Responding to certain stockholder actions can be costly, disruptive and time- consuming, and could also impact our ability to attract, retain and motivate our employees. For example, a proxy contest for our annual meeting of stockholders relating to stockholder proposals or director nominees would require significant time and could divert the attention of our management, other employees and our board of directors. In addition, a proxy contest would require us to incur significant costs, including legal fees and proxy solicitation expenses. The realization of any of the risks described in these " Risk Factors " could have a dramatic and material adverse impact on the market price of our Class A Common Stock. In addition, class action litigation has often been instituted 60**