Risk Factors Comparison 2024-03-07 to 2023-02-28 Form: 10-K

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You should carefully consider the following risk factors, together with the other information contained in this annual report on Form 10- K, including our financial statements and the related notes and " Management' s Discussion and Analysis of Financial Condition and Results of Operations, " before making a decision to purchase or sell shares of our common stock. We cannot assure you that any of the events discussed in the risk factors below will not occur. These risks could have a material and adverse impact on our business, results of operations, financial condition and growth prospects. If that were to happen, the trading price of our common stock could decline. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations or financial condition. In this section, we first provide a summary of the more significant risks and uncertainties we face and then provide a full set of risk factors and discuss them in greater detail. SUMMARY RISKS FACTORS ● We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future; ● We may never ~~generate any revenue or~~ become profitable or, if we achieve profitability, we may not be able to sustain it; ● We ~~will~~ **may** require ~~substantial~~ additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our **commercialization activities,** product development programs, ~~commercialization efforts~~ or other operations ~~; ● We may not be successful in demonstrating to the FDA that we are able to maintain the level of the nitrosamine impurity N- nitroso- vonoprazan below the acceptable daily intake established by the FDA~~ ; ● Our Revenue Interest Financing Agreement could limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations; ● We currently depend entirely on the success of **VOQUEZNA,** ~~products containing vonoprazan including~~ VOQUEZNA TRIPLE PAK and VOQEUZNA DUAL PAK, which **were** ~~have not been~~ launched **in** ~~but are our only approved products, and, if approved, VOQUEZNA for~~ the ~~treatment~~ **fourth quarter** of **2023** ~~erosive GERD~~ . If we are unable to ~~obtain approval of vonoprazan for treatment of erosive GERD, and launch and~~ successfully commercialize these products, or ~~experience significant delays in doing so, or~~ are unable to ~~advance the clinical development of, and~~ obtain regulatory approval for ~~,~~ vonoprazan to treat ~~non~~ **heartburn associated with symptomatic Non** - ~~erosive~~ **Erosive** GERD, our business will be materially harmed; ● ~~Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of prior clinical trials and other investigator- initiated clinical trials of vonoprazan are not necessarily predictive of our future results.~~ Vonoprazan may not have favorable results in our **future** clinical trials, or receive additional regulatory approvals on a timely basis, if at all; ● ~~Vonoprazan~~ **VOQUEZNA, VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK,** and any future product candidates are subject to extensive regulation and compliance obligations, which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize **additional** ~~vonoprazan and any future~~ product candidates; ● We may not be successful in our efforts to expand our pipeline by identifying additional indications and formulations for which to investigate vonoprazan in the future. We may expend our limited resources to pursue a particular indication or formulation for vonoprazan and fail to capitalize on product candidates, indications or formulations that may be more profitable or for which there is a greater likelihood of success; ● We currently have ~~a~~ limited ~~commercial organization, no field sales representatives, and have no~~ experience as a company in commercializing products **. We** ~~, and we~~ may **lack the necessary expertise, personnel and resources to successfully commercialize any of our product candidates that** have **received** ~~to invest significant additional resources to develop these capabilities. If we are unable to establish the necessary commercial capabilities or enter into agreements with third parties to market and sell our~~ **or** ~~products, we~~ may **receive regulatory approval, including VOQUEZNA** ~~not be able to generate product revenue~~ ; ● We rely on third parties to conduct our preclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain additional regulatory approvals for or commercialize vonoprazan and our business could be harmed; ● We currently engage third- party manufacturers for all of our clinical and commercial supplies. The loss of any of these suppliers, or any future single source suppliers, could harm our business; ● We rely on the Takeda License to provide us rights to develop and commercialize vonoprazan in the United States, Europe, and Canada. If the license agreement is terminated, we would lose our rights to develop and commercialize vonoprazan; ● If the scope of any patent protection **or non- patent regulatory exclusivity** we obtain is not sufficiently broad, or if we lose **or fail to obtain** any of our patent protection **or non- patent regulatory exclusivity** , our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected; ● The successful commercialization of VOQUEZNA **, VOQUEZNA** TRIPLE PAK and Voquezna Dual Pak ~~(or, if approved, VOQUEZNA for the treatment of erosive GERD or any future product candidates)~~ will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products successfully and decrease our ability to generate revenue; ● If ~~following commercialization of~~ **we fail to comply with reporting and payment obligations for VOQUEZNA,** VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK ~~(and if approved, VOQUEZNA for the treatment of erosive GERD or any future product candidates) we fail to comply with reporting and payment obligations~~ under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects; ● We are subject to various foreign, federal, and state healthcare

and privacy laws and regulations, and our failure to comply with these laws and regulations could harm our results of operations and financial condition; ● ~~Our business is subject to risks arising from epidemic diseases, such as the COVID- 19 pandemic; ●~~ We are highly dependent on the services of our key executives and personnel, and if we are not able to retain these members of our management or recruit additional management, clinical and commercial personnel, our business will suffer; and ● The trading price of our securities is likely to be volatile, and purchasers of our securities could incur substantial losses. Risks Related to Our Limited Operating History, Financial Position and Capital Requirements We have a limited operating history **as a commercial company** , **which may make it difficult** ~~have incurred significant operating losses since our inception and expect~~ to **evaluate** ~~incur significant losses for~~ the ~~foreseeable~~ **success of our business to date and to assess our** future **viability** . ~~We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it~~ . Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We **received** ~~are a late clinical- stage biopharmaceutical company with a limited operating history upon which you can evaluate~~ our **first regulatory approvals** ~~business and prospects. We commenced operations~~ in ~~2018~~ **2022** , and **prior** to ~~date~~ **our commercialization of VOQUEZNA** , **VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK in the fourth quarter of 2023,** we ~~have focused primarily~~ **had not manufactured products** on ~~organizing and staffing our company, business planning, raising capital, in- licensing our initial product candidate, vonoprazan, meeting with regulatory authorities, conducting our Phase 3 clinical trials of vonoprazan, preparing applications for regulatory approval for vonoprazan and preparing for a potential commercial launch. As a company, we have not yet demonstrated an ability to initial commercial launch a product launch, manufacture~~ a commercial scale ~~product ,~~ or ~~arrange~~ **arranged** for a third party to do so on our behalf ~~,~~ or ~~conduct~~ **conducted** sales and marketing activities necessary for successful ~~product~~ commercialization. Consequently, ~~any~~ predictions ~~made~~ about our future success or viability may not be as accurate as they could be if we had a **longer** history of successfully **developing** ~~obtaining regulatory approvals for~~ and commercializing ~~biopharmaceutical~~ products **. We expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. We have transitioned from a company with solely a clinical development focus to a company also undertaking commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays, and may not be successful in such a transition** . We have incurred significant operating losses since ~~our~~ inception ~~. If vonoprazan is not successfully developed, approved~~ and ~~commercially launched in the United States, Europe and /~~ **anticipate that we will continue to incur substantial operating losses** ~~or~~ **for** ~~Canada, we~~ **the foreseeable future and** may never ~~generate any revenue~~ **achieve or maintain profitability** . ~~We~~ **Since our inception, we** have incurred ~~cumulative~~ **significant operating losses. Our** net ~~losses~~ -- **loss** ~~since our inception and, as~~ **was** ~~of~~ **$ 201. 6 million and $ 197. 7 million for the years ended** December 31, **2023 and** 2022 **, respectively. As of December 31, 2023** , we had an accumulated deficit of $ ~~727~~ **928** . ~~1~~ **7** million. ~~Substantially all of our~~ **We expect to continue to incur expenses and operating** losses ~~have resulted from~~ **for the foreseeable future. It could be several years, if ever, before VOQUEZNA, VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK or other product candidates, if approved, generate significant revenues to offset these** expenses ~~incurred in connection with in- licensing~~ and ~~developing vonoprazan, commercial activities in preparation for a potential product launch, and from general and administrative costs associated with our operations~~ - **operating losses** . ~~Vonoprazan~~ **As a result, we are uncertain when or if we** will **achieve profitability** ~~require substantial additional time~~ and ~~resources before~~ **, if so, whether** we will be able to ~~begin generating revenue~~ **sustain it. The net losses we incur may fluctuate significantly** from **quarter** ~~product sales, and any future product candidates will require substantial additional development time and resources before we will be able~~ to **quarter** ~~apply for or receive regulatory approvals~~ and **year to year** ~~begin generating revenue from product sales~~ . We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as we **: • initiate,** continue **,** ~~our~~ - **or** ~~development~~ **complete planned or ongoing clinical trials** of **vonoprazan** , ~~seek~~ **including related support activities; • make required milestone and royalty payments under license agreements by which we acquired rights to vonoprazan; • make required royalty payments under the Revenue Interest Financing Agreement, or RIFA, entered into in May 2022, as amended; • make required payments under the Loan and Security Agreement with Hercules Capital, Inc., entered into in September 2021, as amended; • initiate clinical trials for VOQUEZNA, vonoprazan or any future product candidates; • build a portfolio of product candidates through the acquisition or in- license of** additional **product candidates or technologies; • pursue** regulatory approvals for **new indications for** ~~, and potentially commercialize~~ vonoprazan and **future** ~~seek to identify, assess, acquire, in- license, or develop additional~~ product candidates **that successfully complete clinical trials; and • incur additional legal, accounting and other expenses in connection with operating as a public company** . To become and remain profitable, we must **successfully** ~~succeed in developing and eventually commercializing~~ **commercialize one or more** ~~products~~ - **product** ~~that generate~~ **candidates with** significant ~~revenue~~ **market potential** . This will require us to be successful in **manufacturing** ~~a range of challenging activities~~ , **marketing** ~~including completing clinical trials~~ and ~~preclinical studies of vonoprazan~~ **selling our currently approved products, particularly VOQUEZNA,** and any future product candidates ~~,~~ **for which we may** ~~obtaining~~ --- **obtain** ~~regulatory~~ **marketing** approval ~~for these product candidates~~ and ~~manufacturing,~~ **satisfying any post-** marketing **requirements** ~~and selling any products~~ . We are ~~still~~ **only** in the early stages of **many** ~~a number~~ of these activities ~~. We may never succeed in these activities~~ and, **in some cases** ~~even if we do~~ , ~~may never generate revenues that are significant enough to achieve profitability. In addition, we~~ have not yet **commenced certain** ~~demonstrated an ability to successfully overcome many~~ of ~~the~~ **these activities** ~~risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. For example, we have not been able to demonstrate to FDA that we can produce commercial product in which the level of an identified nitrosamine impurity remains below its acceptable daily intake limit throughout the shelf- life of the product. Because of this and the other numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to initiate product~~

~~commercialization and achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis~~ . Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, continue our product development efforts, diversify our product candidate pipeline or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment. We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development programs, commercialization efforts or other operations. The development and commercialization of biopharmaceutical product candidates is capital- intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we ~~prepare~~ **continue** to ~~commercialize vonoprazan~~ **achieve product sales** for **VOQUEZNA** ~~H. pylori~~ and ~~, if~~ **our other** approved **products** ~~, erosive GERD~~ and progress our ~~non~~ **Non** - ~~erosive~~ **Erosive** GERD development program. In addition, **we** ~~if one or more products containing vonoprazan~~ are ~~commercialized, we will be~~ required to make milestone and royalty payments to Takeda, from whom we have in- licensed the rights to develop and commercialize vonoprazan in the United States, Europe, and Canada pursuant to the Takeda License. Furthermore, if and to the extent we seek to acquire or in- license additional product candidates in the future, we may be required to make significant upfront payments, milestone payments, and / or royalty payments. If we obtain additional regulatory approvals for vonoprazan or regulatory approval for any future product candidate, we also expect to incur significant **additional** commercialization expenses related to product manufacturing, marketing, sales and distribution. Because the outcome of any clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of vonoprazan ~~or~~ **for** ~~any future~~ **additional populations, such as patients with Non- Erosive GERD or EoE, or other** product ~~candidate~~ **candidates** . Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts. We believe that our existing cash and cash equivalents together with the drawdown of the remaining $ ~~100~~ **160** million under our loan and security agreement, or the Loan Agreement, with Hercules Capital, or Hercules, are sufficient to fund operations for at least the next ~~twelve~~ **12** months and **, along with anticipated product** ~~receipt of the $ 175 million milestone under our revenue~~ **revenues** ~~interest financing agreement following approval of vonoprazan for the treatment of erosive GERD~~ , will ~~enable us~~ **be sufficient** to fund our operations through **the end of** ~~2024~~ **2026** . In particular, we expect that these funds will allow us to **finance the ongoing** launch **of VOQUEZNA, including for the treatment of heartburn associated with symptomatic Non- Erosive GERD, if approved, VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, and complete the clinical development of** vonoprazan **as an as needed treatment** for **Non-** ~~H. pylori and erosive~~ **Erosive** GERD ~~subject to approval of our resubmissions~~ . We have based these estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other capital sources, including potentially collaborations, licenses and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day- to- day activities, which may adversely affect our ability to develop vonoprazan or any future product candidates. Our future capital requirements will depend on many factors, including: • the costs ~~and timing~~ of ~~establishing or securing additional~~ sales and marketing ~~capabilities~~ **activities** in ~~advance~~ **support** of ~~initiating~~ **the** commercial launch of **VOQUEZNA,** VOQUEZNA TRIPLE PAK, **and** VOQUEZNA DUAL PAK, ~~and, if approved, VOQUEZNA for the treatment of erosive GERD~~ or any future product candidate; • the initiation, type, number, scope, results, costs and timing of ~~,~~ our clinical trials of vonoprazan, and preclinical studies or clinical trials of other potential product candidates we may choose to pursue in the future, including feedback received from regulatory authorities; • the costs and timing of manufacturing for vonoprazan or any future product candidates, including commercial scale manufacturing if any product candidate is approved; • the costs, timing and outcome of regulatory review of our ~~resubmissions following receipt of complete response letters for our post approval supplement for VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK and our~~ NDA for ~~VOQUEZNA~~ **vonoprazan** for the treatment of **heartburn associated with symptomatic Non-** ~~erosive~~ **Erosive** GERD, and the costs, timing and outcome of regulatory review of any future product candidates; • the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights; • our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting; • the costs associated with hiring additional personnel and consultants as our business grows particularly commercial personnel; • the timing and amount of the milestone or other payments we must make to Takeda and any future licensors; • our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third- party payers and adequate market share and revenue for any approved products; • patients' willingness to pay out- of- pocket for any approved products in the absence of coverage and / or adequate reimbursement from third- party payers; • the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and • the costs associated with any products or technologies that we may in- license or acquire. Conducting clinical trials and preclinical studies is a time consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval ~~and achieve~~ **of future** product ~~sales~~ **candidates** . In addition **, VOQUEZNA** , VOQUEZNA TRIPLE PAK ~~,~~ **and** VOQUEZNA DUAL PAK, ~~and, if approved, VOQUEZNA for the treatment of erosive GERD~~ or any future product candidate, may not achieve commercial success. Our commercial revenues **will** , ~~if any~~ **for the foreseeable future** , ~~would initially~~ be derived **exclusively** from sales of products containing vonoprazan in the United States. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may

seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through equity offerings, our Loan Agreement with Hercules, our ~~revenue~~ **Revenue** ~~interest~~ **Interest** ~~financing~~ **Financing** ~~agreement~~ **Agreement** , other debt financings, or other capital sources, including potential collaborations, licenses and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Our Loan Agreement and our Revenue Interest Financing Agreement include, and any future debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures or declaring dividends. For example, our Loan Agreement with Hercules contains minimum cash financial covenants. If ~~on or prior to March 31, 2024, we have not received FDA approval of our NDA for vonoprazan for the treatment of erosive GERD, raised additional funding, or significantly reduced our operating expenses, we may be in violation of these covenants. If we default on such indebtedness, with Hercules or a future lender, we could lose such assets and intellectual property. If~~ we raise funds through future collaborations, licenses and other similar arrangements, we may have to relinquish valuable rights to our future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and / or that may reduce the value of our common stock. Risks Related to **Commercialization** ~~the Development and Regulatory Approval~~ of **VOQUEZNA, VOQUEZNA TRIPLE PAK, VOQUEZNA DUAL PAK and Any Future** Product Candidates We ~~Commercialization of Vonoprazan~~ **may lack the necessary expertise,personnel** and ~~Any~~ **resources to successfully commercialize VOQUEZNA,VOQUEZNA TRIPLE PAK,VOQUEZNA DUAL PAK,and any** ~~Future~~ **future** ~~Product~~ **product** ~~Candidates~~ **candidates that may** ~~Even if we~~ receive regulatory approval **,on our own or together with collaborators.Until 2023,our operations were primarily limited to organizing and staffing our company,business planning,raising capital,acquiring the rights to,and undertaking clinical trials of,vonoprazan.Although we started developing marketing and distribution capabilities in 2021 in advance of the planned commercialization of VOQUEZNA,VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK,due to approval and launch delays,we did not hire our field force until late 2023.The success of the commercialization of our approved products in the United States and any of our future product candidates that may be approved by the FDA will depend on such marketing,sales and distribution capabilities.Factors that may affect our ability to commercialize our approved products and future product candidates successfully on our own include obtaining access to or persuading adequate numbers of physicians to prescribe our products.Building and maintaining a sales and marketing organization has required,and will continue to require,significant investment,and is time- consuming.Our sales and marketing organization may prove not to be effective.If we are unable to maintain effective sales and marketing capabilities** for ~~any~~ **our approved** ~~product~~ **products** ~~candidate~~ **including VOQUEZNA** , **or to find suitable partners for such commercialization,** we ~~will be~~ **may have difficulties generating revenue from them.Following receipt of regulatory approval,we are** subject to ongoing regulatory obligations and continued regulatory review,which may result in significant additional expense.With respect to **VOQUEZNA** ~~our approved products~~ ,VOQUEZNA TRIPLE PAK ~~and~~ **,** VOQUEZNA DUAL PAK, ~~and,if approved,VOQUEZNA~~ and any future product candidates,the FDA,EMA or other comparable regulatory authority may impose significant restrictions on a product' s indicated uses or marketing or impose ongoing requirements for potentially costly and time- consuming post- approval studies,post- market surveillance or clinical trials to monitor the safety and efficacy of the product.The FDA and comparable regulatory authorities may also require a REMS or similar risk management measures as a condition of approval of any ~~additional products containing vonoprazan or~~ future product candidates,which could include requirements for a medication guide,physician communication plans or additional elements to ensure safe use,such as restricted distribution methods,patient registries and other risk minimization tools.In addition,for our approved products or future products that obtain approval,particularly following commercial launch of any such products,the manufacturing processes,labeling,packaging,distribution,adverse event reporting,storage,advertising,promotion,import,export and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements.These requirements include submissions of safety and other post- marketing information and reports,registration,as well as continued compliance with cGMPs and similar requirements and GCP requirements for any clinical trials that we conduct post- approval.Later discovery of previously unknown problems with our products,including adverse events of unanticipated severity or frequency,or with our third- party manufacturers or manufacturing processes,or failure to comply with regulatory requirements,may result in,among other things:• restrictions on the marketing or manufacturing of our products,withdrawal of the product from the market or voluntary or mandatory product recalls;• restrictions on product distribution or use,or requirements to conduct post- marketing studies or clinical trials **;** • fines,restitutions,disgorgement of profits or revenues,warning letters,untitled letters or holds on clinical trials;• refusal by the FDA or comparable foreign regulatory authority to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;• product seizure or detention,or refusal to permit the import or export of our products;and • injunctions or the imposition of civil or criminal penalties.The occurrence of any event or penalty described above may inhibit our ability to commercialize **our current** products ~~containing vonoprazan~~ and any future product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.The FDA' s and other regulatory authorities' policies may change,and additional government regulations may be enacted that could prevent,limit or delay regulatory approval of **any future product candidates or** additional **indications for our current** ~~products containing vonoprazan and any future product~~ **products** ~~candidates~~ .If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies,or if we are not able to maintain regulatory compliance,we may lose any marketing approval that we may have obtained,may be subject to

enforcement action,and we may not achieve or sustain profitability .For instance,the EU has adopted the Clinical Trials Regulation,or CTR,in April 2014,which became applicable on 31 January 2022.The CTR is directly applicable in all EU member states,repealing the current Clinical Trials Directive.The CTR harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System,which will notably contain a centralized EU portal and database.It is currently unclear to what extent the United Kingdom,or UK,will seek to align its regulations with the EU.The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law,through secondary legislation).A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and / or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK .Additionally,the EU pharmaceutical legislation is currently undergoing a complete review process,in the context of the Pharmaceutical Strategy for Europe initiative,launched by the European Commission in November 2020.A proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration currently and VOQUEZNA DUAL PAK,and,if approved,VOQUEZNA and any future product candidates,the FDA,EMA or other comparable regulatory authority may impose significant restrictions on a product' s indicated uses or marketing or impose ongoing requirements for potentially costly and time- consuming post- approval studies,post- market surveillance or clinical trials to monitor the safety and efficacy of the product.The FDA and comparable regulatory authorities may also require a REMS or similar risk management measures as a condition of approval of any additional products containing vonoprazan or future product candidates,which could include requirements for a medication guide,physician communication plans or additional elements to ensure safe use,such as restricted distribution methods,patient registries and other risk minimization tools.In addition,for our approved products or future products that obtain approval,particularly following commercial launch of any such products,the manufacturing processes,labeling,packaging,distribution,adverse event reporting,storage,advertising,promotion,import,export and recordkeeping for our products will be subject to extensive and ongoing regulatory requirements.These requirements include submissions of safety and other post- marketing information and reports,registration,as well as continued compliance with cGMPs and similar requirements and GCP requirements for any clinical trials that we conduct post- approval.Later discovery of previously unknown problems with our products,including adverse events of unanticipated severity or frequency,or with our third- party manufacturers or manufacturing processes,or failure to comply with regulatory requirements,may result in,among other things:• restrictions on the marketing or manufacturing of our products,withdrawal of the product from the market or voluntary or mandatory product recalls;• restrictions on product distribution or use,or requirements to conduct post- marketing studies or clinical trials • fines,restitutions,disgorgement of profits or revenues,warning letters,untitled letters or holds on clinical trials;• refusal by the FDA or comparable foreign regulatory authority to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;• product seizure or detention,or refusal to permit the import or export of our products;and • injunctions or the imposition of civil or criminal penalties.The occurrence of any event or penalty described above may inhibit our ability to commercialize products containing vonoprazan and any future product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.The FDA' s and other regulatory authorities' policies may change,and additional government regulations may be enacted that could prevent,limit or delay regulatory approval of additional products containing vonoprazan and any future product candidates.If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies,or if we are not able to maintain regulatory compliance,we may lose any marketing approval that we may have obtained,may be subject to enforcement action,and we may not achieve or sustain profitability.For instance,the EU has adopted the Clinical Trials Regulation,or CTR,in April 2014,which became applicable on 31 January 2022.The CTR is directly applicable in all EU member states,repealing the current Clinical Trials Directive.The CTR harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System,which will notably contain a centralized EU portal and database.It is currently unclear to what extent the United Kingdom,or UK,will seek to align its regulations with the EU.The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law,through secondary legislation).A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and / or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK.Additionally,the EU pharmaceutical legislation is currently undergoing a complete review process,in the context of the Pharmaceutical Strategy for Europe initiative,launched by the European Commission in November 2020. A **The European Commission' s** proposal for revision of several legislative instruments related to medicinal products (potentially **reducing the duration of regulatory data protection,** revising the duration of regulatory exclusivity, eligibility for expedited pathways,etc.) **was published on April 26,** is expected to be adopted by the European Commission by the end of 2022 **2023** .The proposed revisions **remain to be** ,once they are agreed and adopted by the European Parliament and European Council (**and the proposals may therefore be substantially revised before adoption,which is** not expected **anticipated** before **early** the end of 2024 **2026**) **.The revisions** may **however** have a significant impact on the biopharmaceutical --- **pharmaceutical** industry **and our business** in the long term.The commercial success of vonoprazan **our current products** or any future product candidates will depend upon the degree of market acceptance of such product candidates by physicians,patients,healthcare payers and others in the medical community. Vonoprazan **VOQUEZNA,VOQUEZNA TRIPLE PAK,VOQUEZNA DUAL PAK,** and any future product candidates **,if approved,** may not be commercially successful.The commercial success of vonoprazan **our current products** or any future product candidates ,if approved, will depend significantly on the broad adoption and use of such product by physicians and patients for approved indications.The degree of market acceptance of vonoprazan **our current products** or any future products,if approved,will depend on a number of factors,including:• demonstration of clinical efficacy and safety compared to other more- established products;• the indications

for which ~~vonoprazan~~ **our current** or any future product candidates are approved;• the limitation of our targeted patient population and other limitations or warnings contained in any FDA- approved labeling or comparable approved labeling;• acceptance of a new drug for the relevant indication by healthcare providers and their patients;• the pricing and cost-effectiveness of our products,as well as the cost of treatment with our products in relation to alternative treatments and therapies;• our ability to obtain and maintain sufficient third- party coverage and adequate reimbursement from government healthcare programs,including Medicare and Medicaid,private health insurers and other third- party payers;• the willingness of patients to pay all,or a portion of,out- of- pocket costs associated with our products in the absence of sufficient third- party coverage or adequate reimbursement;• any restrictions on the use of our products,and the prevalence and severity of any adverse effects;• potential product liability claims;• the timing of market introduction of our products as well as competitive drugs;• the effectiveness of our or any of our potential future collaborators' sales and marketing strategies;and • unfavorable publicity relating to the product.If ~~either of~~ our current ~~approved products,and if approved,any additional product~~ **products** ~~containing vonoprazan~~ or any future product ~~candidate~~ **candidates ,if approved** ,does not achieve an adequate level of acceptance by physicians,hospitals,healthcare payers or patients,we may not generate sufficient revenue from that product and may not become or remain profitable.Our efforts to educate the medical community and third- party payers regarding the benefits of our products may require significant resources and may never be successful.Takeda has the right to develop and commercialize vonoprazan outside of the United States,Europe,and Canada and has received marketing approval for vonoprazan in ~~certain~~ **numerous** countries in Asia and Latin America as well as in Russia.We have little or no control over Takeda' s commercialization activities with respect to vonoprazan outside of our licensed territories even though those activities could impact our ability to successfully commercialize vonoprazan.For example,Takeda can make statements or use promotional materials with respect to vonoprazan outside of our licensed territories that are inconsistent with our positioning of the product in the United States,Europe,and Canada,and could sell vonoprazan in foreign countries at prices that are dramatically lower than the prices we would charge in our licensed territories.These activities and decisions,while occurring outside of our licensed territories,could harm our commercialization strategy.In addition,product recalls or safety issues with vonoprazan outside our licensed territories could result in serious damage to the brand and impair our ability to successfully market **our products containing** vonoprazan in our licensed territories.The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses.If we are found or alleged to have improperly promoted off- label uses,we may become subject to significant liability.The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products such as our currently approved products,and any additional ~~products~~ **product candidates** containing vonoprazan and any future product candidates,if approved.In particular,a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product' s approved labeling.For example,the FDA has approved ~~both~~ VOQUEZNA ~~TRIPLE PAK~~ **for the treatment for healing** and ~~VOQUEZNA DUAL PAK~~ **maintenance of healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults and,in combination with either amoxicillin,** ~~for~~ **or** ~~the~~ **amoxicillin and clarithromycin,** treatment of H.pylori infection in adults,and we are not currently permitted to promote ~~these~~ **this** ~~products~~ **product** for any other uses ~~,~~ unless and until such uses are approved by the FDA.For any product for which we have obtained a marketing approval,however,physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label.If we are found to have promoted such off- label uses,we may become subject to significant liability.The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off- label promotion.The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.If we cannot successfully manage the promotion of **our current** products ~~containing vonoprazan~~ or any ~~future~~ product candidates ~~,if approved~~ ,we could become subject to significant liability,which would materially adversely affect our business and financial condition.The successful commercialization of ~~VOQUEZNA TRIPLE PAK,VOQUEZNA DUAL PAK,or~~ **our current products** ~~if approved,VOQUEZNA~~ or any future product ~~candidates~~ **candidate** ,will depend in part on the extent to which governmental authorities and health insurers establish coverage,adequate reimbursement levels and favorable pricing policies.Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products and decrease our ability to generate revenue.The availability of coverage and the adequacy of reimbursement by governmental healthcare programs,such as Medicare and Medicaid,private health insurers and other third-party payers are essential for most patients to be able to afford prescription medications such as VOQUEZNA **,VOQUEZNA** TRIPLE PAK,VOQUEZNA DUAL PAK ~~,or,if approved,VOQUEZNA~~ or any future product candidates **that may be approved** .Our ability to achieve coverage and acceptable levels of reimbursement for our products by third- party payers will have an effect on our ability to successfully commercialize those products.Even if we obtain coverage for a given product by a third-party payer,the resulting reimbursement payment rates may not be adequate or may require co- payments that patients find unacceptably high.We cannot be sure that coverage and reimbursement in the United States,the European Union **,** or elsewhere will be available for any product that we may develop,and any reimbursement that may become available may be decreased or eliminated in the future.Third- party payers increasingly are challenging prices charged for pharmaceutical products and services,and many third- party payers may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available.It is possible that a third- party payer may consider our products as substitutable and only offer to reimburse patients for the less expensive product.Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our products,pricing of existing drugs may limit the amount we will be able to charge for our products.These payers may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development.If reimbursement is not available or is available only at limited levels,we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on products that we

may develop.There is significant uncertainty related to third- party payer coverage and reimbursement of newly approved products.In the United States,third- party payers,including private and governmental payers,such as the Medicare and Medicaid programs,play an important role in determining the extent to which new drugs will be covered.Some third- party payers may require pre- approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies.It is difficult to predict at this time what third- party payers will decide with respect to the coverage and reimbursement for our products.Obtaining and maintaining reimbursement status is time consuming,costly and uncertain.The Medicare and Medicaid programs increasingly are used as models for how private payers and other governmental payers develop their coverage and reimbursement policies for drugs.However,no uniform policy for coverage and reimbursement for products exists among third- party payers in the United States.Therefore,coverage and reimbursement for products can differ significantly from payer to payer.As a result,the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payer separately,with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.Furthermore,rules and regulations regarding reimbursement change frequently,in some cases at short notice,and we believe that changes in these rules and regulations are likely.Outside the United States,international operations are generally subject to extensive governmental price controls and other market regulations,and we believe the increasing emphasis on cost- containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products.In many countries,the prices of medical products are subject to varying price control mechanisms as part of national health systems.Other countries allow companies to fix their own prices for medical products but monitor and control company profits.Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products.Accordingly,in markets outside the United States,the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.Moreover,increasing efforts by governmental and third- party payers in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and,as a result,they may not cover or provide adequate payment for our products.We expect to experience pricing pressures in connection with the sale of any of our products due to the trend toward managed healthcare,the increasing influence of health maintenance organizations and additional legislative changes.The downward pressure on healthcare costs in general,particularly prescription drugs and surgical procedures and other treatments,has become very intense.As a result,increasingly high barriers are being erected to the entry of new products.If ~~following commercialization of products containing vonoprazan (or any future product candidates,if approved)~~ we fail to comply with reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs,we could be subject to additional reimbursement requirements,penalties,sanctions and fines,which could have a material adverse effect on our business,financial condition,results of operations and growth prospects. **We** ~~If we successfully commercialize products containing vonoprazan and,if approved,any future product candidates,we will likely~~ participate in **various** governmental programs,such as **the** Medicaid **Drug Rebate Program** ,that impose extensive drug price reporting and payment obligations on pharmaceutical manufacturers.Medicaid is a joint federal and state program that is administered by the states for low- income and disabled beneficiaries.Medicare is a federal program that is administered by the federal government covering individuals age 65 and over as well as those with certain disabilities.Under the Medicaid Drug Rebate Program,or MDRP,as a condition of having federal funds being made available to the states for covered outpatient drugs under Medicaid **and,if applicable,Medicare Part B** ,pharmaceutical manufacturers must enter into an agreement with the Secretary of Health and Human Services to pay a rebate to state Medicaid programs for each unit of covered outpatient drug dispensed to a Medicaid beneficiary and paid for by the state Medicaid program.Medicaid drug rebates are based on pricing data that pharmaceutical manufacturers report on a monthly and quarterly basis to the U.S.Centers for Medicare & Medicaid Services,or CMS,which is the federal agency that administers the MDRP and Medicare programs.For the MDRP,these data include the average manufacturer price,or AMP,for each drug and,in the case of innovator products,the Best Price,or BP,which represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure,calculated to include all applicable sales and associated rebates,discounts and other price concessions.If a manufacturer becomes aware that its MDRP government price reporting submission for a prior quarter was incorrect or has changed as a result of recalculation of the pricing data,the manufacturer must resubmit the corrected data for up to three years after those data originally were due.If a manufacturer fails to provide information timely or is found to have knowingly submitted false information to the government,the manufacturer may be subject to civil monetary penalties and other sanctions,including termination from the MDRP.Federal law requires that any company that participates in the MDRP also participate in the Public Health Service' s 340B drug pricing program,or the 340B program,in order for federal funds to be available for the manufacturer' s drugs under Medicaid **and,if applicable,Medicare Part B** .The 340B program is administered by the Health Resources and Services Administration,or HRSA,and requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B " ceiling price " for the manufacturer' s covered drugs used in an outpatient setting.These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service,as well as hospitals that serve a disproportionate share of low - income patients.The 340B ceiling price is calculated using a statutory formula,which is based on the **AMP** ~~average manufacturer price~~ and rebate amount for the covered outpatient drug as calculated under the MDRP.In general,products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement.Manufacturers must report 340B ceiling prices to HRSA on a quarterly basis,and HRSA publishes them to 340B covered entities.HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B - eligible drugs.HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges,and through which

manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs.In addition,legislation may be introduced that,if passed,would further expand the 340B program,such as adding further covered entities or requiring participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.In order to be eligible to have drug products paid for with federal funds under Medicaid and **,if applicable,Medicare Part B,and** purchased by certain federal agencies and grantees,a manufacturer must also participate in the U.S.Department of Veterans Affairs,or VA,Federal Supply Schedule,or FSS,pricing program.Under the VA / FSS program,a manufacturer must report the Non- Federal Average Manufacturer Price,or Non- FAMP,for its covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price,which is calculated based on Non- FAMP using a statutory formula.These federal agencies are the VA,the U.S.Department of Defense,the U.S.Coast Guard,and the U.S.Public Health Service (including the Indian Health Service).The manufacturer must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program.If a manufacturer participating in the FSS program fails to provide timely information or is found to have knowingly submitted false information,the manufacturer may be subject to civil monetary penalties.Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs,including the cost of prescription drugs and combination products.A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies.Requirements under such laws include advance notice of planned price increases,reporting price increase amounts and factors considered by manufacturers in taking such increases,wholesale acquisition cost disclosure to prescribers,purchasers,and state agencies,and new product notice and reporting.Such legislation could limit the price or payment for certain drugs,and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements,including the untimely,inaccurate,or incomplete reporting of drug pricing information.If we are found to have violated state law requirements,we may become subject to penalties or other enforcement mechanisms,which could have a material adverse effect on our business.Pricing and rebate calculations vary across products and programs,are complex,and are often subject to interpretation by pharmaceutical manufacturers,governmental or regulatory agencies,and the courts,which can change and evolve over time.Such pricing calculations and reporting,along with any necessary restatements and recalculations,could increase costs for complying with the laws and regulations governing the MDRP and other governmental programs,and under the MDRP could result in an overage or underage in Medicaid rebate liability for past quarters.Price recalculations under the MDRP also may affect the ceiling price at which manufacturers are required to offer products under the 340B program.Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government,if we ~~are found to have made a misrepresentation in the reporting of ASP,if we~~ fail to submit the required price data on a timely basis,or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price.CMS could also terminate our Medicaid drug rebate agreement,in which case federal payments may not be available under Medicaid for our covered outpatient drugs.We cannot assure you that our submissions will not be found to be incomplete or incorrect.We face significant competition,and if our competitors develop technologies or product candidates more rapidly than we do or their technologies are more effective,our ability to develop and successfully commercialize products may be adversely affected.The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies,intense competition and a strong emphasis on proprietary and novel products and product candidates.Our competitors have developed,are developing or may develop products,product candidates and processes competitive with ~~vonoprazan~~ **VOQUEZNA** .Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.We believe that a significant number of products are currently under development,and may become commercially available in the future,for the treatment of GI diseases for which we may attempt to develop vonoprazan or any future product candidates.Our competitors include larger and better funded pharmaceutical,biopharmaceutical,biotechnological and therapeutics companies.Moreover,we may also compete with universities and other research institutions who may be active in the indications we are targeting and could be in direct competition with us.We also compete with these organizations to recruit management,scientists and clinical development personnel,which could negatively affect our level of expertise and our ability to execute our business plan.We will also face competition in establishing clinical trial sites,enrolling patients for clinical trials and in identifying and in- licensing new product candidates.Smaller or early- stage companies may also prove to be significant competitors,particularly through collaborative arrangements with large and established companies.We expect that **,** ~~VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK~~ for the treatment of H.pylori infection, **healing and maintenance of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis** and,if approved, **treatment of heartburn associated with symptomatic Non-Erosive GERD,** VOQUEZNA ~~,for the treatment of erosive GERD,~~ will primarily compete with generic PPIs marketed by multiple pharmaceutical companies in both the prescription and OTC markets. ~~Additionally~~ **In addition to generic PPI- based triple and quad therapies** , ~~in March 2020,RedHill Biopharma Ltd.launched~~ **we expect VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK will compete with** Talicia,a co- formulated capsule comprising generic omeprazole,amoxicillin,and rifabutin for the treatment of H.pylori infection **,launched in March 2020 by RedHill Biopharma Ltd** .We are aware of other PCABs in development in the United States,as well as a number of other PCABs in territories outside of the United States that if developed and approved in our territories may compete with vonoprazan.In the United States, ~~Neurogastrx previously announced its intention to commence a Phase 3 erosive GERD trial for fexuprazan,under an exclusive license from~~ Daewoong Pharmaceutical Co.,Ltd.,or Daewoong **is looking for a strategic partner to advance the development of fexuprazan** .In addition,Cinclus Pharma AG,or Cinclus,received QIDP designation for linaprazan glurate in combination with antibiotics for the treatment of H.pylori infection,completed a Phase 2 dose selection study for ~~erosive~~ **Erosive** GERD in November 2022,and plans to initiate **a** Phase 3 ~~studies~~ **study** in ~~2023~~ **2024** for the treatment of **Erosive** GERD ~~and H.pylori infection~~ .Finally,Sebela

Pharmaceuticals,which acquired development and commercialization rights in United States and Canada to tegoprazan from HK inno.N,a South Korean company,has initiated two Phase 3 studies in the United States,one for ~~non~~ **Non** - ~~erosive~~ **Erosive** GERD and the other for healing and maintenance of healing of ~~erosive~~ **Erosive** GERD.The **earliest** estimated completion date for these studies is ~~May~~ **during** 2024 ~~and December 2024,respectively~~ .Outside the United States,in 2022 Daewoong launched fexuprazan in South Korea for the treatment of ~~erosive~~ **Erosive** GERD under the brand name Fexuclue,has submitted applications for regulatory approval in additional countries in Asia and Latin America,and has out- licensed rights to develop fexuprazan in China to Shanghai Haini,a subsidiary of China' s Yangtze River Pharmaceutical Group.Also outside the United States,revaprazan is marketed by Yuhan Corporation in South Korea,and tegoprazan is **co-** marketed by HK inno.N **and Boryung Corp.** in South Korea,is also marketed in China ~~and ,~~ Indonesia, **Mexico,Mongolia,Philippines and Singapore** and is currently **under health authority review in Argentina and Thailand as well as** in development by RaQualia Pharma,Inc.in Japan **and by Dr.Reddy' s in Russia** .Additionally,Jeil Pharm has initiated a Phase 3 trial in South Korea of its PCAB candidate,JP- 1366,in ~~erosive~~ **Erosive** GERD,and Cinclus' linaprazan glurate has completed a Phase 2 clinical trial in Europe.To our knowledge,none of these compounds have demonstrated superiority to PPIs in a Phase 3 clinical trial.Additionally,we are aware of several clinical- stage PPIs in territories outside of the United States that if developed and approved in our licensed territories may compete with vonoprazan.These include Dexa Medica' s DLBS- 2411,currently launched in the Philippines and in Phase 3 in Indonesia,Sihuan Pharmaceutical' s anaprazole,currently in Phase 3 in China,and Eisai' s azeloprazole,currently in a Phase 2 in China.In July 2012,the Food and Drug Administration Safety and Innovation Act was passed,which included the **Generating Antibiotic Incentives Now Act,or** GAIN Act.The GAIN Act is intended to provide incentives for the development of new,qualified infectious disease products.In December 2016,the 21st Century Cures Act was passed,providing additional support for the development of new infectious disease products.These incentives may result in more competition in the market for new antibiotics and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of product candidates that could be competitive with vonoprazan or any future product candidates.Many of our competitors have significantly greater financial,technical,manufacturing,marketing,sales and supply resources or experience than we do. **We will face competition** ~~If we initial commercial launch of VOQUEZNA TRIPLE PAK,VOQUEZNA DUAL PAK,or~~ **for** ~~if approved,VOQUEZNA or~~ **our current products and** any future product ~~candidate~~ **candidates** ~~,we will face competition~~ based on many different factors,including the safety and effectiveness of our products,the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration,the ~~timing and~~ scope of regulatory approvals for these products,the availability and cost of manufacturing,marketing and sales capabilities,price,reimbursement coverage and patent position.Competing products could present superior treatment alternatives,including by being more effective,safer,more convenient,less expensive or marketed and sold more effectively than any products we may develop.Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing ~~vonoprazan~~ **our current products** or any future product candidates.If we are unable to compete effectively,our opportunity to generate revenue from the sale of our products we may develop,if approved,could be adversely affected.If the market opportunities for ~~vonoprazan~~ **VOQUEZNA,VOQUEZNA TRIPLE PAK,VOQUEZNA DUAL PAK,** or any future ~~products~~ **product candidates** are smaller than we believe they are,our revenue may be adversely affected,and our business may suffer.The precise incidence and prevalence for all the conditions we aim to address with ~~vonoprazan~~ **our current products** or any future product candidates are unknown.Our projections of both the number of people who have these diseases,as well as the subset of people with these diseases who have the potential to benefit from treatment of ~~vonoprazan~~ **our current products** or any future product candidates,are based on our beliefs and estimates.These estimates have been derived from a variety of sources,including the scientific literature,surveys of clinics or market research,and may prove to be incorrect.Further,new trials may change the estimated incidence or prevalence of these diseases.The total addressable market across ~~vonoprazan~~ **indications for our current products** and any future product candidates will ultimately depend upon,among other things,the diagnosis criteria included in the final label for each of ~~vonoprazan~~ **product** and any future product candidates approved for sale for these indications,the availability of alternative treatments and the safety,convenience,cost and efficacy of ~~vonoprazan~~ **our current products** and any future product candidates relative to such alternative treatments,acceptance by the medical community and patient access,drug pricing and reimbursement.The number of patients in the United States and other major markets and elsewhere may turn out to be lower than expected,patients may not be otherwise amenable to treatment with our products or new patients may become increasingly difficult to identify or gain access to,all of which would adversely affect our results of operations and our business.We **have only recently built out our marketing,sales and distribution infrastructure.If our efforts in developing and maintaining sales,marketing and distribution capabilities are unsuccessful,or if we fail to achieve adequate pricing or reimbursement,we will not be successful in commercializing our current products or any future product candidates.We have only recently expanded our marketing,sales and distribution capabilities in advance of the launch of VOQUEZNA,VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK.This expansion greatly increased our expenses and was very time consuming for management.We** currently **market,sell and distribute VOQUEZNA,VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK through our own sales and marketing organization.Our current sales force may not be sufficient in size and may not** have ~~a limited~~ **adequate expertise in the medical markets we intend to target.Any deficiency in our sales,** marketing and **distribution capabilities or delay in the future development of such capabilities would adversely impact the commercialization of our products.To the extent that in the future we enter into any collaboration agreements with respect to marketing,** sales ~~organization~~ **or distribution for our current products** and **any future** ~~have no experience as a company in commercializing products~~ - **product** ~~,and~~ **candidates our product revenue may be lower than if** we ~~may have~~ **directly marketed or sold any approved products.We plan on entering into collaboration agreements with respect** to ~~invest significant resources to develop~~ **marketing,sales and**

distribution of our products in Europe and Canada.Any revenue we receive in these ~~capabilities~~ **markets will depend in whole or in part upon the efforts of these third- party collaborators,which may not be successful and are generally not within our control** .If we are unable to ~~establish marketing and sales capabilities or~~ enter into ~~agreements~~ **these arrangements on acceptable terms or at all,we may not be able to successfully commercialize any approved products.If we are not successful in commercializing any approved products,either on our own or through collaborations** with **one or more** third parties **,our future product revenue will suffer,and we may incur significant additional losses.Our future growth may depend,in part,on our ability to operate in foreign markets,particularly Europe and Canada,where we would be subject to additional regulatory burdens and other risks and uncertainties.Our future growth may depend,in part,on our ability to develop and commercialize our current products and any future product candidates in foreign markets,particularly Europe and Canada.We are not permitted** to market **or promote vonoprazan** and **any future product candidates before we receive regulatory approval from applicable regulatory authorities in foreign markets,and we may never receive such regulatory approvals for vonoprazan or any future product candidates.To obtain separate regulatory approval in any other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing,among other things,clinical trials,commercial sales,pricing and distribution of vonoprazan and any future product candidates.If we obtain regulatory approval of our current products and any future product candidates and ultimately commercialize our products in foreign markets,we would be subject to additional risks and uncertainties,including:• different regulatory requirements for approval of drugs in foreign countries;• reduced protection for intellectual property rights;• the existence of additional third- party patent rights of potential relevance to our business;• unexpected changes in tariffs,trade barriers and regulatory requirements;• economic weakness,including inflation,public health emergencies or political instability in particular foreign economies and markets;• compliance with tax,employment,immigration and labor laws for employees living or traveling internationally;• foreign currency fluctuations,which could result in increased operating expenses and reduced revenues,and other obligations incident to doing business in another country;• foreign reimbursement,pricing and insurance regimes;• workforce uncertainty in countries where labor unrest is common;• production shortages resulting from any events affecting raw material supply or manufacturing capabilities internationally;and • business interruptions resulting from geopolitical actions,including war and terrorism,or natural disasters including earthquakes,typhoons,floods and fires.Risks Related to the Development and Regulatory Approval of Product Candidates We** depend entirely on the success of **VOQUEZNA and other products containing** vonoprazan ~~, which is contained in our only approved products and product candidate~~ . If we **do not** ~~are unable to successfully launch and commercialize vonoprazan, obtain additional, required regulatory approvals and advance the clinical development of vonoprazan in additional indications, or experience significant delays in doing any of the foregoing, our business will be materially harmed. We currently have two approved products and one product candidate, all of which contain vonoprazan, which we in- licensed from Takeda. Our current business depends entirely on our ability to successfully develop,~~ obtain regulatory approval for **vonoprazan for the treatment of heartburn symptoms associated with Non- Erosive GERD** , ~~and~~ **or if we do not successfully** commercialize ~~products containing~~ **VOQUEZNA for Erosive GERD or, if approved, Non- Erosive GERD, or we experience significant delays in doing so, we may never become profitable. We expect that a substantial portion of our efforts and expenses over the next few years will be devoted to the commercialization of** vonoprazan ~~in a timely manner. This may make an~~ **and the** ~~investment in our company riskier than similar companies that have multiple approved products or product candidates in active~~ development **and regulatory** ~~that may be able to better sustain failure of a single product. In May 2022, the FDA approved~~ **approval of vonoprazan for additional indications; specifically,** the **ongoing review of the** ~~NDAs~~ **NDA** for vonoprazan **as** ~~triple therapy, under the brand name VOQUEZNA TRIPLE PAK and vonoprazan dual therapy, under the brand name VOQUEZNA DUAL PAK. In August 2022, prior to the launch of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, we announced that, consistent with current FDA Guidance for Industry: Control of Nitrosamine Impurities in Human Drug Products, we initiated testing to determine whether nitrosamine impurities were present in our initial commercial drug product for VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK. These tests revealed trace levels of~~ a **once** ~~nitrosamine impurity, N- nitroso- vonoprazan, or NVP, that is not described within the FDA Guidance document. In January 2023, we announced that, although the FDA established an acceptable daily intake (AI) for NVP at 96 ng / day, the FDA (Division of Gastroenterology) advised us that it would not be acting on our erosive GERD NDA on or prior to the Prescription Drug User Fee Act (PDUFA) target action date of January 11, 2023. Rather, the FDA requested additional stability data demonstrating that the levels of NVP will remain at or below the AI throughout the proposed shelf life of the product. In February 2023, we received complete response letters from the FDA relating to our erosive GERD NDA and post approval supplement relating to our approved H. pylori NDAs, both of which address specifications and controls for NVP. These letters formalize FDA' s prior request that we provide additional stability data to demonstrate that levels of NVP will remain at or below the AI throughout the proposed shelf life of the product. No additional deficiencies were cited by the FDA in either letter. We have scheduled a meeting with the FDA in March 2023 to discuss our resubmission plan and timeline. If we are unable to demonstrate to the FDA that we will be able to maintain NVP levels at or below the AI, launches of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK will be further delayed and approval of our erosive GERD NDA will continue to be delayed, which could substantially increase our costs and delay or put at risk our ability to generate revenue and adversely affect our commercial prospects. Also in January 2023, we reported positive topline results from PHALCON- NERD- 301, a Phase 3 study evaluating the safety and efficacy of vonoprazan for the~~ daily treatment of ~~adults~~ **heartburn associated** with ~~non~~ **symptomatic Non** - ~~erosive~~ **Erosive** GERD **and** ~~. We are also in discussions with~~ the **planned** ~~FDA regarding the design of a~~ Phase 3 trial **studying for** ~~to evaluate the novel dosing regimen of~~ vonoprazan as an as needed treatment for ~~episodic~~ heartburn **symptoms associated** ~~relief in patients~~ with ~~non~~ **Non** - ~~erosive~~ **Erosive** GERD ~~,~~ **. As** a **result, our business currently depends heavily on the successful development, regulatory approval and, if**

approved, commercialization of vonoprazan for this additional indication and dosing regimen ~~not~~ **. We cannot be certain that we will be able to submit or obtain** ~~approved~~ **approval** ~~in the U. S.~~ for **any additional NDA** ~~PPIs. This trial would constitute our~~ **or** ~~fourth Phase 3 trial~~ **NDA supplement, or sNDA,** for vonoprazan **within the timeframes** ~~. In February 2022,~~ we ~~reported positive topline results~~ **expect, that any NDAs or sNDAs we submit will be accepted by the FDA for filing in a timely manner or at all, or that any of our product candidates will receive regulatory approval or will be successfully commercialized even if they receive regulatory approval. The testing, manufacturing, safety, efficacy, labeling, approval, sale, marketing and distribution of our product candidates are, and will remain, subject to comprehensive regulation by the FDA and similar foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. Failure to obtain regulatory approval for additional indications for vonoprazan or future product candidates in the United States will prevent us** from ~~PHALCON- NERD- 201, a Phase 2 proof- of- concept study evaluating this novel dosing regimen. Our assumptions about the commercial~~ **commercializing** ~~potential of~~ **and marketing** vonoprazan **for** ~~are based in part on the~~ **these indications** ~~commercial experience of vonoprazan in Japan. However, our~~ **or our product candidates** ~~assumptions may prove to be wrong, and we may encounter a materially and adversely different development and commercial experience~~ . The success of vonoprazan **for future indications and our product candidates** will depend on several **additional** factors, including ~~the following~~ : • **completing clinical trials that** ~~demonstrating~~ **demonstrate their efficacy and** safety ~~and efficacy to the satisfaction of applicable regulatory authorities, including without limitation, demonstrating to the FDA that levels of NVP will remain below the AI throughout the shelf- life of our products~~ ; • **receiving marketing approvals** ~~acceptance by the FDA or comparable foreign regulatory authorities of the proposed design of our clinical trials; • the willingness of the FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities to accept the data~~ from **applicable** ~~the clinical trials and preclinical studies and clinical trials conducted outside of our licensed territories by Takeda and independent investigators as part of the basis for review and approval of vonoprazan; • the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA, and other comparable foreign~~ regulatory authorities; • **completing any post- marketing studies** ~~receipt of additional regulatory approvals, including approvals~~ required **by** ~~to initiate distribution and sale of products containing vonoprazan, from~~ applicable regulatory authorities ~~including the FDA~~ ; • ~~making and / or~~ maintaining ~~arrangements~~ **adequate commercial manufacturing capabilities; • maintaining successful commercial sales, marketing and distribution operations; • the prevalence and severity of adverse events experienced** with **vonoprazan and** ~~Takeda, Catalent, Sandoz, Evonik or~~ **our** ~~any~~ future **product candidates; • acceptance of VOQUEZNA and our future product candidates by patients, the medical community and** third- party **payers** ~~manufacturers for, or establishing, commercial manufacturing capabilities and receiving / importing commercial supplies approved by FDA and other regulators from Takeda, Catalent, Sandoz, Evonik or any future third- party manufacturer~~ ; • **a continued** ~~establishing sales, marketing and distribution capabilities and, following required approval, commercializing vonoprazan, whether alone or in collaboration with others; • establishment and maintenance of patent and trade secret protection or regulatory exclusivity for vonoprazan; • maintaining an~~ acceptable safety profile ~~of vonoprazan~~ following approval; ~~and~~ • **obtaining and** maintaining ~~and growing~~ **healthcare coverage** ~~an~~ **and adequate reimbursement for VOQUEZNA** ~~organization of people who can develop~~ and **our future product candidates; • competing effectively with other therapies, including with respect to the sales and marketing of our product candidates** , if approved **;** ~~, commercialize, market,~~ and ~~sell~~ **• qualifying for, maintaining, enforcing and defending our intellectual property rights and claims. Many of these factors are beyond our control, including the time needed to adequately complete clinical testing, the regulatory submission process, potential threats to our intellectual property rights and changes in the competitive landscape. It is possible that no new indications for** vonoprazan ~~to physicians, patients, healthcare payers,~~ and **no** ~~others in the medical community. If we are unable to demonstrate to FDA' s satisfaction our ability to maintain the level of NVP below the AI throughout the shelf- life of our products, the launches of our approved products may be further delayed and approval and launch of our erosive GERD NDA may also be further delayed, which could substantially increase our costs and put at risk our ability to generate revenue and adversely affect our commercial prospects. The success of our business, including our ability to finance our company and generate any revenue in the~~ future ~~,~~ **product candidates** will **ever obtain** ~~primarily depend on the successful completion of clinical development,~~ regulatory approval **even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or** ~~and~~ **an inability to** ~~commercialization of vonoprazan, including~~ successfully ~~addressing~~ **complete clinical trials** ~~, to the FDA' s and the medical community' s satisfaction, the formation of nitrosamine impurities in commercial batches of vonoprazan drug product, which may be significantly delayed beyond our current expectations and may never occur. Although we have obtained~~ -- **obtain** ~~marketing~~ **regulatory** approval ~~of two vonoprazan- based treatment regimens for one indication, we have not yet succeeded in launching and successfully commercializing vonoprazan. Any inability to obtain required, additional regulatory approvals for,~~ or, if approved, ~~successfully~~ commercialize **additional** vonoprazan **indications or any other product candidates** , **which** would materially **harm** ~~and adversely affect~~ our business, financial condition ~~, prospects~~ and ~~operating~~ results **of operations** . Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Even if we believe the results of our clinical trials are positive, obtaining regulatory approval may not occur on a timely basis, if at all. The results from clinical trials or preclinical studies of a product candidate may not predict the results of later clinical trials of the product candidate, and interim results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy

characteristics despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after the product candidate achieved promising results in earlier clinical trials. The results of our trials may not be comparable to those achieved previously, whether as a result of differences in trial design, patient population or otherwise. For example, in our Phase 3 clinical trial for the treatment of H. pylori infection, the vonoprazan dual therapy arm was not double- blinded because patients in this arm were administered amoxicillin three times daily, versus twice daily for the triple therapy regimens. Both triple therapy regimens were double- blinded. The inability to double- blind the dual therapy arm may impact how regulatory agencies or healthcare payers interpret such results. For example, the EMA has noted that it expects additional analyses of treatment compliance and drop- out rates in the dual therapy arm because it will not be double- blinded. Further, in July 2019, we received scientific advice from the EMA on our Phase 3 clinical trial of vonoprazan in the healing and maintenance of healing of ~~erosive~~ **Erosive** GERD. For the healing phase of the study, the EMA recommended that we include an endoscopy to assess healing at Week 4 in addition to the planned endoscopies at Week 2 and Week 8 because the summary of product characteristics for lansoprazole suggests four weeks of treatment to assess healing in ~~erosive~~ **Erosive** GERD. We decided not to incorporate this change into the study design given the additional burden on study subjects to return for a third endoscopy in an eight- week period. This decision may impact the future summary of product characteristics for vonoprazan or may cause the EMA to require us to conduct additional clinical trials for vonoprazan to support marketing approval. In addition, Takeda, a third party over which we have no control, has the right to develop and commercialize vonoprazan outside of the United States, Europe, and Canada. Takeda has marketing approval for vonoprazan in certain countries in Asia and Latin America, and Takeda has ongoing clinical trials of vonoprazan in certain indications that we are also pursuing. If such ongoing trials fail to meet their primary endpoints, have serious adverse events or encounter other problems, the development potential of vonoprazan could be materially and adversely affected. In addition, if serious adverse events or other problems occur with patients using vonoprazan marketed outside of our licensed territories, or if the results of ongoing or future clinical trials of vonoprazan conducted by Takeda or others generate negative results or results that conflict with the results of our clinical trials, the FDA or other regulatory authorities may delay, limit, or deny approval of vonoprazan, require us to conduct additional clinical trials as a condition to marketing approval, or withdraw their approval of vonoprazan or otherwise restrict our ability to market and sell vonoprazan, if approved. In addition, treating physicians may be less willing to prescribe vonoprazan due to concerns over such trial results or adverse events, which would limit our ability to commercialize vonoprazan **. In addition, the FDA' s and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the EU Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state in which the clinical trial takes place, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application for multi- center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR foresees a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the EU Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the EU Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our developments plans. It is currently unclear to what extent the United Kingdom, or UK, will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). A decision by the UK not to closely align its regulations with the new approach that has been adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries** . For the foregoing reasons, our ongoing and future clinical trials and our efforts to obtain additional regulatory approvals for vonoprazan may not be successful. Further, any safety concerns observed in any one of our ongoing or future clinical trials for the targeted indications could limit the prospects for additional regulatory approvals of vonoprazan or any future product candidates in those and other indications, which could have a material adverse effect on our business, financial condition and results of operations. Any difficulties or delays in the commencement or completion, or termination or suspension, of our ongoing or future clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects. Before obtaining marketing approvals from regulatory authorities for the sale of vonoprazan for additional indications or approval of any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of vonoprazan in such new indication or of any future product candidates in humans. We do not know whether any ongoing studies will be completed on schedule, if at all, or if any future clinical trials will begin on time. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to: • the FDA, EMA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials and reaching consensus among the FDA and EMA over the design of the same clinical trial; • any failure or delay in obtaining regulatory authorizations to commence a trial; • any failure or delay in reaching an agreement with contract research organizations, or CROs, and clinical

trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; • institutional review boards, or IRBs, or other reviewing bodies refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial; • changes to clinical trial protocols; • clinical sites deviating from trial protocols or dropping out of a trial; • manufacturing or obtaining sufficient quantities of vonoprazan and any future product candidates; • inability to obtain and deliver sufficient quantities of vonoprazan and any future product candidates to clinical sites; • subjects failing to enroll or remain in our trials at the rate we expect, or failing to return for post- treatment follow- up; • subjects choosing an alternative treatment for the indication for which we are developing vonoprazan and any future product candidates, or participating in competing clinical trials; • lack of adequate funding to continue the clinical trial; • subjects experiencing severe or unexpected drug- related adverse effects; • occurrence of serious adverse events in trials of the same class of agents conducted by other companies; • selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data; • a facility manufacturing vonoprazan or any future product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing, or cGMP, regulations or other applicable requirements, or infections or cross- contaminations of product candidates in the manufacturing process; • any changes to our manufacturing process that may be necessary or desired; • third- party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices, or GCP, or other regulatory requirements; • third- party contractors not performing data collection or analysis in a timely or accurate manner; or • third- party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted or by the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities may impose a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing, or successful completion of a clinical trial. Further, conducting clinical trials in foreign countries, as we have done for vonoprazan and may do for any future product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Moreover, principal investigators for our clinical trials currently serve and may continue to serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the clinical trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of vonoprazan or any future product candidates. If we experience delays in the completion of, or termination of, any clinical trial of vonoprazan or any future product candidates, the commercial prospects of vonoprazan and any future product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. We may make formulation or manufacturing changes to vonoprazan or any future product candidates, in which case we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize vonoprazan or any future product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of vonoprazan and any future product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition, and prospects significantly. We may find it difficult to enroll patients in our clinical trials. If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected. We may not be able to initiate or continue clinical trials for vonoprazan or any future product candidates if we are unable to identify and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the risk that enrolled patients will not complete a clinical trial, our ability to recruit clinical trial investigators with the appropriate competencies and experience, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new

drugs that may be approved for the indications we are investigating as well as any drugs under development. We will be required to identify and enroll a sufficient number of patients for each of our clinical trials. Potential patients for any planned clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for such trials. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for our clinical trials and monitoring such patients adequately during and after treatment. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible patients to participate in the clinical trials required by the FDA or comparable foreign regulatory authorities. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow- up periods. The eligibility criteria of our clinical trials further limits the pool of available trial participants. If patients are unwilling to participate in our trials for any reason, including the existence of concurrent clinical trials for similar patient or the availability of approved therapies, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of vonoprazan and any future product candidates may be delayed. ~~Further, public health emergencies, such as the COVID- 19 pandemic have and may continue to negatively affect site activation, as well as patient enrollment and retention.~~ Our inability to enroll a sufficient number of patients for any of our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Our assumptions used in determining expected clinical trial timelines may not be correct, and we may experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines. Use of **products or product candidates containing** vonoprazan or any future product candidates could be associated with side effects, adverse events or other properties or safety risks, which could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon a product candidate, limit the commercial profile of an approved label or result in other significant negative consequences that could severely harm our business, prospects, operating results and financial condition. As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with **VOQUEZNA' s or** vonoprazan' s or any future product candidates' use. Results of our ongoing or future clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by vonoprazan and any future 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 FDA or comparable foreign regulatory authorities. The drug- related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, and prospects significantly. Moreover, if vonoprazan or any other future product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective, which may limit the commercial expectations for the product candidate, if approved. We may also be required to modify our study plans based on findings in our clinical trials. ~~As of December 2022, more than 9, 000 subjects have been exposed to vonoprazan in completed and ongoing Phase 1 to 3 clinical trials. The doses studied have ranged from 1 to 120 mg with durations up to one year. In our Phase 3 clinical trial for EE, the most common adverse reactions (≥ 2 %) in vonoprazan- treated patients in the healing phase were abdominal pain and diarrhea and in the maintenance phase were gastritis, diarrhea, abdominal pain, dyspepsia, gastroesophageal reflux disease, hypertension, abnormal liver function test, and nausea. Of these, only two adverse events, both in the maintenance phase, exceeded 5 %: gastritis (6. 4 %, vonoprazan 10 mg) and abdominal pain (5. 4 %, vonoprazan 20 mg). In our Phase 3 clinical trial evaluating vonoprazan in combination with amoxicillin and clarithromycin or amoxicillin, most common adverse reactions (≥ 2 %) in vonoprazan triple therapy- treated patients were dysgeusia, diarrhea, headache, abdominal pain, vulvovaginal candidiasis and hypertension and with vonoprazan dual therapy- treated patients were diarrhea, abdominal pain and nasopharyngitis. Certain earlier generation PCABs previously under development by other companies may have been discontinued in part due to their hepatic safety profile. These hepatic safety concerns may be compound- specific and not generalizable to the PCAB class. Vonoprazan has shown similar hepatic safety results to lansoprazole across all comparative clinical studies conducted by Takeda, in which 1. 0 % of subjects treated with vonoprazan 10 mg or 20 mg and 0. 8 % of subjects treated with lansoprazole 15 mg or 30 mg had ALT or AST elevations greater than three times the upper limit of normal or bilirubin elevations greater than two times the upper limit of normal. Similarly, in the healing phase of PHALCON- EE, transient elevations in ALT or AST greater than 3 times the upper limit of normal were observed in 0. 4 % of subjects treated with vonoprazan 20 mgs and 0. 2 % of subjects treated with lansoprazole. In the maintenance phase, ALT or AST greater than three times the upper limit of normal were observed in 1 % of subjects treated with vonoprazan 10 mg, 0. 3 % of subjects treated with vonoprazan 20 mg, and 2 % of subjects treated with lansoprazole. The most recent post- marketing safety report from December 2022 includes an estimate of over 50 million patients who have received vonoprazan in Japan and other countries in Asia since launch. Based on the post- marketing experience, the clinically significant adverse reactions section of the Japanese prescribing information for vonoprazan was updated to include shock, anaphylaxis, hepatic impairment, skin reactions such as toxic epidermal necrolysis, Steven- Johnson syndrome, and erythema multiforme, and events of pancytopenia, agranulocytosis, leukocytopenia, and thrombocytopenia. The incidence of these reactions was considered extremely rare (less than 1 in 100, 000 patients) and a causal relationship to vonoprazan could not be ruled out. Although serious hepatic adverse events have been observed among patients exposed to vonoprazan in Japan in the post- marketing setting, these cases were typically confounded by comorbidities or other concomitant medications and are believed to be idiosyncratic reactions. The post- marketing safety data, including the December 2022 post- marketing safety report and the reported hepatic safety events, have been submitted to the PMDA. We may also observe hepatic- related events in our clinical trials.~~ It is possible that as we continue to test vonoprazan and any future product candidates in our clinical trials, or as the use of ~~vonoprazan~~ **VOQUEZNA** and any future product candidates becomes more widespread **following any** ~~if they~~

~~receive~~ regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. If any such side effects become known later in development or upon approval, such findings may harm our business, financial condition and prospects significantly. Further, if a serious safety issue is identified in connection with use of vonoprazan commercially or in third- party clinical trials in Asia or elsewhere, such issues may adversely affect the development potential of vonoprazan or result in regulatory authorities restricting our ability to develop vonoprazan **for** ~~. In addition~~ **additional indications. If** ~~, if vonoprazan or~~ any ~~future~~ **of our** ~~product~~ **products** ~~candidate~~ **that** receives marketing approval, ~~and we or others later identify~~ **including VOQUEZNA, is discovered to cause** undesirable side effects ~~caused by such products~~, a number of potentially significant negative consequences could result, including: • **withdrawal, suspension or limitation by** regulatory authorities **of** ~~may withdraw, suspend or limit~~ approvals of such product ~~, or seek an injunction against its manufacturer~~ ; • ~~we may be required to~~ **seizure of the product by regulatory authorities; •** recall ~~a~~ **of the** product or ~~change~~ **changes to** the ~~way such product~~ **manner in which it** is administered ~~to patients~~ ; • **restrictions on the marketing of the product or the manufacturing process for any component thereof; • requirement by** regulatory authorities **of** ~~may require~~ additional warnings on the label, such as a " black box " warning or ~~a contraindication~~ **contraindications** ; • **requirement that** we ~~may be required to~~ implement a ~~Risk Evaluation and Mitigation Strategy, or~~ REMS ~~, or similar risk management measures~~ or create a medication guide outlining the risks of such side effects for distribution to patients; • **commitment** ~~we may be required~~ to **expensive** ~~change the way a product is distributed or administered, conduct~~ additional **safety studies prior** ~~clinical trials or change the labeling of a product or be required~~ to ~~conduct additional~~ **approval or** post- marketing studies ~~or surveillance~~ **required by regulatory authorities of such product** ; • ~~we could be sued~~ **the product may become less competitive; • initiation of regulatory investigations** and **government enforcement actions; • initiation of legal action against us to** ~~held~~ **hold us** liable for harm caused to patients; **and** • **harm to** ~~sales of the product may decrease significantly or the product could become less competitive; and •~~ our reputation ~~may suffer~~ **and resulting harm to physician or patient acceptance of our products** . Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, **financial condition, and** results of operations ~~and prospects~~ . **Our current** ~~As a company, we have only received regulatory approval for two~~ products ~~, VONOPRAZAN TRIPLE PAK and VONOPRAZAN DUAL PAK, for which we have not initiated commercial launch, and may be unable to obtain additional regulatory approvals for vonoprazan or approval of any future product candidates. Although we have completed our pivotal Phase 3 clinical trials for vonoprazan for treatment of H. pylori infection, erosive GERD, and non- erosive GERD, and have obtained regulatory approvals for VONOPRAZAN TRIPLE PAK and VONOPRAZAN DUAL PAK for the treatment of H. pylori infection, we still need to obtain regulatory approval from the FDA for VOQUEZNA for the treatment of erosive GERD and have not yet submitted our submission for regulatory approval for non- erosive GERD. Moreover, due to the formation of the nitrosamine NVP in vonoprazan drug product, we have not been able to launch either of our approved products. As a company, we may be unable to successfully control the formation of NVP and as a result would not be able to launch our approved products or obtain approval of vonoprazan for erosive GERD. In addition, we may not be able to obtain regulatory approval of any future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to timely obtain regulatory approvals could delay us in commercializing vonoprazan or any future product candidates. Vonoprazan~~ and any future product candidates are subject to extensive regulation and compliance obligations **that are** ~~, which is~~ costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize vonoprazan ~~and~~ **for additional indications or** any future product candidates. The clinical development, manufacturing, labeling, storage, record- keeping, advertising, promotion, import, export, marketing and distribution of ~~vonoprazan~~ **our current approved products, including VOQUEZNA,** and any future product candidates are subject to extensive regulation by the FDA in the United States and by comparable foreign regulatory authorities in other foreign markets. In the United States, we are not permitted to market vonoprazan ~~and~~ **for additional indications or** any future product candidates until we receive the necessary regulatory approval from the FDA and in the EU, we are not permitted to market ~~vonoprazan and~~ **any of our approved products or** any future product candidates until we receive a marketing authorization from the European Commission or competent authorities of the EU member states. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels and the ability to hire and retain key personnel. In addition, approval policies or regulations may change, and the FDA and EMA and comparable regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. For example, in February 2023, we received complete response letters from the FDA relating to our ~~erosive~~ **Erosive** GERD NDA and post approval supplement to our approved H. pylori NDAs ~~, both of which address nitrosamine specifications and controls~~ . As a result, the approval of ~~vonoprazan~~ **VOQUEZNA** for treatment of ~~erosive~~ **Erosive** GERD **was delayed until November 2023,** and our ability to launch **VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK was** ~~our approved products for the treatment of H. pylori infection have been~~ delayed **until October 2023** . Prior to obtaining approval to commercialize a product candidate in the United States or internationally, we must demonstrate with substantial evidence from adequate and well- controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for **additional regulatory approvals for** vonoprazan ~~and~~ **or for** any future product

candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities, as the case may be, may also require us to conduct additional preclinical studies or clinical trials for vonoprazan ~~and~~ **or** any future product candidates either prior to or post- approval, or may object to elements of our clinical development program. The FDA, EMA or other comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including: • such authorities may disagree with the design or implementation of our clinical trials; • negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA, EMA, or other comparable foreign regulatory agencies for approval; • serious and unexpected drug- related side effects may be experienced by participants in our clinical trials or in clinical trials conducted by Takeda or others outside of our licensed territories, or by patients using vonoprazan or drugs similar to vonoprazan; • the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval; • such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States; • we may be unable to demonstrate to the satisfaction of such authorities that a product candidate is safe and effective for its proposed indication and that a product candidate' s clinical and other benefits outweigh its safety risks; • such authorities may disagree with our interpretation of data from preclinical studies or clinical trials; • such authorities may not agree that the data collected from clinical trials of vonoprazan, including data collected from clinical trials conducted by Takeda and independent investigators outside of our licensed territories, and any future product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval, and such authorities may impose requirements for additional preclinical studies or clinical trials; • such authorities may disagree regarding the formulation, labeling and / or the specifications of vonoprazan and any future product candidates; • approval may be granted only for indications that are significantly more limited than what we apply for and / or with other significant restrictions on distribution and use; • such authorities may find deficiencies in the manufacturing processes or facilities of ~~Takeda~~ **Evonik, Catalent** , Sandoz, ~~Evonik, Catalent~~ or any future third- party manufacturers with which we contract for clinical and commercial supplies; • regulations of such authorities may significantly change in a manner rendering our or any of our potential future collaborators' clinical data insufficient for approval; or • such authorities may not accept a submission due to, among other reasons, the content or formatting of the submission. With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA, EMA, and other comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy, or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our potential future collaborators from commercializing vonoprazan and any future product candidates. Of the large number of drugs in development, only a small percentage successfully complete the FDA, EMA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain **additional** regulatory ~~approval~~ **approvals** to market vonoprazan and any future product candidates, which would significantly harm our business, financial condition, results of operations and prospects. **With respect to our** ~~Even if we eventually receive approval~~ **approvals** ~~of~~ **in the U. S., the FDA has granted approvals,** ~~an~~ **and may grant** ~~NDA or foreign marketing application for vonoprazan and any~~ future **approvals** ~~product candidates~~ , **with** ~~the FDA or other~~ -- **the** ~~comparable~~ **requirement that we perform additional costly clinical trials including pediatric trials.** ~~foreign~~ **Foreign** regulatory ~~authority~~ **authorities** may ~~grant~~ **also make their** ~~approval~~ **approvals** contingent on **similar requirements** ~~the performance of costly additional clinical trials, including confirmatory Phase 3 clinical trials, Phase 4 clinical trials, and / or the implementation of a REMS or risk management measures, which may be required to ensure safe use of the drug after approval~~ . The FDA or other comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or other comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product. Any delay in obtaining, or inability to obtain, ~~applicable~~ **additional** regulatory ~~approval~~ **approvals** would delay or prevent commercialization of that **indication or** product candidate and would materially adversely impact our business and prospects. We may not be successful in our efforts to expand our pipeline by identifying and successfully developing vonoprazan for additional indications and formulations. We may expend our limited resources to pursue a particular indication or formulation for vonoprazan and fail to capitalize on product candidates, indications or formulations that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on specific indications and formulations for ~~vonoprazan~~ **VOQUEZNA** . As a result, we may fail to generate additional clinical development opportunities for vonoprazan for a number of reasons, including, vonoprazan may in certain indications, on further study, be shown to have harmful side effects, limited to no efficacy, or other characteristics that suggest it is unlikely to receive marketing approval and achieve market acceptance in such additional indications. For example, we believe the rapid onset of ~~action~~ **acid suppression observed in clinical studies** of vonoprazan may enable as needed use for the management of ~~non~~ **heartburn symptoms associated with Non** - ~~erosive~~ **Erosive** GERD. However, no proton pump inhibitor has received approval from the FDA for this ~~indication~~ **dosing regimen** . We may be incorrect in our belief regarding the potential of vonoprazan as an as needed treatment for ~~non~~ **Non** - ~~erosive~~ **Erosive** GERD and any future clinical trial we conduct studying as needed dosing of vonoprazan in ~~non~~ **Non** - ~~erosive~~ **Erosive** GERD patients may not succeed including as a result of our design and enrollment criteria. Furthermore, research programs to identify additional indications for vonoprazan require substantial technical, financial and human resources. We may also pursue additional formulations and packaging for vonoprazan, such as orally disintegrating tablets and other oral dosage forms for patients with difficulty swallowing, and an intravenous formulation for in- hospital applications. However, we may not successfully develop

these additional formulations for chemistry- related, stability- related or other reasons. If we do not accurately evaluate the commercial potential or target market for vonoprazan or any future product candidates, we may relinquish valuable rights to that product candidate through future collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Additionally, we may pursue additional in- licenses or acquisitions of development- stage assets or programs, which entails additional risk to us. Identifying, selecting and acquiring promising product candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular product candidate, potentially resulting in a diversion of our management' s time and the expenditure of our resources with no resulting benefit. We enrolled patients in Europe in our ~~erosive~~ **Erosive** GERD and H. pylori trials. Additionally, we may conduct future clinical trials outside of the United States. However, the FDA and other comparable foreign regulatory authorities may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business. We enrolled patients in Europe in our ~~erosive~~ **Erosive** GERD and H. pylori trials, and we may conduct one or more of our future clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States and not subject to an IND, acceptance of this data is subject to certain conditions imposed by the FDA. For example, where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will not approve the application on the basis of foreign data alone unless those data are applicable to the United States population and United States medical practice; the trials were performed by clinical investigators of recognized competence; and the data are considered valid without the need for an on- site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. Similar requirements may apply in foreign jurisdictions. For trials that are conducted only at sites outside of the United States and not subject to an IND, the FDA requires the clinical trial to have been conducted in accordance with GCP and the FDA must be able to validate the data from the clinical trial through an on- site inspection if it deems such inspection necessary. For such trials not subject to an IND, the FDA generally does not provide advance comment on the clinical protocols for the trials, and therefore there is an additional potential risk that the FDA could determine that the trial design or protocol for a non- United States clinical trial was inadequate, which could require us to conduct additional clinical trials. In addition, such foreign trials would be subject to the applicable local laws of the foreign regulatory agency and legal requirements where the trials are conducted. There can be no assurance the FDA will accept data from clinical trials conducted outside of the United States. If the FDA or comparable regulatory authority does not accept data from our clinical trials of vonoprazan and any future product candidates, it would likely result in the need for additional clinical trials, which would be costly and time consuming and delay or permanently halt our development of vonoprazan **for additional indications** and any future product candidates. Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with: • additional foreign regulatory requirements; • foreign exchange fluctuations; • compliance with foreign manufacturing, customs, shipment and storage requirements; • cultural differences in medical practice and clinical research; and • diminished protection of intellectual property in some countries. Interim, top- line and preliminary data from clinical trials that we or others announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we or others, such as Takeda, may publicly disclose preliminary or top- line data from clinical trials **that** ~~, which~~ are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top- line or preliminary results that we or others report may differ from future results of the same clinical trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top- line and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data previously published. As a result, top- line and preliminary data should be viewed with caution until the final data are available. From time to time, we or others may also disclose interim data from clinical trials. Interim data from clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary, top- line or interim data and final data could significantly harm our business prospects. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the top- line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, vonoprazan and any future product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition. Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business. The ability of the FDA and other government agencies to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, a government agency' s ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the government agency' s ability to perform routine

functions. Average review times at the FDA and other government agencies have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA, may also slow the time necessary for new drugs and or modifications to approved drugs or to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the United States government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Separately, in response to the COVID- 19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed ~~stand~~ **standard** inspection operations ~~of domestic facilities where feasible~~ , ~~the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic, and~~ any resurgence of the virus or emergence of new variants may lead to further inspectional **or administrative** delays ~~. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID- 19 pandemic~~ . If a prolonged government shutdown occurs, or if global health concerns ~~continue to~~ hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Risks Related to Our Reliance on Third Parties We rely on the Takeda License to provide us rights to develop and commercialize vonoprazan in the United States, Europe, and Canada. If the license agreement is terminated, we would lose our rights to develop and commercialize vonoprazan. Pursuant to the Takeda License, we have secured an exclusive license from Takeda to commercialize vonoprazan products using specified formulations for all human therapeutic uses in the United States, Europe, and Canada, and a non- exclusive license to develop and manufacture vonoprazan products anywhere in the world (subject to Takeda' s consent as to each country) for the purposes of commercializing the vonoprazan products in the United States, Europe, and Canada. The Takeda License will continue until the expiration of the obligation to pay royalties in all countries and on all products, unless terminated earlier. We may terminate the Takeda License in its entirety without cause upon prior written notice. We and Takeda may terminate the Takeda License in the case of the other party' s insolvency or for the other party' s material uncured breach. Takeda may terminate the Takeda License in its entirety if we challenge the licensed patents, or if we assist any third party in challenging such patents. In addition, if any of the commercial milestones or other cash payments become due under the terms of the Takeda License, we may not have sufficient funds available to meet our obligations, which would allow Takeda to terminate the Takeda License. If the license agreement is terminated, we would lose our rights to develop and commercialize **products containing** vonoprazan, which in turn would have a material adverse effect on our business, operating results and prospects. We rely on third parties to conduct our clinical trials. Any failure by a third party to conduct the clinical trials according to GCPs and other requirements and in a timely manner may delay or prevent our ability to seek or obtain **additional** regulatory ~~approval~~ **approvals** for ~~or commercialize~~ vonoprazan and **regulatory approvals for** any future product candidates. We are dependent on third parties to conduct our preclinical and clinical trials ~~, including our completed and ongoing Phase 3 clinical trial of vonoprazan~~ . Specifically, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, CROs and consultants to conduct our clinical trials in accordance with our clinical protocols and regulatory requirements. These CROs, investigators and other third parties will play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have agreements governing the activities of our third- party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for vonoprazan and any future product candidates that reach clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP or similar regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. CROs, investigators or other third parties may not devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed, or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable regulatory authority concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any NDA or similar marketing application we submit by the FDA or by comparable regulatory authority. Any such delay or rejection could prevent us from commercializing vonoprazan **for additional indications** and any future product candidates. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms. Switching or adding additional CROs, investigators and other third parties involves additional cost and requires management time and focus.

In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, we may encounter challenges or delays in the future and these delays or challenges may have a material adverse impact on our business, financial condition and prospects. We currently rely on **, and expect to rely on for the foreseeable future, Evonik and** Catalent ~~and Takeda~~ for the manufacture of vonoprazan **drug substance and drug product** for clinical development and **commercial sale, and we** expect to rely ~~on Catalent, Evonik and other third parties for clinical supplies for the foreseeable future, and we expect to rely on Takeda, Catalent, Evonik and other third parties to produce commercial supplies of vonoprazan drug substance and drug product, and~~ on Sandoz for commercial supplies of **VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK and the** amoxicillin and clarithromycin **in those products** ~~for our convenience packs~~. This reliance on third parties increases the risk that we will not have sufficient quantities of **finished product** ~~vonoprazan, amoxicillin, and / or clarithromycin,~~ which could delay, prevent or impair our development or commercialization efforts. We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. **We have** ~~Pursuant to the Takeda License, we~~ entered into ~~a clinical manufacturing and~~ **an** ~~supply agreement with Takeda for the supply of vonoprazan for our clinical trials. In addition, we entered into a commercial supply agreement with Takeda for the commercial supply of bulk drug product and / or drug substance, a commercial supply~~ agreement with Catalent for the ~~commercial~~ supply of **finished** drug product, **an** ~~a commercial supply~~ agreement with Evonik for the supply of drug substance, and ~~a commercial supply and~~ **an** ~~packaging~~ agreement with Sandoz for commercial supply of amoxicillin, clarithromycin and finished convenience packs containing ~~vonoprazan~~ **VOQUEZNA** and one or both of those antibiotics. As a result, we currently rely, and expect to continue to rely, on third parties for the manufacture of vonoprazan and **supply of** related raw materials for clinical development and commercial ~~supply~~ **sale**. If ~~Takeda,~~ Catalent, Evonik or Sandoz fails to fulfill its obligations under its respective supply agreement ~~(s)~~, or if any of the vonoprazan drug product or drug substance supplied by ~~Takeda,~~ Catalent or Evonik cannot be utilized due to quality or cGMP or similar concerns, adverse findings during regulatory inspections or other reasons, our development plans and commercialization of vonoprazan, if approved, could be significantly delayed or otherwise adversely affected. The facilities used by ~~Takeda,~~ Catalent and Evonik to manufacture vonoprazan and by Sandoz to manufacture amoxicillin and clarithromycin and to package the antibiotics and vonoprazan must be approved by the FDA and foreign regulatory authority pursuant to inspections that may be conducted after we submit marketing authorizations to the FDA and comparable foreign regulatory authorities. We do not control the manufacturing process of, and are completely dependent on ~~, Takeda~~, Catalent, Evonik and Sandoz for compliance with applicable cGMP or similar requirements. If ~~Takeda,~~ Catalent, Evonik, Sandoz, or any other third- party manufacturer we contract with in the future, cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, including requirements related to the manufacturing of high potency compounds, they will not be able to secure and / or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over ~~Takeda' s,~~ Catalent' s, Evonik' s, Sandoz' s, or any other third- party manufacturer' s ability to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve of facilities of the third- party manufacturer for the manufacture of vonoprazan or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to **continue to** develop, obtain **additional** regulatory ~~approval~~ **approvals** for or **continue to** market **our current** ~~vonoprazan, if approved. For example, in June 2020, the FDA issued a warning letter to Takeda following a routine inspection of aseptic (sterile) drug product~~ **products** ~~manufacturing at Takeda' s manufacturing facility located in Hikari, Yamaguchi, or the Hikari Facility. Although it is not an aseptic product, Takeda also manufactures vonoprazan drug substance and drug product at the Hikari Facility. The warning letter indicated that the FDA was not satisfied with Takeda' s response to an FDA Form 483 issued to Takeda following the inspection and cited significant violations of cGMP for finished aseptic pharmaceuticals. Due to the issues relating to the Hikari Facility, we did not include the Hikari Facility, as a contract manufacturing site in the H. pylori NDAs we submitted to FDA in September 2021. In October 2021, the FDA revised the inspection classification of the Hikari Facility to Voluntary Action Indicated, or VAI. Takeda has reported that this revision means the FDA determined that the conditions in the warning letter dated June 2020 have been sufficiently addressed. We have not experienced any clinical supply constraints to date as a result of the issues at the Hikari Facility, and we currently do not expect these issues will have an effect on our ongoing or future clinical trials or commercial supplies~~. Our failure, or ~~Takeda' s,~~ Catalent' s, Evonik' s, Sandoz' s or any other third- party manufacturer' s failure, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. ~~Furthermore, Takeda may choose to prioritize the manufacture of vonoprazan for its markets over the manufacture of vonoprazan for our licensed markets.~~ Our or ~~Takeda' s,~~ Catalent' s, Evonik ~~'~~ **'** s or Sandoz' s failure, or the failure of any future third- party manufacturer, to execute on our manufacturing requirements, to do so on commercially reasonable terms and comply with cGMP **or similar foreign requirements,** could adversely affect our business in a number of ways, including: • an inability to initiate and continue clinical trials of vonoprazan or any future product candidates; • delay in submitting regulatory applications, or receiving marketing approvals ~~,~~ **for new indications** for vonoprazan ~~and~~ **or for** any future product candidates; • subjecting third- party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities; • requirements to cease development or to recall batches of ~~vonoprazan~~ **our current products** and any future product candidates; and • ~~in the event of approval to market and commercialize vonoprazan or any future product candidates,~~ an inability to meet commercial demands for ~~vonoprazan~~ **our current products** or any future product candidates. Reliance on third- party manufacturers entails additional risks, including: • failure of third- party manufacturers to comply with regulatory requirements and maintain quality assurance; • breach of the manufacturing agreement by the third party; • failure to manufacture our product

according to our specifications; • failure to manufacture our product according to our schedule or at all; • misappropriation of our proprietary information, including our trade secrets and know- how; and • termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us. ~~Vonoprazan~~ **Our current products, including VOQUEZNA,** and any ~~products~~ **product candidates** that we may develop **,** may compete with other product candidates and products for access to manufacturing facilities. Moreover, there may be a limited number of manufacturers that operate under cGMP or similar regulations and that might be capable of manufacturing for us. Any performance failure on the part of ~~Takeda,~~ Catalent, Evonik, Sandoz or any future manufacturers could delay clinical development or **additional** marketing ~~approval~~ **approvals**, and any related remedial measures may be costly or time consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials used in the manufacture of **our current** ~~vonoprazan and any future product~~ **products** ~~candidates~~. If ~~Takeda,~~ Catalent, Evonik, or Sandoz cannot perform as agreed, we may be required to replace them and we may be unable to replace them on a timely basis or at all. Further ~~, Takeda~~, Catalent, Evonik, Sandoz and any other third- party manufacturers we may use may experience manufacturing or shipping difficulties due to resource constraints or as a result of natural disasters, labor disputes, unstable political environments, or public health emergencies such as the COVID- 19 pandemic or ongoing hostilities in the Ukraine **and the Middle East**. If ~~Takeda,~~ Catalent, Evonik, Sandoz or other third- party manufacturers were to encounter any manufacturing or shipping difficulties or delays due to these factors, our ability to provide vonoprazan to patients in clinical trials, or to provide product for treatment of patients if approved, would be jeopardized. Our current and anticipated future dependence upon others for the manufacture of ~~vonoprazan~~ **our current products** or any future product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis. Our reliance on third parties, including ~~Takeda~~ **Sandoz**, Catalent and Evonik, requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. Because we rely, and expect to continue to rely **,** on ~~Takeda~~ **Sandoz**, Catalent and Evonik to manufacture ~~vonoprazan~~ **our current approved products** and to perform quality testing, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements, consulting agreements or other similar agreements with our advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are intentionally or inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets and despite our efforts to protect our trade secrets, a competitor' s discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects. We may seek to enter into collaborations, licenses and other similar arrangements and may not be successful in doing so, and even if we are, we may not realize the benefits of such relationships. We may seek to enter into collaborations, joint ventures, licenses and other similar arrangements for the development or commercialization of ~~vonoprazan and~~ **our current products or** any future product candidates ~~,~~ due to **, for example,** capital costs required to develop or commercialize ~~vonoprazan and~~ **our current products or** any future product candidates **,** or manufacturing constraints. We may not be successful in our efforts to establish such collaborations ~~for vonoprazan and any future product candidates~~ because **, among other reasons,** ~~vonoprazan and any future product candidates may be deemed to be at too early of a stage of development for collaborative effort or~~ third parties may not view ~~vonoprazan and any~~ **our current products or** future product candidates as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time consuming and complex. Further, any future collaboration agreements may restrict us from entering into additional agreements with potential collaborators. Following a strategic transaction or license, we may not achieve an economic benefit that justifies such transaction. Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development or approval of a product candidate is delayed, the safety of a product candidate is questioned or sales of an approved product candidate are unsatisfactory. In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able ~~to~~ adequately **to** protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of vonoprazan and any future product candidates ~~, if approved,~~ and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations ~~related to vonoprazan or any future product candidates~~, could delay **or impair** the **further** development and commercialization of vonoprazan or **the development and commercialization of** any future product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations. Risks Related to Commercialization of Vonoprazan and Any Future Product..... floods and fires. Risks Related to Our Business Operations and Industry Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide. Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to: • the timing and cost of, and level of investment in, research, development, regulatory approval and commercialization activities relating to ~~VOQUEZNA TRIPLE PAK~~ **our current products**, ~~VOQUEZNA DUAL PAK, VOQUEZNA~~ or any future product candidates, which may change from time to time; • coverage and reimbursement policies with respect to ~~VOQUEZNA TRIPLE PAK~~ **our current products**, ~~VOQUEZNA DUAL~~

~~PAK, and, if approved, VOQUEZNA~~ or any future product candidates, and potential future drugs that compete with such products, if approved; • the cost of manufacturing ~~vonoprazan~~ **of our current products** or any future product candidates, which may vary depending on the quantity of production and the terms of our agreements with ~~Takeda,~~ Catalent, Evonik, Sandoz and any future third- party manufacturers; • business interruptions resulting from geopolitical actions, including war, such as the ongoing hostilities in the Ukraine **or the Middle East** , and terrorism, or natural disasters such as earthquakes, typhoons, floods and fires or public health emergencies or pandemics such as the ~~ongoing~~ COVID- 19 pandemic; • the timing and amount of the milestone or other payments we will be required to pay to Takeda pursuant to the Takeda License; • expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies; • the level of demand for any approved products, which may vary significantly; • future accounting pronouncements or changes in our accounting policies; and • the timing and success or failure of **additional** ~~preclinical studies or~~ clinical trials for vonoprazan or **preclinical studies or clinical trials for** any future product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners. The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period- to- period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide. Our business is subject to risks arising from epidemic diseases, such as the ~~ongoing~~ COVID- 19 pandemic. A public health pandemic, such as COVID- 19, has the potential to impact worldwide economic activity and poses the risk that we or our employees, contractors, including our CROs, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time, including due to spread of the disease within these groups or due to shutdowns that may be requested or mandated by governmental authorities. In March 2020, due to efforts to combat the COVID- 19 pandemic, we announced a temporary pause in randomization of new patients in our Phase 3 trials and did not recommence randomizations in either trial until June 2020. While it is not possible at this time to estimate the full impact that ~~COVID- 19 or~~ a future public health pandemic could have on our business, ~~the~~ measures taken by the governments of countries affected could, in addition to disrupting our **commercial activities and** clinical trials, disrupt the supply chain and the manufacture or shipment of drug substance and finished drug product of vonoprazan for use in our clinical trials or in commercial distribution, which could delay our ongoing clinical trials and increase development costs, or impair our ability to successfully commercialize **our** ~~vonoprazan following regulatory approval~~ **approved products** , and in either case have a material adverse effect on our business, financial condition and results of operations. The COVID- 19 pandemic and mitigation measures ~~had~~ had an adverse impact on global economic conditions and mitigation measures regarding ~~a~~ **any** future public health pandemic could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed. The extent to which ~~COVID- 19 or~~ a future public health pandemic impacts our results will depend on future developments that are highly uncertain and cannot be predicted. Our indebtedness may limit our flexibility in operating our business and adversely affect our financial health and competitive position, and all of our obligations under our indebtedness are secured by substantially all of our assets, excluding our intellectual property and certain other assets. If we default on these obligations, our lenders could foreclose on our assets. In September 2021, we entered into **, and in December 2023 we increased** the **amounts available under and extended the maturity date of, a** Loan Agreement with Hercules. We borrowed $ 100 ~~. 0~~ million at the inception of the Loan Agreement **, $ 40 million in December 2023,** and may be eligible to borrow up to an additional $ **160** ~~100. 0~~ million. All obligations under the Loan Agreement are secured by a first priority lien on substantially all of our assets, including intellectual property and certain other assets. As a result, if we default on any of our obligations under the Loan Agreement, Hercules could foreclose on its security interest and liquidate some or all of the collateral, which would harm our business, financial condition and results of operations and could require us to reduce or cease operations. In order to service our current indebtedness and any additional indebtedness we may incur in the future, we need to generate cash from our operating activities or other financings. Our ability to generate cash is subject, in part, to our ability to successfully execute our business strategy, as well as general economic, financial, competitive, regulatory and other factors beyond our control. Our business may not be able to generate sufficient cash flow from operations, and future borrowings or other financings may not be available to us in an amount sufficient to enable us to service our indebtedness and fund our other liquidity needs. To the extent we are required to use cash from operations or the proceeds of any future financing to service our indebtedness instead of funding working capital or other general corporate purposes, we will be less able to plan for, or react to, changes in our business, industry and in the economy generally. This could place us at a competitive disadvantage compared to our competitors that have less indebtedness. The Loan Agreement contains customary affirmative and negative covenants that limit our ability to engage in certain transactions that may be in our long- term best interest. The affirmative covenants include, among others, covenants requiring us to maintain certain levels of cash subject to a control agreement in favor of Hercules, and commencing on ~~November 15~~ **September 30** , ~~2023~~ **2024** , certain levels of trailing three- month net product revenue from the sale of ~~vonoprazan~~ **VOQUEZNA** and **other** products containing vonoprazan, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding our operating accounts. The negative covenants include, among others, limitations on our ability to incur additional indebtedness and liens, merge with other companies or consummate certain changes of control, acquire other companies, engage in new lines of business, make certain investments, pay dividends, transfer or dispose of assets, amend certain material agreements or enter into various specified transactions. While we believe we are currently in compliance with the covenants contained in the Loan Agreement, we may breach these covenants in the future. Our ability to comply with these covenants may be affected by events

and factors beyond our control. In the event that we breach one or more covenants, the lenders may choose to declare an event of default and require that we immediately repay all amounts outstanding under the applicable agreement, terminate any commitment to extend further credit and foreclose on the collateral. The occurrence of any of these events could have a material adverse effect on our business, financial condition and results of operations. Our Revenue Interest Financing Agreement could limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations. In May 2022, we entered into a Revenue Interest Financing Agreement with the Initial Investors pursuant to which we can receive up to $ 260 **. 0** million in funding from the Initial Investors, and in October 2022, we entered into the Joinder Agreement under which we can receive up to $ 40 million from the Additional Investor, bringing the total funding available under the Revenue Interest Financing Agreement to up to $ 300 million. Under the terms of the Revenue Interest Financing Agreement and Joinder Agreement, we received $ 100 million at the initial closing and ~~can receive~~ **received** an additional $ 175 million ~~upon~~ **in November 2023 following** FDA approval of vonoprazan for treatment of ~~erosive~~ **Erosive** GERD ~~on or before March 31, 2024~~. In addition, we are eligible for $ 25 **million** ~~, 000, 000~~ in additional funding for achievement of a sales milestone. Under the Revenue Interest Financing Agreement, the investors are entitled to receive a 10 % royalty on net sales of products containing vonoprazan. The royalty rate is subject to a step- down on net sales exceeding certain annual thresholds and if we receive FDA approval for vonoprazan for an indication relating to the treatment of heartburn associated with ~~non~~ **Non** - ~~erosive~~ **Erosive** GERD. The investors' right to receive royalties on net sales will terminate when the investors have aggregate payments equal to 200 % of the Investment Amount. ~~In addition, at any time after the earlier of (i) April 30, 2024 and (ii) the date that the payment for erosive GERD regulatory approval is made, we have the right to make a cap payment equal to 200 % of the Investment Amount less any royalties already paid, at which time the agreement will terminate.~~ If the investors have not received aggregate payments of at least 100 % of the Investment Amount by December 31, 2028, and at least 200 % of the Investment Amount by December 31, 2037, each a Minimum Amount, then we will be obligated to make a cash payment to the investors in an amount sufficient to gross the investors up to the applicable Minimum Amount. Pursuant to the Revenue Interest Financing Agreement, we also agreed to specified affirmative and negative covenants, including covenants to use commercially reasonable efforts to promote products containing vonoprazan in the United States and covenants requiring us to maintain certain levels of cash. The Revenue Interest Financing Agreement also contains representations and warranties, other covenants, indemnification obligations, and other provisions customary for transactions of this nature. In the event of an event of default under the Revenue Interest Financing Agreement, the investors may be entitled to foreclose on the pledged collateral which includes the applicable royalty under the Royalty Interest Financing Agreement from net sales of **VOQUEZNA and other** ~~product~~ **products** containing vonoprazan. ~~We are~~ **Our future growth and ability to compete** ~~dependent~~ **depends** on **retaining** ~~the services of~~ our **key** ~~current management and other clinical and scientific~~ personnel ~~,~~ and ~~if we are not able to retain these individuals or recruit~~ **recruiting** additional ~~management or clinical and scientific personnel, our business will suffer. Our success depends in part on our continued ability to attract, retain and motivate highly~~ qualified ~~management, clinical and scientific~~ personnel. We are highly dependent ~~upon~~ **on the management, commercial, development, clinical, and financial experience of** our ~~current~~ senior management ~~team and our development personnel. The loss of services of any of these individuals or personnel could delay or prevent the successful development of our product pipeline, completion of our ongoing clinical trials, initiation or completion of future clinical trials, or the commercialization of vonoprazan or any other future product candidates~~. Although we have ~~executed~~ **entered into** employment agreements ~~or offer letters~~ with **our executive officers,** each ~~member~~ of ~~our senior management team~~ - **them may** ~~, these agreements are terminable~~ **terminate their employment with us** at **any time** ~~will with or without notice and, therefore, we may not be able to retain their services as expected~~. We do not ~~currently~~ maintain " key person " ~~life~~ insurance **for any** ~~on the lives~~ of our executives or ~~any of our~~ employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals. ~~We will continue to expand and need to effectively manage our managerial, operational, financial and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition~~ **Competition** for qualified personnel ~~among~~ **in the** ~~pharmaceutical~~ **biopharmaceutical field is intense** , ~~biotechnology~~ and **our future success depends upon our ability to attract, retain and motivate highly skilled commercial, scientific, technical and managerial employees. We face competition for personnel from** other **biopharmaceutical companies and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to implement** ~~businesses --~~ **business strategy, which could harm our business. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating and implementing our development and commercialization strategy** . Our ~~industry has experienced a high rate of turnover of management personnel in recent years~~ **consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us** . If we are ~~not able~~ **unable to continue** to attract ~~, integrate~~ , retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede ~~the~~ achievement of our **commercial and** development objectives, our ability to raise additional capital and our ability to implement our business strategy ~~. We have recently substantially increased the size of our organization, and we may encounter difficulties in managing our growth and expanding our operations successfully~~ . We have substantially increased **the size of** our organization **over the past year, and we may encounter difficulties in managing our growth and expanding our operations successfully. Our number of employees increased substantially in 2023 to prepare for the commercialization of VOQUEZNA, VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK. This expansion of our operations has resulted in a significant increase in our commercial organization, which may divert our management and business development resources** from **our clinical** ~~seventy- three full- time employees in December 2021 to one hundred and twelve full- time~~

~~employees as of December 31, 2022. As we continue~~ development **group** ~~and pursue the potential commercialization of vonoprazan and any future product candidates, as well as function as a public company, we will continue to expand our marketing, sales, financial, regulatory, and manufacturing capabilities or contract with third parties to provide these capabilities for us~~ . **To** ~~As our operations expand, we expect that we will need to~~ manage ~~additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to develop and commercialize vonoprazan and any future product candidates and to compete effectively will depend, in part, on our ability to manage~~ our recent ~~substantial~~ growth and ~~any~~ **anticipated** future growth **, we must continue to implement and improve our managerial, operational and financial systems, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to** effectively **manage the expansion of our operations or recruit and train additional qualified personnel. Any inability to manage growth could delay the execution of our business plans or disrupt our operations** . We are subject to various foreign, federal, and state healthcare laws and regulations, and our failure to comply with these laws and regulations could harm our results of operations and financial condition. Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third- party payers, patient organizations and customers expose us to broadly applicable foreign, federal and state fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any products for which we obtain marketing approval. Such laws include, but are not limited to: • the U. S. federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, or order, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service, for which payment may be made, in whole or in part, under any U. S. federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti- Kickback Statute or specific intent to violate it in order to have committed a violation; • the U. S. civil and criminal federal false claims laws, including the civil False Claims Act, which can be enforced through civil whistleblower or qui tam actions, and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making or causing to be made a false statement to avoid, decrease or conceal an obligation to pay money to the U. S. federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act; • the U. S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U. S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate it in order to have committed a violation; • the U. S. federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children' s Health Insurance Program (with certain exceptions) to report annually to ~~the Centers for Medicare & Medicaid Services, or~~ CMS, information related to certain payments and other " transfers of value " made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; and • analogous state and foreign laws and regulations, such as state anti- kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payers, including private insurers, or by the patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information or which require tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities. We may also be subject to additional regulation in the conduct of our business. For example, we may be subject to the U. S. Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, U. S. companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof. Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U. S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions,

disgorgement, imprisonment, contractual damages, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations. Enacted and future legislation and healthcare reform measures may increase the difficulty and cost for us to ~~obtain marketing approval for and~~ commercialize vonoprazan and any future product candidates and may affect the prices we may set. In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system, including cost- containment measures **,** that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U. S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Patient Protection and Affordable Care Act, ~~as amended by the Health Care and Education Reconciliation Act, collectively~~ the Affordable Care Act, was enacted in the United States **, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry** . Among ~~the~~ **other things** ~~provisions of the Affordable Care Act of importance to our potential product candidates~~ , the Affordable Care Act includes: • an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs; • a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point- of- sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer' s outpatient drugs to be covered under Medicare Part D; • an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23. 1 % and 13. 0 % of the **AMP** ~~average manufacturer price~~ for branded and generic drugs, respectively; • a methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; • an extension of a manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations; • expansion of the entities eligible for discounts under the **340B drug** ~~Public Health Service~~ pharmaceutical pricing program; • a new Patient- Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and • establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial and political challenges to certain aspects of the Affordable Care Act. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ~~ACA~~ **Affordable Care Act** without specifically ruling on the constitutionality of the ~~ACA~~ **Affordable Care Act** . **Thus** ~~Prior to the Supreme Court' s decision~~ , **the Affordable Care Act will remain in effect in its current** ~~President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for~~ **form** ~~purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA~~ . In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. ~~These changes included aggregate reductions to~~ **For example, beginning April 1, 2013,** Medicare payments to providers **were reduced under the sequestration required by the Budget Control Act** of **2011** ~~2 % per fiscal year~~ , which ~~went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute~~ will remain in effect through ~~2030~~ **2032** ~~, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022~~ , unless additional Congressional action is taken. ~~On~~ **Additionally, on** January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, **further** reduced Medicare payments to several providers, including hospitals, **imaging centers and cancer treatment centers,** and increased the statute of limitations period for the government to recover overpayments to providers from three to five years **. On March 11, 2021, the American Rescue Plan Act of 2021 was signed into law, which eliminates the statutory Medicaid drug rebate cap, beginning January 1, 2024. Previously, the rebate was capped at 100 % of a drug' s AMP** . Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs. At the federal level, such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. Most ~~recently~~ **significantly** , on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law **. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the Affordable Care Act in 2010** . Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services **, or HHS,** to implement many of these provisions through guidance, as opposed to regulation, for the initial years **HHS has and will continue to issue and update guidance as these programs are**

implemented . ~~For~~ **On August 29, 2023, HHS announced the list of the first ten drugs** that ~~and~~ **will be subject to price negotiations, although** ~~other~~ -- **the** ~~reasons, it~~ **Medicare drug price negotiation program** is currently ~~unclear how~~ **subject to legal challenges. The impact of** the IRA ~~will~~ **on the pharmaceutical industry cannot yet** be ~~effectuated~~ **fully determined, but is likely to be significant** . The likelihood of implementation of these and other reform initiatives is uncertain. In the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our product candidates. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Furthermore, there has been increased interest by third party payers and governmental authorities in reference pricing systems and publication of discounts and list prices. These reforms could reduce the ultimate demand for vonoprazan and any future product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects. We expect that these healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize vonoprazan and any future product candidates, if approved. We and any of our third- party manufacturers or suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly. We and any of our third- party manufacturers or suppliers will use biological materials, potent chemical agents and may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety of the environment. Our operations and the operations of our third- party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended. Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work- related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products. We **are exposed to potential** ~~face an inherent risk of~~ product liability ~~as a result of~~ **risks that are inherent in** the **development, manufacturing, marketing, and use of pharmaceutical products. The current and future use of product candidates by us in** clinical trials **, and the sale** of ~~vonoprazan~~ **VOQUEZNA, VOQUEZNA TRIPLE PAK, VOQUEZNA DUAL PAK,** and any **other approved products in the** future **, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies, or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend or settle, and could compromise the market acceptance of our** product candidates **or** ~~and will face an~~ **any** ~~even greater risk~~ **prospects for the commercialization of our products and,** if ~~we commercialize vonoprazan or, following approval~~ **approved** , ~~any future~~ product candidates. ~~For example~~ **Although the clinical trial process is designed to identify and assess potential side effects** , ~~we~~ **it is always possible that a drug, even after regulatory approval,** may ~~be sued if vonoprazan or~~ **exhibit unforeseen side effects. If** any ~~future~~ **of our** product candidates ~~allegedly~~ **were to** cause **adverse side effects** ~~injury or are found to be otherwise unsuitable~~ during **clinical trials** ~~product testing, manufacturing,~~ or **after approval** ~~sale. Any such product liability claims may include allegations~~ of ~~defects in manufacturing, defects in design, a failure to warn of dangers inherent in~~ the product candidate, **we** ~~negligence, strict liability and a breach of warranties. Claims~~ may be **exposed to substantial liabilities. Physicians and** ~~brought against us by clinical trial participants,~~ patients **may not comply with any warnings** ~~or others using, administering or selling products~~ that **identify known potential adverse effects and patients who should not use our product candidates** ~~may be approved in the future. Claims could also be asserted under state consumer protection acts~~ . If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in: • decreased demand for our products; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial participants; • costs to defend the related litigation; • a diversion of management' s time and our resources; • substantial monetary awards to trial participants or patients; •

product recalls, withdrawals or labeling, marketing or promotional restrictions; • significant negative financial impact; • the inability to commercialize ~~vonoprazan~~ **our current products** and any future product candidates; and • a decline in our stock price. **Although we** ~~Our inability to~~ maintain ~~sufficient~~ product liability ~~insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, and, if approved, VOQUEZNA and additional products we may develop. Although we maintain such~~ insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts **in which case our business operations could be impaired** . Moreover, 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 ~~. As a result of receiving marketing approval for, VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, we have expanded our insurance coverage to include the commercialization of these products as well as, if approved, vonoprazan; however, we may be unable to continue to obtain this liability insurance on commercially reasonable terms and such insurance may be insufficient to cover our exposure~~ . We and others, including any of our potential future collaborators, will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business. **The** ~~If we or any of our potential future collaborators are successful in commercializing VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, or, if approved, VOQUEZNA or any future product candidates, the~~ FDA and foreign regulatory authorities ~~would~~ **will** require that we and Takeda (with respect to products containing vonoprazan) and any of our ~~current or~~ potential future collaborators, report certain information about adverse medical events **for our approved products** if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We, Takeda and any of our potential future collaborators or CROs may fail to report adverse events within the prescribed timeframe. If we, Takeda or any of our potential future collaborators or CROs fail to comply with such reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval of future products. **Compliance** ~~Actual or perceived failures to comply~~ with applicable data protection, privacy and security laws, regulations, standards and other requirements **involves significant expenditure and resources, and any actual or perceived failures by us, our partners or vendors to comply** could adversely affect our business, results of operations, and financial condition. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous **federal,** state ~~, federal~~ and foreign laws, **regulations, standards and other** requirements ~~and regulations~~ governing the collection, use, disclosure, retention, ~~and~~ security **and other processing** of personal data, such as information that we may collect in connection with **our marketing activities in the U. S. and** clinical trials in the U. S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer **,** use ~~and ,~~ share **and otherwise process** personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws ~~or ,~~ regulations **or standards** , our internal policies and procedures or our contracts ~~governing~~ **relating to privacy, security or** our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties **, material penalties, significant legal liability, changes in how we operate** and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business. As our operations and business grow, we may become subject to or affected by new or additional data protection **, privacy and security** laws ~~and ,~~ regulations **, standards and other requirements,** and face increased scrutiny or attention from regulatory authorities. In the U. S., HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information **. While we are not a covered entity under HIPAA, we interact with healthcare providers regulated by HIPAA as covered entities** . Certain states have also adopted ~~comparable~~ **comprehensive and health- specific** privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. ~~In addition~~ **For example** , California enacted the CCPA on June 28, 2018, which went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of ~~entities~~ **covered businesses** handling ~~certain~~ personal information **about California residents** . It provides for civil penalties for violations, as well as a private right of action **and statutory damages** for **certain** data breaches ~~that is expected to increase data breach litigation. Further, the CPRA recently passed in California~~ . The CPRA ~~will impose~~ **amended the CCPA effective January 1, 2023, imposing** additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, ~~new audit requirements for higher risk data,~~ and opt outs for certain uses of sensitive data. It ~~will~~ also ~~create~~ **created** a new California data protection agency authorized to issue substantive regulations ~~and could~~ **, which will likely** result in increased privacy and ~~information security~~ **cybersecurity** enforcement ~~. The majority of the provisions will go into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required~~ . Similar laws ~~have passed~~ **are already** in **effect in other states including** Virginia, Connecticut, Colorado and Utah **,** and have been **enacted or** proposed in other states and at the federal level, reflecting a trend toward more stringent ~~privacy legislation~~

regulation in the United States **of the collection, use, disclosure and other processing of personal information** . The enactment of such laws ~~could have~~ **creates the potential for a patchwork of overlapping, but different and** potentially conflicting **,** requirements that ~~would~~ **may** make compliance challenging. In the event that we ~~are~~ **become** subject to ~~or affected by~~ HIPAA, the CCPA **and similar state** ~~, the CPRA or other domestic~~ privacy ~~and data protection~~ laws, **compliance will likely involve significant expenditure and resources, and** any ~~liability from~~ **failure or perceived** failure to comply with the requirements of these laws could adversely affect our **business, results of operations and** financial condition. Furthermore, the FTC and many state Attorneys General continue to enforce federal and state consumer protection laws against ~~companies for online collection, use, dissemination~~ **in relation to a variety of data privacy** and security ~~practices that appear~~ **issues, such as promises made in privacy policies or failures** to ~~be~~ **appropriately protect information about individuals, as** unfair or deceptive ~~. For example, according to the FTC, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair~~ acts or practices in or affecting commerce in violation of Section 5 (a) of the Federal Trade Commission Act **or similar state laws** . The FTC expects a company' s ~~data security~~ **cybersecurity** measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. ~~In~~ **Given our past sponsorship of clinical trials at sites in** Europe, **we are also subject to the European Union General Data Protection Regulation, or the EU** GDPR, ~~went into effect in May~~ **and to the United Kingdom General Data Protection Regulation and Data Protection Act** 2018 **, or collectively, the UK GDPR, (the EU GDPR** and **UK GDPR together referred to as the " GDPR ") which** ~~imposes~~ **impose** ~~strict requirements for~~ **comprehensive data privacy compliance obligations in relation to** processing the personal data of individuals within the EEA **and UK** . Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million **/ GBP 17. 5 million** or **up to** 4 % of the annual global revenues of the noncompliant company, whichever is greater. In addition, the GDPR increases the scrutiny of transfers of personal data from the EEA **and UK** to the United States and other jurisdictions that the European Commission does not recognize as having " adequate " data protection laws. **Case law** ~~In 2016, the EU and United States agreed to a transfer framework for data transferred~~ from the ~~EU to the United States called the Privacy Shield, but in July 2020 the~~ Court of Justice of the ~~EU~~ **European Union** , or ~~the~~ CJEU, ~~limited how organizations could lawfully transfer personal data from the EEA to the United States~~ **states that reliance** ~~by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions~~ on ~~use of~~ the standard contractual clauses ~~–~~ **a standard form** ~~, or SCCs. While the CJEU upheld the adequacy~~ of **contract approved by** ~~the SCCs, it made clear that reliance on them~~ **the European Commission as an adequate personal data transfer mechanism –** alone may not necessarily be sufficient in all circumstances **and that transfers** ~~. Use of the SCCs~~ must ~~now~~ be assessed on a case- by- case basis **. On October 7** ~~taking into account the legal regime applicable in the destination country~~ , ~~in particular applicable surveillance laws~~ **2022, President Biden signed** ~~and~~ **an Executive Order on ' Enhancing Safeguards** ~~rights of individuals and additional measures and / or~~ **for** ~~contractual provisions may need~~ **United States Intelligence Activities' which introduced new redress mechanisms and binding safeguards** to **address** ~~be put in place, however, the nature of these~~ **the concerns raised by the** ~~additional measures is currently uncertain. The~~ CJEU ~~went~~ **in relation to data transfers from the EEA to the United States and which formed the basis of the new EU- US Data Privacy Framework, or DPF, as released** on **December 13** ~~to state that if a competent supervisory authority believes that the SCCs cannot be complied with in the destination country and the required level of protection cannot be secured by other means~~ , **2022** ~~such supervisory authority is under an obligation to suspend or prohibit that transfer~~ . The European Commission ~~issued revised SCCs~~ **adopted its Adequacy Decision in relation to the DPF** on ~~June 4~~ **July 10** , ~~2021~~ **2023 , rendering** ~~to account for~~ the **DPF effective as** ~~decision of the CJEU and~~ **an** ~~recommendations made~~ **EU GDPR transfer mechanism to U. S. entities self- certified under the DPF. On October 12, 2023, the UK Extension to the DPF came into effect (as approved** by the **UK Government), as a UK GDPR** ~~European Data Protection Board. The revised SCCs must be used for relevant new~~ data ~~transfers~~ **transfer mechanism to U. S. entities self- certified under the UK Extension to the DPF. In the future, as applicable, we expect to rely on the DPF to transfer certain personal data** from ~~September 27, 2021; existing~~ **the EEA to the United States and on the UK Extension to the DPF to transfer certain personal data from the UK to the United States. In the past we have relied on EU** standard contractual clauses **and** ~~arrangements must be migrated to~~ the ~~revised~~ **UK Addendum to the EU standard contractual** clauses **as relevant** ~~by December 27, 2022. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers~~ to ~~non- EEA entities subject to the GDPR. The revised SCCs apply only to the~~ transfer ~~of~~ personal data outside ~~of~~ the EEA and ~~not~~ the UK ~~;~~ **with respect to third party transfers. We expect** the **existing legal complexity and uncertainty regarding international personal** ~~UK' s Information Commissioner' s Office launched a public consultation on its draft revised~~ data transfers ~~mechanisms in August 2021~~ **to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators** . As **the regulatory** ~~supervisory authorities issue further~~ guidance ~~on personal~~ **and enforcement landscape in relation to** data **transfers continue to develop** ~~export mechanisms, including circumstances where the SCCs cannot be used, and / or start taking enforcement action~~ , we could suffer additional costs, complaints and / or regulatory investigations or fines, **we may have to stop using certain tools and vendors and make other operational changes, we have had to and will have to implement revised standard contractual clauses for existing customer and vendor arrangements within required time frames,** and / or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. ~~The European Commission issued revised SCCs on June 4, 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board. The revised SCCs must be used for relevant new data~~

~~transfers from September 27, 2021; existing standard contractual clauses arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom; the United Kingdom' s Information Commissioner' s Office launched a public consultation on its draft revised data transfers mechanisms in August 2021. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non- EEA entities subject to the GDPR. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the SCCs cannot be used, and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.~~ Our internal ~~computer~~ **information** systems, or those of any of our CROs, **contract** manufacturers, service providers, other contractors or consultants or potential future collaborators, may fail or suffer ~~security~~ **cybersecurity incidents or** breaches, which could result in a material disruption of our product development programs. The United States federal and various state and foreign governments have adopted or proposed requirements regarding the collection, distribution, use, security, and storage of personally identifiable information and other data relating to individuals, and federal and state consumer protection laws are being applied to enforce regulations related to the online collection, use, and dissemination of data. Despite the implementation of ~~security~~ **cybersecurity** measures, our internal ~~computer~~ **information** systems and those of our current and any future CROs **, contract manufacturers,** and other service providers, contractors, consultants and collaborators are vulnerable to **numerous and evolving cybersecurity risks that threaten the confidentiality, integrity and availability of our information systems and confidential Information, including from diverse threat actors, such as state- sponsored organizations, opportunistic hackers and hacktivists, as well as through diverse attack vectors, such as social engineering / phishing, malware (including ransomware), malfeasance by insiders, human or technological error, and as a result of malicious code embedded in open- source software, or misconfigurations,' bugs' or other vulnerabilities in commercial software that is integrated into our (or our suppliers' or service providers') IT systems, products or services, alongside** damage from ~~computer viruses, cybersecurity threats, unauthorized access,~~ natural disasters, terrorism, war and telecommunication and electrical failures. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives ~~and~~ **,** expertise **, technique and tools – including artificial intelligence – to circumvent security controls, evade detection and remove forensic evidence** . ~~As~~ **For example, on February 22, 2024, UnitedHealth Group, or UHG, disclosed that** a **suspected nation** ~~result of the COVID- 19 pandemic~~ **state associated cyber security threat actor had gained access to some of the information technology systems at Change Healthcare** , ~~we may~~ **one of UHG' s affiliates that provides numerous services to the healthcare industry such as payment systems, claims submission, benefits verification, and prior authorization. This breach has, among other things, disrupted the processing of transactions under our patient co- pay assistance card program, and the ability of certain pharmacies to fill prescriptions, including prescriptions for VOQUEZNA. At present, UHG is unable to estimate the duration or extent of the disruption. If this disruption persists, it could have a material adverse effect on our business and financial condition. We** also face increased cybersecurity risks due to our reliance on internet technology and the increased number of our employees **(and employees of our vendors, contractors and other organizations with whom we have formed strategic relationships)** who are working remotely, which may create additional opportunities for ~~cybercriminals~~ **threat actors** to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience ~~security~~ **cybersecurity incidents or data** breaches that may remain undetected for an extended period. If such an event were to occur and cause interruptions in our operations ~~or~~ **,** result in the unauthorized **access to,** disclosure ~~of~~ **, loss, processing** or ~~access to other compromise of,~~ ~~personally- -~~ **personal** ~~identifiable~~ information or individually identifiable health information (violating certain privacy laws such as GDPR) **or confidential information, or jeopardize the confidentiality, integrity, or availability of our information systems or any information residing therein** , it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of **certain** ~~security~~ **cybersecurity** breaches involving particular ~~personally- -~~ **personal** ~~identifiable~~ information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Even though we may have contractual protections with such vendors, contractors, or other organizations, notifications and follow- up actions related to a ~~security~~ **cybersecurity** breach could impact our reputation, cause us to incur significant costs, including legal expenses, harm customer confidence, hurt our expansion into new markets, cause us to incur remediation costs, or cause us to lose existing customers. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. We also rely on third parties to manufacture vonoprazan and any future product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. **There can no assurance that our cybersecurity risk management program and processes, including our policies, controls or procedures, will be fully implemented, complied with or effective in protecting our information systems and personal or confidential Information.** To the extent that any disruption or ~~security~~ **cybersecurity** ~~breach~~ **incident** were to **jeopardize the confidentiality, integrity, or availability of our information systems, or** result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, the further development and commercialization of vonoprazan and any future product candidates could be delayed, and we could be subject to significant fines, penalties or liabilities for any noncompliance

to certain privacy and ~~security~~ **cybersecurity** laws. Our employees and independent contractors, including principal investigators, CROs, consultants and vendors, may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements. We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants and vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and / or negligent conduct or other unauthorized activities that violate: (i) the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies, (ii) manufacturing standards, including cGMP and similar requirements, or (iii) federal and state healthcare, security, fraud and abuse laws, data privacy and ~~security~~ **cybersecurity** laws, and other similar non- U. S. laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other U. S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non- compliance, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. We are subject to U. S. and certain foreign export and import controls, sanctions, embargoes, anti- corruption laws and anti- money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We could face criminal liability and other serious consequences for violations, which could harm our business. We are subject to export control and import laws and regulations, including the U. S. Export Administration Regulations, U. S. Customs regulations, and various economic and trade sanctions regulations administered by the U. S. Treasury Department' s Office of Foreign Assets Controls, and anti- corruption and anti- money laundering laws and regulations, including the U. S. Foreign Corrupt Practices Act of 1977, as amended, the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act, the USA PATRIOT Act, and other state and national anti- bribery and anti- money laundering laws in the countries in which we conduct activities. Anti- corruption laws are interpreted broadly and prohibit companies and their employees, agents, clinical research organizations, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We have engaged, and may engage in the future, third parties for clinical trials outside of the United States, and may engage third parties to sell our products abroad once we enter a commercialization phase, and / or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, clinical research organizations, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management. From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out- licensing or in- licensing of intellectual property, products or technologies, similar to our approach in in- licensing and acquiring our current product candidates. Any future transactions could increase our near and long- term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in- process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin- offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits of the acquisition. Accordingly, although we may not undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects. Risks Related to Our Intellectual Property Our success depends on our ability to protect our intellectual property and our proprietary technologies. Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for **our current products containing** vonoprazan and any future product candidates, proprietary technologies and their uses as well as our ability to operate without infringing upon the proprietary rights of others. If we are unable to protect our intellectual property rights or if our intellectual property rights are inadequate for our technology or vonoprazan or any future product candidates, our competitive position could be harmed. We generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to vonoprazan or any future product candidates, proprietary

technologies and their uses that are important to our business. We do not currently own any issued patents or pending patent applications. We also seek to protect our proprietary position by acquiring or in- licensing relevant issued patents or pending patent applications from third parties. We have in- licensed from Takeda a number of United States, European, and Canadian patents and patent applications relating to the compound vonoprazan as well as the use and manufacture of vonoprazan products. Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our future patent applications or the patent applications of our current and future licensors will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents if issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties and / or limitations in our ability to properly protect the intellectual property rights relating to vonoprazan and any future product candidates could have a material adverse effect on our financial condition and results of operations. We cannot be certain that the claims in our licensor' s U. S. pending patent applications, corresponding international patent applications and patent applications in certain foreign countries will be considered patentable by the United States Patent and Trademark Office, or USPTO, courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our licensor' s issued patents will not be found invalid or unenforceable if challenged. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting vonoprazan and any future product candidates by obtaining and defending patents. These risks and uncertainties include the following: • the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction; • patent applications may not result in any patents being issued; • patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage; • our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or block our ability to make, use and sell vonoprazan and any future product candidates; • there may be significant pressure on the U. S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and • countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing products. The patent prosecution process is also expensive and time consuming, and we and our licensor may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we and our licensor will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances such as under the Takeda License, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, directed to technology that we license from third parties. We may also require the cooperation of our licensors in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such applications. If they fail to do so, this could cause us to lose rights in any applicable intellectual property that we in- license, and as a result our ability to develop and commercialize products or product candidates may be adversely affected and we may be unable to prevent competitors from making, using and selling competing products. In addition, although we enter into non- disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third- party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, including our rights in vonoprazan licensed from Takeda, or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. We are a party to the Takeda License under which we are granted rights to intellectual property that are important to our business and we may enter into additional license agreements in the future with other third parties. The Takeda License imposes, and we expect that any future license agreements where we in- license intellectual property, will impose on us, various development, regulatory and / or commercial diligence obligations, payment of milestones and / or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy- related proceedings, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Additionally, if a future license agreement includes a sublicense from a third party who is not the original licensor of the intellectual property at issue, then we must rely on our direct licensor to comply with its obligations under the primary license agreements under which such licensor obtained rights in the applicable intellectual property, where we may have no relationship with the original licensor of such rights. If such a licensor fails to comply with its obligations under its upstream license agreement, the original third- party licensor may have the right to terminate the original license, which may terminate our sublicense. If this were to occur, we would no longer have rights to the applicable intellectual

property unless we are able to secure our own direct license with the owner of the relevant rights, which we may not be able to do on reasonable terms, or at all, which may impact our ability to continue to develop and commercialize vonoprazan and any future product candidates incorporating the relevant intellectual property. We may need to obtain further licenses from third parties to advance our research or allow commercialization of vonoprazan and any future product candidates, and we cannot provide any assurances that third- party patents do not exist which might be enforced against vonoprazan and any future product candidates in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • our right to sublicense patents and other rights to third parties; • our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of vonoprazan and any future product candidates, and what activities satisfy those diligence obligations; • our right to transfer or assign the license; and • the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business. In addition, certain of our agreements may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, if we choose to sublicense or assign to any third parties our rights under our existing license agreement with Takeda with respect to any licensed product, we may be required to wait for a certain period or until the occurrence of certain funding or development milestones. If the scope of any patent protection **or non- patent regulatory exclusivity** we obtain is not sufficiently broad, or if we lose **or fail to obtain** any of our patent protection **or non- patent regulatory exclusivity** , our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our in- licensed pending and future patent applications may not result in patents being issued which protect vonoprazan or any future product candidates or which effectively prevent others from commercializing competitive product candidates. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own in the future or license currently issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any future patents that we own or license, now or in the future, may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether vonoprazan or any future product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our future patents or the patents of our current and future licensors by developing similar or alternative technologies or products in a non- infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our future patents or the patents of our current and future licensors may not cover vonoprazan or any future product candidates or may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party pre- issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post- grant review, or PGR, and inter partes review, or IPR, or other similar proceedings in the USPTO or foreign patent offices challenging our patent rights. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we or our predecessors and the patent examiner were unaware during prosecution. There is no assurance that all potentially relevant prior art relating to our in- licensed patents and patent applications has been found. There is also no assurance that there is not prior art of which we, our predecessors or licensors are aware, but which we do not believe affects the validity or enforceability of a claim in our in- licensed patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize vonoprazan or any future product candidates and compete directly with us, without payment to us. It is possible that defects of form in the preparation or filing of our or our current and future licensors' patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If there are material defects in the form, preparation, prosecution, or enforcement of our future patents or future patent applications or our current and future licensors' patents or patent applications, such patents may be invalid and / or unenforceable, and such applications may never result in valid, enforceable patents. Any loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of vonoprazan or any future product candidates, which could materially and adversely impact our business. Such proceedings also

may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our future patents and future patent applications or the patents and patent applications of our current and future licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize vonoprazan or any future product candidates **. In addition to patent exclusivity, the successful commercialization of our products also depends, in part, on our ability to obtain and maintain periods of non- patent exclusivity during which time the FDA is precluded from accepting new drug applications, or NDAs, submitted under Section 505 (b) (2) of the FDCA or abbreviated new drug applications, or ANDAs, for certain competitive products. In May 2021, FDA granted qualified infectious disease product, or QIDP, designations to vonoprazan tablets in combination with both amoxicillin capsules and clarithromycin tablets, and with amoxicillin capsules alone, respectively, for the treatment of H. pylori infection. On May 3, 2022, the FDA approved our NDAs for these products, branded as VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, respectively. Because these approvals were for QIDP- designated drugs containing the active moiety, vonoprazan, which had not previously been approved, the FDA granted five- years of NCE exclusivity, which was extended by an additional five- years pursuant to the GAIN Act, resulting in a total of ten- years of NCE exclusivity, until May 3, 2032. In November 2023, we received approval for VOQUEZNA, which also contains vonoprazan. NCE exclusivity protects against the submission and the FDA' s acceptance of a 505 (b) (2) NDA or ANDA referencing that NCE for the duration of the exclusivity period, and the FDA interprets this form of exclusivity to attach to the active moiety such that the submission and the FDA' s acceptance of ANDAs and 505 (b) (2) NDAs for a drug with that active moiety may not occur until the innovator' s exclusivity has expired, whether or not FDA has approved other versions of the drugs entitled to exclusivity, and regardless of the specific listed drug product to which the ANDA or 505 (b) (2) application refers. Consequently, we believe that VOQUEZNA, because it contains vonoprazan, should benefit from the same extended period of NCE exclusivity granted in connection with our NDAs for VOQUEZNA DUAL PAK and VOQUEZNA TRIPLE PACK, until May 3, 2032. The FDA publication, " Approved Drug Products with Therapeutic Equivalence Evaluations, " referred to as the Orange Book, identifies that VOQUEZNA benefits from the same five- year period of NCE exclusivity as VOQUEZNA DUAL PAK and VOQUEZNA TRIPLE PAK, but does not currently identify the GAIN Act extension of an additional five- years of NCE exclusivity to which we believe it is entitled. We informally requested that the FDA correct the VOQUEZNA listings to reflect the same extended NCE exclusivity period as VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK. However, the FDA so far declined to update those listings. We are therefore further engaging with the FDA regarding VOQUEZNA' s Orange Book listings and the application to VOQUEZNA of the extended NCE exclusivity tied to vonoprazan. If the FDA ultimately concludes that the GAIN Act extension of NCE exclusivity granted in connection with our VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK NDAs does not extend to our VOQUEZNA NDA, there is the potential we could be subject to competition much earlier than we currently anticipate. If this occurs, it would have a material adverse effect on our business and financial condition** . The patent protection and patent prosecution for vonoprazan or any future product candidates may be dependent on third parties. We may rely on third parties to file and prosecute patent applications and maintain patents and otherwise protect the licensed intellectual property under certain current and future license agreements, such as the Takeda License. Under such arrangements, we may not have primary control over these activities for certain of licensed patents or patent applications and other intellectual property rights. We cannot be certain that such activities by third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents or other intellectual property rights. In addition, our current and future licensors may not be fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, which could compromise such patent rights. We may in the future enter into license agreements where the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. Even if we are not a party to these legal actions, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. If any of our licensors or any of our future licensors or future collaborators fail to appropriately prosecute and maintain patent protection for patents covering ~~vonoprazan~~ **VOQUEZNA** or any future product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control prosecution of patent applications or enforcement of patents we have acquired or licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our predecessors or licensors and their counsel that took place prior to us assuming control over such activities. Third parties may retain certain rights to the technology that they license to us, including the right to use the underlying technology for noncommercial academic and research use, to publish general scientific findings from research related to the technology, and to make customary scientific and scholarly disclosures of information relating to the technology. For example, under the Takeda License, Takeda retained the rights to the inventions in all countries other than the United States, Europe, and Canada. Takeda also retained the right to develop certain drug products that contain vonoprazan where vonoprazan is not the only active pharmaceutical ingredient. It is difficult to monitor whether our predecessors or licensors limit their use of the technology to these uses, and we could incur substantial expenses to enforce our rights to our licensed technology in the event of misuse. If we are limited in our ability to utilize acquired or licensed technologies, or if we lose our rights to critical in- licensed technology, we may be unable to successfully develop, out- license, market and sell our products, which could prevent or delay new product introductions. Our business strategy depends on the successful development of licensed and acquired technologies into commercial products.

Therefore, any limitations on our ability to utilize these technologies may impair our ability to develop, out- license or market and sell our product candidate. Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to develop products that are similar to ~~vonoprazan~~ **VOQUEZNA** or any future product candidates but that are not covered by the claims of the patents that we own in the future or license; • we or our current and future licensors or predecessors might not have been the first to make the inventions covered by the issued patents or patent applications that we own in the future or license; • we or our current and future licensors or predecessors might not have been the first to file patent applications covering certain of the claimed inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that the pending patent applications we own or license will not lead to issued patents; • issued patents that we own in the future or license may be held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; and • the patents of others may have an adverse effect on our business. Should any of these events occur, it could significantly harm our business, results of operations and prospects. Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts. Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import ~~vonoprazan~~ **VOQUEZNA** and any future product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and / or foreign patent offices. Numerous third- party U. S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third- party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of ~~vonoprazan~~ **VOQUEZNA** and any future product candidates. As the biopharmaceutical industry expands and more patents are issued, the risk increases that ~~vonoprazan~~ **VOQUEZNA** and any future product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published we may be unaware of third- party patents that may be infringed by commercialization of ~~vonoprazan~~ **VOQUEZNA** and any future product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that ~~vonoprazan~~ **VOQUEZNA** and any future product candidates may infringe. In addition, identification of third- party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Any claims of patent infringement asserted by third parties would be time consuming and could: • result in costly litigation that may cause negative publicity; • divert the time and attention of our technical personnel and management; • cause development delays; • prevent us from commercializing **, or continuing to commercialize, VOQUEZNA (and / or other approved products containing** vonoprazan **),** and any future product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law; • require us to develop non- infringing technology, which may not be possible on a cost- effective basis; • subject us to significant liability to third parties; or • require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology. Although no third party has asserted a claim of patent infringement against us as of the date of this annual report, others may hold proprietary rights that could prevent ~~vonoprazan~~ **VOQUEZNA** and any future product candidates from being marketed. Any patent- related legal action against us claiming damages and seeking to enjoin activities relating to ~~vonoprazan~~ **VOQUEZNA** and any future product candidates or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or develop ~~vonoprazan~~ **VOQUEZNA** and any future product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign ~~vonoprazan~~ **VOQUEZNA** and any future product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing ~~vonoprazan~~ **VOQUEZNA** and any future product candidates, which could harm our business, financial condition and operating results. Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative

proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. We may not be successful in obtaining or maintaining necessary rights to ~~vonoprazan~~ **our current products** and any future product candidates through acquisitions and in- licenses. Because our development programs may in the future require the use of proprietary rights held by other third parties, the growth of our business may depend in part on our ability to acquire, in- license, or use these third- party proprietary rights. We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify as necessary for ~~vonoprazan~~ **our current products, including VOQUEZNA,** and any future product candidates. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third- party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third- party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer. We may be involved in lawsuits to protect or enforce our future patents or the patents of our current and future licensors, which could be expensive, time consuming and unsuccessful. Further, our future issued patents or the patents of our current and future licensors could be found invalid or unenforceable if challenged in court. Competitors may infringe our intellectual property rights or those of our current and future licensors. To prevent infringement or unauthorized use, we and / or any such licensors may be required to file infringement claims, which can be expensive and time consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own or license is not valid, is unenforceable and / or is not infringed. If we or any of our current and future licensors were to initiate legal proceedings against a third party to enforce a patent directed at ~~vonoprazan~~ **VOQUEZNA** and any future product candidates, the defendant could counterclaim that our patent or the patent of our current or future licensor is invalid and / or unenforceable in whole or in part. In patent litigation, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, non- enablement, or obviousness- type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our future patents and future patent applications or those of our current and future licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline. During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business. Derivation or interference proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party. Derivation or interference proceedings provoked by third parties or brought by us or declared by the USPTO or similar proceedings in foreign patent offices may be necessary to determine the priority of inventions with respect to our future patents or future patent applications or those of our current and future licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of such proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our **commercial activities,** clinical trials ~~, continue our research programs~~ , license necessary technology from third parties or enter into development or manufacturing partnerships that would help us **continue commercializing our current products and** bring ~~vonoprazan and~~ any future product candidates to market. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our future patent applications or those of our current and future licensors and the enforcement or defense of our future issued patents or those of

our current and future licensors. On September 16, 2011, the Leahy- Smith America Invents Act, or Leahy- Smith Act, was signed into law. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy- Smith Act, the United States transitioned in March 2013 to a " first inventor to file " system in which, assuming that other requirements of patentability are met, the first inventor to file a patent application will be entitled to the patent regardless of whether a third party was first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013 but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we may not be certain that we or our current and future licensors are the first to either (1) file any patent application related to ~~vonoprazan~~ **VOQUEZNA** and any future product candidates or (2) invent any of the inventions claimed in the patents or patent applications. The Leahy- Smith Act also includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post- grant proceedings, including PGR, IPR, and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our future patent applications or those of our current and future licensors and the enforcement or defense of our future issued patents or those of our current and future licensors, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. In 2012, the European Patent Package, or EU Patent Package, regulations were passed with the goal of providing a single pan- European Unitary Patent and a new European Unified Patent Court, or UPC, for litigation involving European patents. Implementation of the EU Patent Package ~~will likely occur~~ **occurred on June 1,** ~~in the first half of~~ 2023. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, will by default automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan- European injunctions **. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize our technology and product candidates and, resultantly, on our business, financial condition, prospects and results of operations** . It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Under the EU Patent Package as currently proposed, we will have the right to opt our patents out of the UPC over the first seven years of the court' s existence, but doing so may preclude us from realizing the benefits of the new unified court. **Moreover, if we do not meet all of the formalities and requirements for opt- out under the UPC, our future European patents could remain under the jurisdiction of the UPC.** Changes in U. S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect ~~vonoprazan~~ **our current products** and any future product candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our future patents or in third- party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. Evolving judicial interpretation of patent law could also adversely affect our business. For example, the U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the U. S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce the existing licensed patents and the patents we might obtain or license in the future. We may be subject to claims challenging the inventorship or ownership of our future patents, the patents of our current and future licensors, or other intellectual property. We may also be subject to claims that former employees or other third parties have an ownership interest in our future patents, the patents of our current and future licensors or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees. Patent terms may be inadequate to protect our competitive position on ~~vonoprazan~~ **VOQUEZNA** and any future product candidates for an adequate amount of time. Patents have a limited lifespan. In

the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non- provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering ~~vonoprazan~~ **our current products including VOQUEZNA** and any future product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of product candidates, patents protecting ~~vonoprazan~~ **our current products** and any future product candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If we do not obtain patent term extension for ~~vonoprazan~~ **our current products** and any future product candidates, our business may be materially harmed. ~~Depending upon~~ **Based on** the **first** ~~timing, duration and specifics of FDA~~ marketing approval ~~of~~ **by the FDA for** vonoprazan ~~and any future product candidates~~, **we believe** one or more of our U. S. patents or those of our current and future licensors, may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch- Waxman Amendments. The Hatch- Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of vonoprazan and any future product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. We may not be able to protect our intellectual property rights throughout our licensed territories. Although we have issued patents and pending patent applications in the United States and certain other countries in which we intend to commercialize our products, filing, prosecuting and defending patents in all relevant countries throughout our licensed territories could be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with ~~vonoprazan~~ **VOQUEZNA** or any future product candidates, and our patents, the patents of our current and future licensors or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our intellectual property rights or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our future patents or the patents of our current and future licensors at risk of being invalidated or interpreted narrowly and our future patent applications or the patent applications of our current and future licensors at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected. Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our future patents and / or future applications and those of our current and future licensors. We have systems in place to remind us to pay these fees, and we rely on third parties to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business. If we are unable to protect the confidentiality of our trade

secrets, our business and competitive position would be harmed. In addition, we rely on the protection of our trade secrets, including unpatented know- how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know- how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. **We may need to share our trade secrets and proprietary know- how with current or future partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and other countries.** Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to protect our trade secret information may be jeopardized. We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers. As is common in the biopharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of vonoprazan and any future product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biopharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations. Any collaboration arrangements that we have or may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our products. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators and partners. Under the Takeda License, for example, Takeda ~~has~~ **had** certain obligations with respect to assisting with the transition of information and materials to us as well as providing clinical and commercial supply of the vonoprazan product. Collaborations and partnerships are subject to numerous risks, which may include that: • collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations; • collaborators may not pursue development and commercialization of our products or may elect not to continue or renew development or commercialization programs based on trial or test results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates; • a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities; • we could grant exclusive rights to our collaborators that would prevent us from collaborating with others; • collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability; • disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources; • collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products; • collaborators may own or co- own intellectual property

covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and • a collaborator' s sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings. Intellectual property discovered through government funded programs may be subject to federal regulations such as " march- in " rights, certain reporting requirements and a preference for U. S.- based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non- U. S. manufacturers. We may acquire or license in the future intellectual property rights that have been generated through the use of U. S. government funding or grant. Pursuant to the Bayh- Dole Act of 1980, the U. S. government has certain rights in inventions developed with government funding. These U. S. government rights include a non- exclusive, non- transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as " march- in rights "). The U. S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U. S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U. S. industry may limit our ability to contract with non-U. S. product manufacturers for products covered by such intellectual property. Risks Related to Our Common Stock The trading price of the shares of our common stock has been, and is likely to continue to be, highly volatile, and purchasers of our common stock could incur substantial losses. The stock market in general and the market for stock of biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price at which they paid. Our common stock has a limited trading history and the market price has fluctuated widely, and may in the future fluctuate widely, depending upon many factors such as those discussed in this " Risk Factors " section and many others, some of which are beyond our control, including the following: • a relatively low- volume trading market for our shares of common stock that could cause trades of small blocks of shares to have a significant impact on the price of our shares of common stock; • market conditions in the biopharmaceutical sector and issuance of securities analysts' reports or recommendations; • establishment of short positions by holders or non- holders of our common stock; • an inability to obtain additional funding; • sales of our stock by insiders and stockholders, including Takeda; • our ability to enroll patients in our ongoing and any future clinical trials; • results of our clinical trials and preclinical studies, the results of clinical trials conducted by Takeda and others for vonoprazan, and the results of trials of our competitors or those of other companies in our market sector; • **additional** regulatory ~~approval~~ **approvals** of vonoprazan and **approvals of** any future product candidates, or limitations to specific label indications or patient populations for ~~its~~ use **of any approved products** , or changes or delays in the regulatory review process; • any termination or loss of rights under the Takeda License; • regulatory developments in the United States and foreign countries; • changes in the structure of healthcare payment systems, especially in light of reforms to the U. S. healthcare system; • the success or failure of our efforts to acquire, license or develop additional product candidates; • innovations or new products developed by us or our competitors; • announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments; • manufacturing, supply or distribution delays or shortages; • any changes to our relationship with any manufacturers, suppliers, licensors, future collaborators or other strategic partners; • achievement of expected product sales and profitability; • variations in our financial results or those of companies that are perceived to be similar to us; • general economic, industry and market conditions, public health emergencies or other events or factors, many of which are beyond our control; • additions or departures of key personnel; • intellectual property, product liability or other litigation against us; • changes in our capital structure, such as future issuances of securities and the incurrence of additional debt; and • changes in accounting standards, policies, guidelines, interpretations or principles. In addition, in the past, stockholders have initiated class action lawsuits against biopharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management' s attention and resources, which could have a material adverse effect on our business, financial condition and results of operations. Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval. Furthermore, many of our current directors were appointed by our principal stockholders. Our executive officers, directors and greater than 5 % stockholders, in the aggregate, own a majority of our outstanding common stock. As a result, such persons acting together have the ability to control or significantly influence all matters submitted to our board of directors or stockholders for approval, including the appointment of our management, the election and removal of directors and approval of any significant transaction, as well as our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders. We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common

stock. We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, under the terms of the Loan Agreement, we are prohibited from paying any cash dividends without the consent of the lenders. Any return to stockholders will therefore be limited to the appreciation of their stock. Shares of our common stock may not appreciate in value or even maintain the price at which stockholders have purchased their shares. Sales of a substantial number of shares of our common stock by our existing stockholders, including Takeda, in the public market could cause our stock price to fall. Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities. As of December 31, ~~2022~~ **2023 , Takeda owned 7, 459, 286 shares of common stock that are eligible for sale in the public market to the extent permitted by Rule 144 under the Securities Act. In addition, as of December 31, 2023** , up to ~~8~~ **9** , ~~780~~ **378** , ~~741~~ **875** shares of common stock that are either subject to outstanding options, warrants or other rights or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, exercise limitations, and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. Further, we filed a registration statement, which became effective on November 17, ~~2020~~ **2023** , registering the resale of up to ~~14~~ **5** , ~~499~~ **827** , ~~416~~ **415** shares of common stock held by ~~Takeda and~~ Frazier Life Sciences IX, L. P., or Frazier ~~, including all shares of our common stock underlying the Takeda Warrant, which warrant has since been exercised in full~~ . As a result of the registration statement, ~~Takeda and~~ Frazier **is** ~~are each~~ able to freely sell some or all of ~~their~~ **its** shares of our common stock. Any sales by these stockholders could have a material adverse effect on the trading price of our common stock. We are an emerging growth company and a smaller reporting company, and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting company may make our common stock less attractive to investors. We are an emerging growth company, as defined in the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the completion of our IPO. However, if certain events occur prior to the end of such five- year period, including if we become a " large accelerated filer " as defined in Rule 12b- 2 under the Exchange Act, our annual gross revenues exceed $ 1. 235 billion or we issue more than $ 1 ~~. 0~~ billion of non- convertible debt in any three- year period, we will cease to be an emerging growth company prior to the end of such five- year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include: • being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced " Management' s Discussion and Analysis of Financial Condition and Results of Operations " disclosure; • not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting pursuant to the Sarbanes- Oxley Act; • not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements, unless the SEC, determines the new rules are necessary for protecting the public; • reduced disclosure obligations regarding executive compensation; and • exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. Investors may find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. We are also a smaller reporting company as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non- voting common stock held by non- affiliates is less than $ 250 ~~. 0~~ million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $ 100 ~~. 0~~ million during the most recently completed fiscal year and our voting and non- voting common stock held by non- affiliates is less than $ 700 ~~. 0~~ million measured on the last business day of our second fiscal quarter. Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management. Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following: • a classified board of directors with three- year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors; • no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates; • the exclusive right of our board of directors, unless the board of directors grants such right to the stockholders, to elect a director 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; • the required approval of at least 66- 2 / 3 % of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause; • the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a

hostile acquiror; • the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval; • the required approval of at least 66- 2 / 3 % of the shares entitled to vote to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors; • a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders; • an exclusive forum provision providing that the federal district courts will be the exclusive forum for actions and proceedings a cause of action arising under the Securities Act of 1933, as amended, and that the Court of Chancery of the State of Delaware will be the exclusive forum for certain other actions and proceedings; • the requirement that a special meeting of stockholders may be called only by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and • advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror' s own slate of directors or otherwise attempting to obtain control of us. We are also subject to the anti- takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15 % or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction. Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf under Delaware statutory or common law, including any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided, that, this provision would not apply to suits brought to enforce a duty or liability created by the Securities Act or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. The choice of forum provisions in our amended and restated certificate of incorporation may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. By agreeing to these provisions, however, stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder. Furthermore, the enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable. If a court were to find the choice of forum provisions in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. Our ability to use net operating loss carryforwards and other tax attributes may be limited. We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward **and, subject** to **limitations,** offset future taxable income, if any, until such unused losses expire (if at all). Under **prevailing** ~~recently enacted~~ U. S. tax ~~legislation~~ **law** , federal net operating loss, or NOL, carryforwards generated in periods after December 31, 2017, may be carried forward indefinitely but may only be used to offset 80 % of our taxable income annually. Our NOL carryforwards are subject to review and possible adjustment by the Internal Revenue Service, or the IRS, and state tax authorities. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, our federal NOL carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three- year period in excess of 50 percentage points. Our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities may be limited as a result of ownership changes, including ~~potential~~ changes in connection with our IPO or future offerings. Similar rules may apply under state tax laws. We have not yet determined the amount of the cumulative change in our ownership resulting from our IPO or other transactions, or any resulting limitations on our ability to utilize our NOL carryforwards and other tax attributes. If we earn taxable income, such limitations could result in increased future tax liability to us and our future cash flows could be adversely affected. We have recorded a full valuation allowance related to our NOLs and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets. Recent U. S. tax legislation may materially adversely affect our financial condition, results of operations and cash flows. The Tax **Cuts and Jobs** Act **of 2017** has significantly changed the U. S. federal income taxation of U. S. corporations, including by reducing the U. S. corporate income tax rate and revising the rules governing NOLs. Many of these changes became effective beginning in 2018, without any transition periods or grandfathering for existing transactions. The legislation is unclear in many respects and may continue to be subject to potential amendments and technical corrections, as well as interpretations and implementing regulations by the U. S. Treasury Department and the IRS, which have lessened or increased certain adverse impacts of the legislation and may do so in the future. We continue to work with our tax advisors to determine the full impact that the recent tax legislation as a whole will have on us. We urge our investors to consult with their legal and tax advisors with respect to such legislation and the potential tax consequences of investing in our common stock. General Risk Factors Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses. Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical

epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self- insured. We rely **, and expect to continue to rely,** on third- party manufacturers to produce vonoprazan **, including VOQUEZNA, VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK** and any future product candidates. Our ability to obtain clinical supplies of vonoprazan and any future product candidates could be disrupted if the operations of these suppliers were affected by a **manmade** ~~man- made~~ or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. Our failure to meet the continued listing requirements of the Nasdaq could result in a delisting of our common stock. If we fail to satisfy the continued listing requirements of the Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, any action taken by us to restore compliance with listing requirements may not allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non- compliance with Nasdaq' s listing requirements. We incur significant costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives. As a public company, we incur significant legal, accounting and other expenses ~~that we did not incur as a private company~~. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes- Oxley Act, as well as rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes- Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd- Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC has adopted additional rules and regulations in these areas, such as mandatory " say on pay " voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The costs we incur as a public company will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage in the future. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline. The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. If securities or industry analysts do not continue coverage of our company, the trading price for our stock would be negatively impacted. In addition, if one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline. If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in our financial reporting and the trading price of our common stock may decline. Pursuant to Section 404 of Sarbanes- Oxley, our management is required to report upon the effectiveness of our internal control over financial reporting. When we lose our status as an " emerging growth company " and reach an accelerated filer threshold, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we are in the process of implementing additional financial and management controls, reporting systems and procedures; and hiring additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting and the trading price of our common stock may decline. There could be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begin its Section 404 reviews, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets. We could be subject to securities class action litigation. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us, because we, like many other biotechnology and pharmaceutical companies, have recently experienced significant stock price volatility. If we face such

litigation, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. ~~142~~ **108**