UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

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

For the transition period from _____ to

Commission file number: 001-39094

PHATHOM PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**82-4151574**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
100 Campus Drive, Suite 102 Florham Park, New Jersey	**07932**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (877) 742-8466

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	**PHAT**	**The Nasdaq Global Select Market**

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

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

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

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

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

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

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

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

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

As of June 30, 2021, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $684.2 million, based on the closing price of the registrant's common stock on the Nasdaq Global Select Market of $33.85 per share.

As of February 24, 2022, the registrant had 31,712,742 shares of common stock ($0.0001 par value) outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain sections of the registrant's definitive proxy statement for the 2022 annual meeting of stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K are incorporated by reference into Part III of this Form 10-K.

PHATHOM PHARMACEUTICALS, INC.

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PART I

This annual report on Form 10-K contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this annual report, including statements regarding our future results of operations and financial position, business strategy, research and development plans and costs, the timing and likelihood of regulatory filings and approvals, commercialization plans, pricing and reimbursement, the potential to develop future product candidates, the timing and likelihood of success of the plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This annual report on Form 10-K also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this annual report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, operating results, business strategy, and short term and long term business operations and objectives. These forward-looking statements speak only as of the date of this annual report and are subject to a number of risks, uncertainties and assumptions, including those described in Part I, Item 1A, “Risk Factors.” The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

This annual report includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this annual report appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and tradenames.

We maintain a website at www.phathompharma.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission, or SEC, are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this report or our other filings with the SEC.

Item 1. Business

Overview

We are a late clinical-stage biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal, or GI, diseases. Our initial product candidate, vonoprazan, is an oral small molecule potassium-competitive acid blocker, or P-CAB. P-CABs are a novel class of medicines that block acid secretion in the stomach. Vonoprazan has shown rapid, potent, and durable anti-secretory effects and has demonstrated clinical benefits over the current standard of care as a single agent in the treatment of gastroesophageal reflux disease, or GERD, and in combination with antibiotics for the treatment of *Helicobacter pylori*, or *H. pylori*, infection. Takeda Pharmaceutical Company Limited, or Takeda, developed vonoprazan and has received marketing approval in numerous countries in Asia and Latin America as well as Russia. Vonoprazan generated approximately $850 million in net sales in its seventh full year on the market since its approval in Japan in late 2014. In May 2019, we in-licensed the U.S., European, and Canadian rights to vonoprazan from Takeda.

In 2021 we reported topline data from two pivotal Phase 3 clinical trials for vonoprazan: one for the treatment of *H. pylori* infection, or PHALCON-HP, and a second for the treatment of erosive GERD, also known as erosive esophagitis or EE, or PHALCON-EE. In April 2021, we reported positive topline data from PHALCON-HP, and in October 2021, we reported positive topline data from PHALCON-EE. These data are supplemented by the extensive existing clinical data generated by Takeda as part of their development program for vonoprazan in Japan and other markets. In September 2021, we submitted two new drug applications, or NDAs, for the use of vonoprazan in combination with amoxicillin and clarithromycin (vonoprazan triple therapy) and vonoprazan in combination with amoxicillin (vonoprazan dual therapy) for the treatment of *H. pylori* in adults, and in November 2021, the U.S. Food and Drug Administration, or FDA, accepted both NDAs for filing, granted each of them Priority Review, and assigned us a Prescription Drug User Fee Act, or PDUFA, action date of May 3, 2022. Based on the results of the PHALCON-EE trial, we expect to submit an NDA for vonoprazan for the healing of all grades of erosive esophagitis and relief of heartburn, and maintenance of healing of all grades of erosive esophagitis and relief of heartburn in March 2022. In August 2019, we received Qualified Infectious Disease Product, or QIDP, and Fast Track designations from the FDA, for vonoprazan tablets in combination with amoxicillin tablets and clarithromycin tablets and with amoxicillin tablets alone for the treatment of *H. pylori* infection. In January 2021 and May 2021, respectively, we received additional Fast Track and QIDP designations to include amoxicillin capsules in addition to amoxicillin tablets. QIDP designation provides potential extension of any regulatory exclusivity awarded, if approved. We have also initiated development of vonoprazan for the treatment of symptomatic non-erosive GERD, or NERD. In February 2022, we commenced enrollment of patients in a Phase 3 trial studying vonoprazan, dosed on a once-daily basis, for the treatment of NERD, with topline data expected in 2023. Also in February 2022, we reported positive topline data from a Phase 2 trial studying vonoprazan for on-demand treatment of NERD. Vonoprazan has the potential to be the first gastric anti-secretory agent from a novel class approved in the United States, Europe, or Canada in over 30 years.

If approved, we plan to independently commercialize vonoprazan in the United States. We also plan to seek commercial partnerships for vonoprazan in Europe and Canada, expand development of vonoprazan into other indications, dosing regimens and alternative formulations and packaging, and in-license or acquire additional clinical or commercial stage product candidates for the treatment of GI diseases in a capital efficient manner.

GERD and *H. pylori* infection are two of the most common acid-related GI diseases and impact millions of people. The prevalence of GERD is estimated to be 20% of the U.S. population and 15% of the population in the five major countries in Europe (France, Germany, Italy, Spain and the United Kingdom) (collectively, the "EU5"). GERD is a disease that develops when the reflux of acidic stomach contents causes troublesome symptoms and/or complications. Approximately 30% of GERD patients have erosive esophagitis. *H. pylori* is a bacterial pathogen that infects approximately 35% of the U.S. population and 45% of the EU5 population. As a result of the chronic inflammation induced by *H. pylori* infection, approximately 20% of infected patients will develop a range of pathologies, including dyspepsia, peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma.

Over the last thirty years, the proton pump inhibitor, or PPI, class, has been the standard of care for the treatment of acid-related GI diseases. PPIs are generally used as a single agent for the treatment of GERD and in combination with antibiotics for the treatment of *H. pylori* infection. The PPI class includes drugs such as Prilosec (omeprazole), Nexium (esomeprazole), and Prevacid (lansoprazole). Prior to the introduction of generic and over-the-counter, or OTC, alternatives, annual PPI class sales reached approximately $12.5 billion in the United States, and peak sales for individual brands were approximately $3.7 billion for Prilosec, $3.5 billion for Nexium, and $3.4 billion for Prevacid in the United States.

While PPIs are the current standard of care and have experienced significant commercial success, they have significant limitations that result in a large unmet medical need. In GERD, PPI therapy is suboptimal for many patients due to the slow onset and insufficient duration of acid control which can lead to inadequate symptom relief. Approximately 15% to 45% of GERD patients remain inadequately treated with PPIs. In the treatment of *H. pylori* infection, the standard of care consists of a combination of a PPI and at least two oral antibiotics. However, increasing antibiotic resistance has resulted in declining eradication rates with PPI-based therapy. We believe these unmet medical needs are in part driven by limitations associated with the mechanism of action and pharmacokinetics of PPIs.

PPIs reduce gastric acid secretion by irreversibly binding to and inhibiting active proton pumps expressed on the parietal cells. PPIs require activation by gastric acid, but they are unstable in the presence of acid. This instability, combined with the short circulating half-life of PPIs, limits their efficacy. Additionally, because proton pumps continuously switch between active and inactive states, multiple doses of PPIs are required to inhibit enough proton pumps to achieve a clinical benefit. As a result, PPIs have a relatively slow onset of action and limited potency and duration of effect, which may result in patients experiencing only partial relief, increasing PPI dosage, and/or cycling through multiple PPIs seeking relief.

Vonoprazan has a differentiated mechanism of action from PPIs. Unlike PPIs, vonoprazan:

- does not require activation by gastric acid;
- is stable in the presence of acid;
- is designed to selectively concentrate in the parietal cells in both the resting and stimulated states, bind to the active pumps and remain associated with the active and inactive pumps;
- binds to the pumps in a noncovalent and reversible manner; and
- has a long plasma half-life that replenishes the drug at the site of action over the course of the day.

These factors have enabled vonoprazan to demonstrate more rapid and potent acid suppression versus the PPIs esomeprazole and lansoprazole in human subjects two hours after oral dosing and maintain target acid inhibition over a 24-hour period in randomized, open-label, crossover clinical trials. In contrast, PPIs require three to five days to reach steady state acid suppression and do not reliably maintain target acid inhibition over a 24-hour period. In addition, vonoprazan demonstrated approximately 10-to-100-fold better acid control compared to lansoprazole and esomeprazole.

We believe that vonoprazan’s anti-secretory profile may demonstrate clinically meaningful advantages over PPIs, such as:

- faster, more complete, and more durable healing of erosive esophagitis;
- faster, more complete, and more durable control of GERD symptoms;
- higher *H. pylori* eradication rates in combination with antibiotics compared to standard of care triple therapy and the potential for antibiotic-sparing dual therapy; and
- more flexible dosing, including dosing independent of food and time of day, and, in the treatment of patients with non-erosive esophagitis, the potential for rapid symptom relief through on-demand dosing.

Vonoprazan has demonstrated clinical advantages over the PPI lansoprazole in the treatment of erosive esophagitis and *H. pylori* infection in completed Phase 3 clinical trials conducted in the United States, Europe, Japan and other Asian countries.

Erosive esophagitis. In PHALCON-EE, a Phase 3 clinical trial conducted in the United States and Europe assessing vonoprazan versus lansoprazole in the healing and maintenance of healing of erosive esophagitis, vonoprazan met its primary healing endpoint demonstrating non-inferiority to lansoprazole in the number of patients who showed complete healing of erosive esophagitis after eight weeks of treatment. Further, in a pre-specified secondary endpoint, vonoprazan demonstrated superior healing after two weeks of treatment in patients with moderate to severe erosive esophagitis compared to lansoprazole. After two weeks of treatment, 70% of patients with moderate to severe erosive esophagitis were healed after treatment with vonoprazan versus 53% with lansoprazole (p=0.0004). In the maintenance phase of the trial both doses of vonoprazan (10 mg and 20 mg) met the primary endpoint of non-inferiority compared to lansoprazole in the number of all patients who maintained healing of erosive esophagitis through week 24. Further, both vonoprazan doses also met a pre-specified secondary endpoint demonstrating superiority of maintenance of healing versus lansoprazole (79% for vonoprazan 10 mg, 81% for vonoprazan 20 mg compared to 72% for lansoprazole 15 mg) (p<0.0001 for both non-inferiority comparisons; p=0.0218 for vonoprazan 10 mg superiority comparison; p=0.0068 for vonoprazan 20 mg superiority comparison). Both vonoprazan doses also met the pre-specified secondary endpoint of demonstrating superiority of the percentage of patients with moderate-to-severe disease who maintained healing of erosive esophagitis through week 24 (75% vonoprazan 10 mg, 77% vonoprazan 20 mg v. 61% lansoprazole 15 mg) (p=0.0245 for vonoprazan 10 mg superiority comparison; p=0.0098 for vonoprazan 20 mg superiority comparison).

In PHALCON-EE, vonoprazan 20 mg met the secondary endpoint of showing non-inferiority to lansoprazole 30 mg in the mean percentage of 24-hour heartburn free days over the healing period, and both vonoprazan doses met the secondary endpoint of showing non-inferiority to lansoprazole 15 mg in the mean percentage of 24-hour heartburn free days over the maintenance period. Finally, vonoprazan 20 mg was also compared to lansoprazole 30 mg in a superiority test for onset of sustained resolution of heartburn by day 3 of the healing phase but did not achieve statistical significance (p=0.2196).

A p-value is the probability that the reported result was achieved purely by chance, such that a p-value of less than or equal to 0.05 or 0.01 means that there is a 5.0% or 1.0% or less probability, respectively, that the difference between the control group and the treatment group is purely due to chance. A p-value of 0.05 or less typically represents a statistically significant result.

The results from PHALCON-EE were consistent with the results of four Phase 3 clinical trials previously conducted by Takeda, two in each of Japan and China, assessing vonoprazan versus lansoprazole in the healing and maintenance of healing of erosive esophagitis in which vonoprazan met its primary endpoint in demonstrating non-inferiority to lansoprazole.

Non-erosive esophagitis. In PHALCON-NERD, a Phase 2 study evaluating three doses of vonoprazan (10 mg, 20 mg, and 40 mg) as an on-demand therapy for relief of episodic heartburn in subjects with NERD, all three vonoprazan doses successfully met the primary endpoint evaluating the percentage of heartburn episodes completely relieved within three hours with relief sustained for over 24 hours and were statistically significant (p<0.0001) when compared to placebo. Within three hours, vonoprazan 10 mg, 20 mg, and 40 mg achieved complete and sustained relief in 56.0%, 60.6% and 70.0% of evaluable heartburn episodes, respectively, as compared to 27.3% of episodes for placebo. An evaluable heartburn episode is a heartburn episode for which the participant completes a minimum of one timed assessment after taking study medication.

In February 2022, we initiated a Phase 3 study evaluating vonoprazan 10 mg and 20 mg as daily dosing, or QD, therapy for the treatment of NERD, and we expect topline results from this study in 2023. Further, based on the positive Phase 2 NERD on-demand data, we plan to discuss with the FDA a Phase 3 trial design to support the novel dosing regimen for vonoprazan as an on-demand treatment for episodic heartburn relief in patients with NERD, a dosing treatment regimen not approved in the U.S. for PPIs.

H. pylori. We also conducted PHALCON-HP, a Phase 3 clinical trial in the United States and Europe studying two vonoprazan-based treatment regimens for the eradication of *H. pylori* infection, both of which successfully met their primary endpoints and all secondary endpoints. The trial studied vonoprazan triple therapy and vonoprazan dual therapy compared to lansoprazole in combination with amoxicillin and clarithromycin, or lansoprazole triple therapy. The objective of the PHALCON-HP trial was to compare eradication rates in all treated subjects as well as in two pre-identified subgroups of patients: those patients with clarithromycin resistant strains of *H. pylori*, and those patients who did not have clarithromycin or amoxicillin resistant strains of *H. pylori.* For regulatory purposes, the primary endpoint of this study was a non-inferiority comparison in the non-resistant subgroup for each of vonoprazan triple therapy and vonoprazan dual therapy compared to lansoprazole triple therapy.

In PHALCON-HP, both vonoprazan-based regimens successfully met their primary endpoints. In the modified intent-to-treat (mITT) population, *H. pylori* eradication rates were 84.7% for vonoprazan triple therapy and 78.5% for vonoprazan dual therapy compared to 78.8% with lansoprazole triple therapy ($p<0.0001$ and $p=0.0037$, respectively, for non-inferiority). In the pre-specified per protocol population, a subset of the mITT population comprised of patients who were protocol compliant, *H. pylori* eradication rates were 90.4% with vonoprazan triple therapy and 81.2% with vonoprazan dual therapy compared to 82.1% with lansoprazole triple therapy ($p<0.0001$ and $p=0.0077$, respectively, for non-inferiority).

In PHALCON-HP vonoprazan triple therapy and vonoprazan dual therapy also met all secondary endpoints, demonstrating superior eradication rates versus lansoprazole triple therapy in all patients and in the subgroup of patients with clarithromycin resistant strains of *H. pylori*. Among all patients, the *H. pylori* eradication rate of vonoprazan triple therapy was superior to that of lansoprazole triple therapy in both the mITT population (80.8% vs. 68.5%; $p=0.0001$) and the per protocol population (85.7% vs. 70.0%; $p<0.0001$). In the subset of patients with *H. pylori* strains resistant to clarithromycin, the *H. pylori* eradication rate with vonoprazan triple therapy was superior to that of lansoprazole triple therapy in both the mITT population (65.8% vs. 31.9%; $p<0.0001$) and the per protocol population (67.2% vs. 29.0%; $p<0.0001$).

Among all patients, the *H. pylori* eradication rate of vonoprazan dual therapy was superior to that of lansoprazole triple therapy in both the mITT population (77.2% vs. 68.5%; $p=0.0063$) and the per protocol population (81.1% vs. 70.0%; $p=0.0013$). The *H. pylori* eradication rate of vonoprazan dual therapy was also superior to that of lansoprazole triple therapy in the subset of patients with *H. pylori* strains resistant to clarithromycin in both the mITT population (69.6% vs. 31.9%; $p<0.0001$) and the per protocol population (79.5% vs. 29.0%; $p<0.0001$).

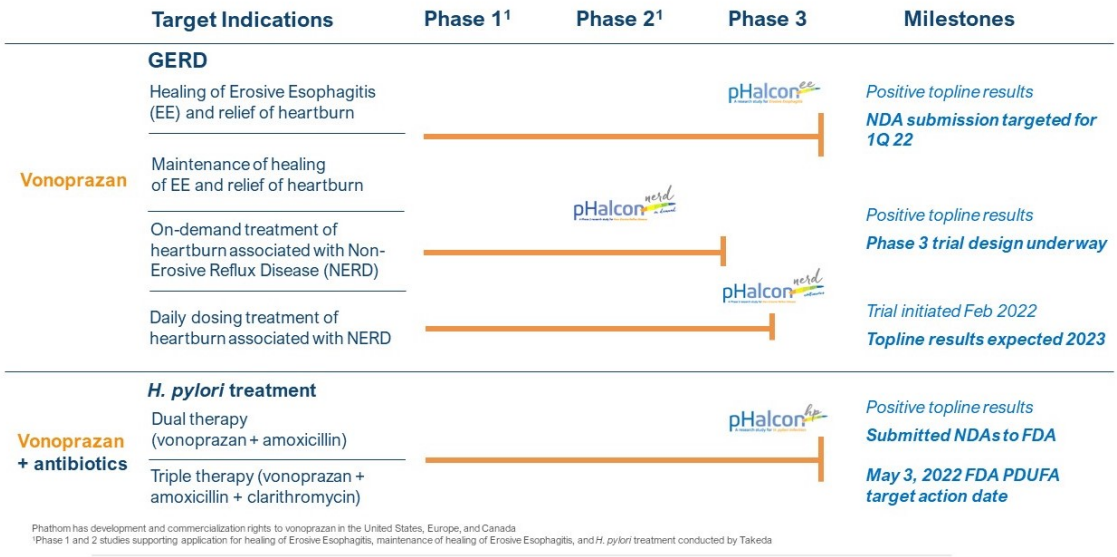
The vonoprazan triple therapy results of PHALCON-HP were consistent with the results of a Phase 3 clinical trial previously conducted by Takeda in Japan assessing vonoprazan in combination with the antibiotics amoxicillin and clarithromycin versus lansoprazole in combination with these same antibiotics in first line treatment of *H. pylori* infection at antibiotic doses and treatment duration (7 days) consistent with local practice in Japan. Vonoprazan dual therapy was not tested in this study.

Our management team has deep expertise in developing GI therapeutics, including anti-secretory agents, and direct experience developing vonoprazan at Takeda. Our Chief Executive Officer, Terrie Curran, has more than 20 years of experience in the biopharmaceutical industry. Ms. Curran served as President, Global Inflammation and Immunology (I&I) Franchise and as a member of the Executive Committee at Celgene Corporation from 2017 to 2019. Ms. Curran joined Celgene in 2013 as the U.S. Commercial Head of the I&I Franchise, built the capabilities and recruited the teams that executed the successful launch of OTEZLA, which was sold to Amgen in November 2019 for $13.4 billion.

Azmi Nabulsi, M.D., M.P.H., our Chief Operating Officer, is the former Deputy Chief Medical and Scientific Officer at Takeda. Our Head of Regulatory, Tom Harris, is the former Senior Vice President and Head of Global Regulatory at Takeda. Dr. Nabulsi and Mr. Harris were extensively involved with the development of vonoprazan at Takeda.

Our Pipeline

The following chart summarizes our current development programs.



Our Strategy

Our mission is to improve the lives of people suffering from gastrointestinal diseases. Our strategy is initially focused on developing and commercializing vonoprazan as a potential first-in-class P-CAB in the United States, Europe, and Canada for the treatment of acid-related GI diseases. Key elements of this strategy include:

- ***Obtain marketing approval of, and commercially launch, vonoprazan in erosive esophagitis and H. pylori infection***. In 2021, we reported positive topline data from Phase 3 clinical trials of vonoprazan in each of erosive esophagitis and *H. pylori* infection. In September 2021, we submitted, and in November 2021, the FDA accepted for filing and granted Priority Review to our NDAs for vonoprazan triple therapy and vonoprazan dual therapy with a PDUFA action date of May 3, 2022. In March 2022 we plan to submit an NDA for vonoprazan in healing of all grades of erosive esophagitis and relief of heartburn, and maintenance of healing of all grades of erosive esophagitis and relief of heartburn. If the NDAs are approved by the PDUFA date, we expect to launch vonoprazan in the treatment of *H. pylori* infection in the second half of 2022, and in erosive esophagitis in 2023. Further, if vonoprazan is approved by the FDA as a new chemical entity, we expect that vonoprazan would receive a five-year period of marketing exclusivity within the United States and QIDP designation could extend the U.S. marketing exclusivity for an additional five years.

- ***Advance the clinical development of vonoprazan in non-erosive reflux disease or NERD and seek marketing approval.*** Non-erosive reflux disease, or NERD, is a major subcategory of GERD and is characterized by reflux-related symptoms in the absence of esophageal mucosal erosions. We are pursuing development of vonoprazan for treatment of NERD as both an on-demand and as a continuously dosed (daily) therapy for patients with NERD. In February 2022, we initiated a Phase 3 trial of vonoprazan in patients with NERD that is evaluating a once-daily dosing regimen and expect to report topline results from that trial in 2023. Also in February 2022, we reported positive topline data from a Phase 2 trial evaluating various doses of vonoprazan as an on-demand therapy for NERD. We intend to discuss the results from this Phase 2 trial with FDA prior to finalizing the design of our Phase 3 NERD on-demand trial.

- ***Commercialize vonoprazan in the United States***. We plan to independently commercialize vonoprazan, if approved, in the United States by building a leading specialty gastroenterology commercial infrastructure to support the adoption of vonoprazan. We believe we can successfully launch vonoprazan in the United States with a focused sales force targeting prescribers of treatments for *H. pylori* and GERD, particularly gastroenterologists. Prescriptions for treatments for *H. pylori* and GERD are both highly concentrated, with approximately 75% of prescriptions in *H. pylori* and 65% of prescriptions in erosive esophagitis being written by 10% of physicians We believe we have an opportunity to achieve significant share of voice and exposure to physicians given the scarcity of actively marketed anti-secretory medicines. Given the limitations of PPIs and current unmet need, we believe the commercial opportunity for vonoprazan is substantial.

- ***Seek commercial partnerships to maximize the vonoprazan opportunity outside of the United States***. To address the opportunity for vonoprazan in Europe and Canada, we plan to seek one or more partners with existing commercial infrastructure and expertise in these markets. We believe this strategy will allow us to realize the value of the market opportunity in Europe and Canada while focusing our resources on the U.S. market.

- ***Further expand the development of vonoprazan across indications, dosing regimens, and alternative formulations and packaging***. In addition to NERD, we plan to pursue vonoprazan lifecycle extension strategies in areas with clear unmet need, clinical rationale, and commercial justification. These strategies may include: (i) additional potential indications, including treatment of gastric ulcers and duodenal ulcers, Barrett's esophagus, and eosinophilic esophagitis; and (ii) alternative formulations and packaging, such as orally disintegrating tablets and other oral dosage forms for patients with difficulty swallowing, and an intravenous formulation for in-hospital applications. Additionally, we believe that vonoprazan has the ideal profile for an OTC product because of the potential for on-demand symptom relief and a well-tolerated safety profile.

- ***In-license or acquire additional clinical or commercial stage product candidates for the treatment of GI diseases in a capital efficient manner***. We intend to take advantage of our management team's GI expertise to opportunistically in-license or acquire additional innovative therapies for diseases treated by gastroenterologists. We plan to leverage our development and planned commercial infrastructure to support multiple assets targeting GI indications.

Acid-Related GI Diseases

Overview

Gastric acid is a digestive fluid formed in the stomach. The highly acidic environment of the stomach causes the unfolding, or denaturing, of food proteins that are subsequently broken down by gastric enzymes. Gastric acid is secreted by the hydrogen potassium ATPase enzyme, which is known as the proton pump. Proton pumps are expressed on the channeled surfaces, or canaliculi, of parietal cells in the stomach, which secrete acid. Proton pumps are continuously synthesized and switch between active and inactive states in response to various stimuli, such as food. When activated, proton pumps increase acid secretion.

GI diseases where treatment is related to acid control, such as GERD, peptic ulcer disease, Zollinger Ellison syndrome, and *H. pylori* infection, are significant medical problems because of their high prevalence, chronic nature and clinical sequelae. GERD results from the effects of acid on compromised mucosal defenses in the gastrointestinal tract. The reflux of gastric acid into the esophagus produces frequent and/or severe heartburn, indigestion, and reflux symptoms. Chronic GERD may damage esophageal tissue and progress to more severe diseases including erosive esophagitis, Barrett's esophagus, and esophageal cancer. GERD and related diseases are associated with impaired quality of life and substantial costs to the healthcare system given their chronic nature and sequelae. In *H. pylori* infection, gastric acid limits the effectiveness of antibiotics used to eradicate infection. Chronic *H. pylori* infection can lead to dyspepsia, peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma.

Prevalence

The prevalence of GI diseases is high. Approximately 20% to 40% of Western adults report chronic heartburn or regurgitation symptoms potentially related to GERD. We estimate that there are approximately 65 million individuals in the United States and 50 million individuals in the EU5 with GERD. In the United States, GERD is the most common gastroenterology-related outpatient diagnosis. Additionally, approximately 35% of the U.S. population and 45% of the EU5 population are infected with *H. pylori*. We estimate that there are approximately 115 million individuals in the United States and 145 million individuals in the EU5 infected with *H. pylori*.

Prevalence of GERD and *H. pylori* Infection

	GERD		*H. pylori* infection	
	Prevalence	Estimated Population	Prevalence	Estimated Population
United States	20%	65 million	35%	115 million
EU5	15%	50 million	45%	145 million

Treatments

Treatments of acid-related GI diseases aim to provide relief of acute symptoms, healing of damaged tissue, and prevention of long-term clinical sequelae associated with chronic acid exposure. Gastric acidity is measured by the pH scale, a logarithmic scale where 7.0 describes a neutral state and lower levels indicate a higher level of acidity. The pH of the stomach typically ranges from 1.5 to 3.5. In patients with acid-related GI diseases, increasing gastric pH has been shown to improve mucosal healing rates and provide more rapid symptom relief for patients. For example, the duration of time that intra-gastric acidity is greater than pH 3.0 correlates with the healing of duodenal and gastric ulcers, and pH greater than 4.0 is correlated with the healing of erosive esophagitis. Similarly, in patients with *H. pylori* infection, a more neutral gastric pH of 6.0 to 8.0 preserves antibiotic function and is optimal for successful eradication.

Drug-induced gastric acid suppression is a key component of the management of acid-related GI diseases. Three classes of drugs with distinct mechanisms of action are principally used for treatment in the United States and Europe: antacids, histamine receptor antagonists, or H2RAs, and PPIs.

Antacids

Antacids, first commercially available in the 1930s, directly neutralize gastric acid to raise intra-gastric pH and can alleviate intermittent, mild symptoms of acid-related GI diseases, such as heartburn, but they are only effective for a short duration and require frequent administrations per day. In addition, antacids do not significantly help heal or prevent complications of acid-related diseases. Antacids include commonly-known OTC products, such as Alka-Seltzer, Pepto-Bismol, Rolaids, and TUMS.

Histamine Receptor Antagonists (H2RAs)

H2RAs, first commercially available in the 1970s, decrease gastric acid secretion in order to raise gastric pH. H2RAs represented a dramatic improvement over antacids in the control of gastric acid and consequently in the management of acid-related GI diseases. H2RAs are also generally safe and well-tolerated. Among the H2RA class were the first commercial blockbuster drugs, Pepcid (famotidine), Tagamet (cimetidine), and Zantac (ranitidine). Zantac was the world's highest-selling prescription drug in the mid-1990s, with peak global sales of $3.7 billion and U.S. sales of $2.2 billion. Prior to the launch of generic H2RAs and increasing competition from PPIs, the H2RA class achieved sales of approximately $3.5 billion in the United States. H2RAs achieved commercial success despite clinical limitations, including unreliable 24-hour acid control, poor control of post-meal symptoms, and loss of efficacy over time.

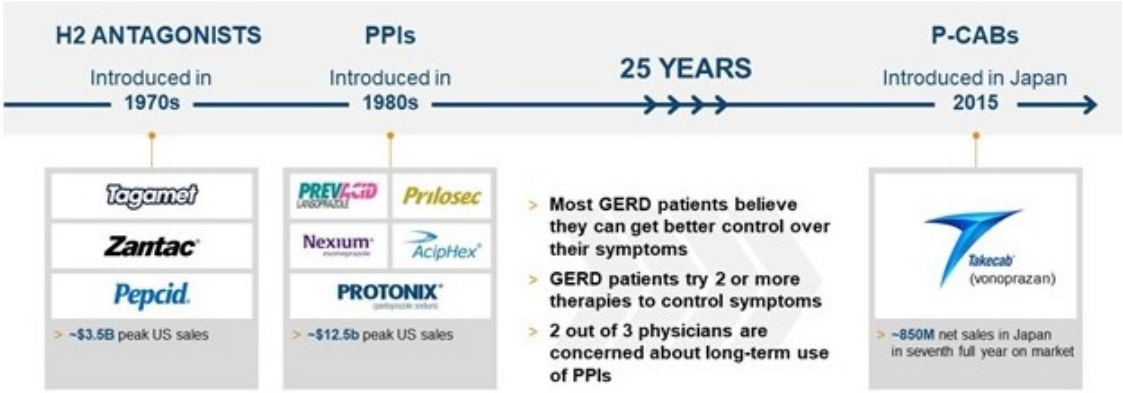
Proton Pump Inhibitors (PPIs)

PPIs, first commercially available in 1989, offered improved acid control over H2RAs. Pharmacodynamic data demonstrated that PPIs maintain gastric pH above target levels for a longer duration than H2RAs. A commonly used benchmark of anti-secretory activity is the percentage of time in a 24-hour period that gastric pH exceeds 4.0, which we refer to as time above pH 4.0, which ranges from 40% to 71% for PPIs versus 33% for H2RAs.

Given this improved pharmacodynamic profile, PPIs demonstrated improved clinical symptom relief and healing over H2RAs. In a meta-analysis of results from 33 randomized clinical trials with over 3,000 GERD patients, a reduction in symptoms was achieved in 83% of patients taking PPIs versus 60% of those on H2RAs. In a second meta-analysis, the eight-week healing rate in patients with erosive esophagitis was 82% for PPIs versus 52% for H2RAs.

The PPI class is currently the first-line treatment of acid-related GI diseases. Prior to the introduction and adoption of generic and OTC alternatives, annual PPI class sales reached approximately $12.5 billion in the United States, and peak sales for individual brands were approximately $3.7 billion for Prilosec, $3.5 billion for Nexium, and $3.4 billion for Prevacid. As recently as 2015, the last branded PPI, Dexilant (dexlansoprazole), reached approximately $530 million in sales in the United States despite limited differentiation from other PPIs. While Dexilant demonstrated a modest improvement in time above pH 4.0 compared to other PPIs, the approved dose did not demonstrate consistent superiority in Phase 3 trials against other PPIs on the healing of erosive esophagitis and has not been tested against PPIs in other indications. We believe that the commercial success of Dexilant highlights the value to physicians and patients of even incremental improvements over other PPIs.

History of Pharmaceutical Agents for Control of Gastric Acid



PPI Limitations

While PPIs provide clinically meaningful symptom relief and healing for millions of patients suffering from acid-related GI diseases, they are inadequate for many patients. The suboptimal anti-secretory profile of PPIs results in slow onset of symptom relief, breakthrough nighttime or postprandial heartburn, and treatment failure. A recent population-based survey with over 70,000 participants in the United States showed that 55% of patients who reported having GERD symptoms were taking PPIs, with 68% taking them daily, and 54% of daily PPI users reported persistent symptoms. This is consistent with earlier studies that have shown that approximately 15% to 45% of GERD patients are inadequately treated with PPIs, experiencing persistent, troublesome symptoms, such as heartburn and regurgitation. In approximately two-thirds of symptomatic GERD patients, reflux symptoms are not adequately controlled after the first dose of a PPI, and nearly 50% of patients still suffer from symptoms three days later. Given these limitations, more than 20% of GERD patients on PPI therapy take their PPI twice daily, which is not FDA approved, or purchase OTC heartburn treatments in addition to their prescription medicine. In a survey of approximately 1,000 GERD patients and 1,000 physicians, approximately one third of GERD patients reported persistent symptoms and were dissatisfied with PPI therapy and 35% of physicians perceived patients as somewhat satisfied to completely dissatisfied with PPI treatment. In addition, in a real world study conducted in 2020 and 2021 evaluating the perspectives and unmet needs of over 400 physicians and patients in the U.S. in the management of acid related disorders, fewer than one-third of the physician participants were satisfied with current treatment options for their patients. Moreover, fewer than 50% of patients in the study reported they were satisfied with their current treatment.

In patients with more severe grades of erosive esophagitis, studies with PPIs have reported failure rates of healing of esophageal erosions exceeding 25%. Additionally, recurrence of erosions is common in healed erosive esophagitis patients receiving maintenance PPI therapy. One study reported recurrence in 15% to 23% of patients with less severe erosive esophagitis and 24% to 41% of patients with more severe erosive esophagitis. We believe that these limitations of PPIs are in part driven by their mechanism of action and pharmacokinetics.

Mechanistic Differences Between PPIs and Vonoprazan

PPIs

After oral dosing, PPIs reach the gastric parietal cells through the bloodstream. PPIs are prodrugs that are converted to their active form in the acidic environment of the secretory canaliculus of the parietal cell but degrade quickly because their active form is unstable in acid. For example, the half-life of omeprazole (Prilosec) is less than 10 minutes at pH 2.0. The active form of a PPI blocks acid production by covalently binding to active proton pumps that have moved to the surface of the secretory canaliculi after activation of the parietal cell with stimuli, such as a meal. Because PPIs bind only to actively secreting pumps, it is generally recommended that they be administered 30 to 60 minutes before a meal to achieve maximal efficacy. Once covalently bound to the proton pumps, the active PPI molecule is no longer available to bind to newly synthesized or activated proton pumps. Furthermore, given the relatively short plasma half-life of most PPIs of one to two hours, resupply of additional PPI molecules from the bloodstream is limited, and newly activated pumps are not inhibited. Due to this profile, PPI dosing over several days is required to inhibit enough proton pumps to increase gastric pH to a clinically meaningful threshold, and PPIs have a limited window of efficacy leading to incomplete acid suppression over the 24-hour dosing interval. In addition, PPIs are primarily metabolized by CYP2C19, an enzyme which has significant interpatient metabolic variability based on genotype. As a result, PPI exposure levels in some patients may not achieve target levels, potentially reducing clinical efficacy.

Vonoprazan

Vonoprazan has a differentiated mechanism of action from PPIs. Vonoprazan is designed to selectively concentrate in the parietal cell in both the resting and stimulated states. In contrast to most PPIs, vonoprazan does not require gastric acid for activation, remains stable in the presence of gastric acid, binds to the active proton pumps in a noncovalent and reversible manner and remains associated with the active and inactive proton pumps, and remains in the secretory canaliculus where it continues to inhibit acid secretion over an extended period. Vonoprazan's prolonged effect is also maintained through a slow dissociation rate from the proton pumps and resupply from the bloodstream due to its seven-hour half-life. These characteristics allow vonoprazan to rapidly achieve target 24-hour acid suppression within two hours of a single dose, unlike PPIs that require three to five days to achieve stable acid suppression. In addition, vonoprazan is primarily metabolized by CYP3A4/5, an enzyme which has less genetic variability than CYP2C19, and may exhibit more consistent activity than PPIs across U.S. and European populations.

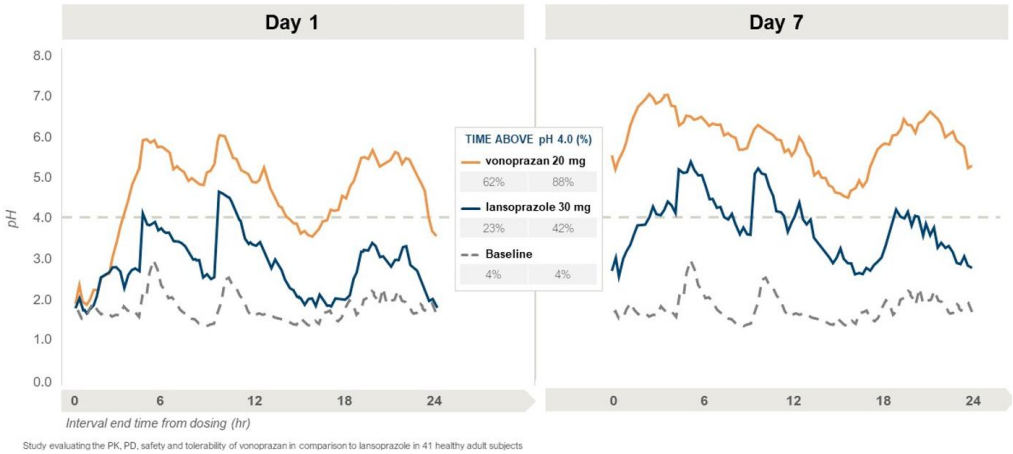
The mechanistic and pharmacologic differences of PPIs and vonoprazan are summarized in the table below.

	PPIs	Vonoprazan
Activation and stability	Prodrugs that require acid for activation yet are unstable in acidic conditions	No activation required and stable in acidic conditions
Binding to proton pump	Irreversibly blocks active proton pumps	Reversibly blocks active proton pumps and remains associated with the active and inactive proton pumps
Half-life	< 2 hours	~7 hours
Onset of action	Steady state anti-secretory effect and complete symptom relief is not achieved for 3 to 5 days (~40% of pumps blocked after a single PPI dose)	Achieves target 24-hour acid suppression within 2 hours of a single dose in a clinical trial in healthy volunteers
Dosing restrictions	Generally administered 30 to 60 minutes before a meal	Dosing independent of meal
Inter-patient variability	Metabolism via CYP2C19	Metabolism via CYP3A4/5

Vonoprazan Pharmacodynamics vs. PPIs

Vonoprazan's more rapid, potent, and durable anti-secretory effects versus the PPI lansoprazole (Prevacid) were demonstrated in a randomized, open-label, crossover clinical trial comparing 20 mg of once daily, or QD, vonoprazan to 30 mg QD of lansoprazole for 7 days in 41 healthy volunteers. As shown below, vonoprazan had a significantly higher 24-hour holding time ratio than lansoprazole for pH>4 on Day 1 (62.4% vs. 22.6%) and Day 7 (87.8% vs. 42.3%) and for pH>6 on Day 1 (33.1 vs. 7.4) and Day 7 (62.5% vs. 16.4%). Mean 24-hour intragastric pH for vonoprazan and lansoprazole was 4.6 and 2.8, respectively, on Day 1, and 5.9 and 3.8, respectively, on Day 7. Gastric pH levels are measured on a logarithmic scale from 0.0 to 14.0, in which each point represents a 10-fold change in acidity and higher pH values represent lower acidity. In this study, vonoprazan maintained an average pH approximately two points higher than lansoprazole at Day 7.

Improved Onset and Potency of pH Control of Vonoprazan vs. Lansoprazole at Day 1 and Day 7



This improved potency and duration of pH control with vonoprazan, as measured by twenty-four hour pH hold time and time above pH 4.0, was evident not only at Day 1, but also at Day 7 when lansoprazole had reached its steady state (see table below).

24-hr Hold Time and Time Above pH 4.0 of Vonoprazan vs. Lansoprazole at Day 1 and Day 7

		Treatment			
	Baseline	Vonoprazan 20 mg QD		Lansoprazole 30 mg QD	
Parameter	Day -1	Day 1	Day 7	Day 1	Day 7
	n=43	n=40	n=40	n=41	n=38
0-24 h pH	1.8	4.6	5.9	2.8	3.8
pH>4 HTR (%)	3.9	62.4	87.8	22.6	42.3

Vonoprazan demonstrated similarly greater time above pH 4.0 versus the PPI esomeprazole (Nexium) in a randomized, open-label, crossover clinical trial comparing 20 mg QD vonoprazan to 20 mg QD of esomeprazole in 20 healthy volunteers. In that trial, greater duration of pH control with vonoprazan, as measured by time above pH 4.0 was observed both on Day 1 and Day 7 (see table below).

Improved Time Above pH 4.0 of Vonoprazan vs. Esomeprazole at Day 1 and Day 7

	Time Above pH 4.0 (%)		
	Baseline	Day 1	Day 7
Vonoprazan 20 mg	11%	71%	86%
Esomeprazole 20 mg	11%	24%	61%

Vonoprazan for the Potential Treatment of Acid-Related GI Diseases

Given the shortcomings of PPI therapy, we believe that there is a significant unmet medical need for a safe and effective anti-secretory agent with rapid, potent, and durable activity. Vonoprazan was developed in markets outside of the United States by Takeda through an extensive clinical program, including 19 Phase 3 clinical trials. As of December 2021, over 8,000 subjects were exposed to vonoprazan in completed and ongoing clinical trials. In head-to-head Phase 3 trials versus a PPI conducted in the U.S. and Europe, vonoprazan demonstrated faster onset of healing in patients with moderate to severe erosive esophagitis, superior maintenance of healing of erosive esophagitis patients across all levels of severity, and superior eradication rates in combination with antibiotics in patients with *H. pylori* infection than PPI-based triple therapy. Vonoprazan received marketing approval in Japan in late 2014 and generated approximately $850 million in net sales in its seventh full year on the market in Japan. In April 2021, we reported positive top-line data from our *H. pylori* trial, and in October 2021, we reported positive top-line data from our erosive esophagitis trial. In September 2021, we submitted NDAs for vonoprazan triple therapy and vonoprazan dual therapy, each for the treatment of *H. pylori* infection in adults, which were granted priority review and received a PDUFA action date of May 3, 2022, and we expect to submit an NDA for vonoprazan for the healing of all grades of erosive esophagitis and relief of heartburn, and maintenance of healing of all grades of erosive esophagitis and relief of heartburn, in March 2022.

Vonoprazan in GERD

Based on the significant unmet medical need, previous Phase 3 trial results from Japan and Asia, and commercial potential, we have prioritized the development and commercialization of vonoprazan in GERD, specifically:

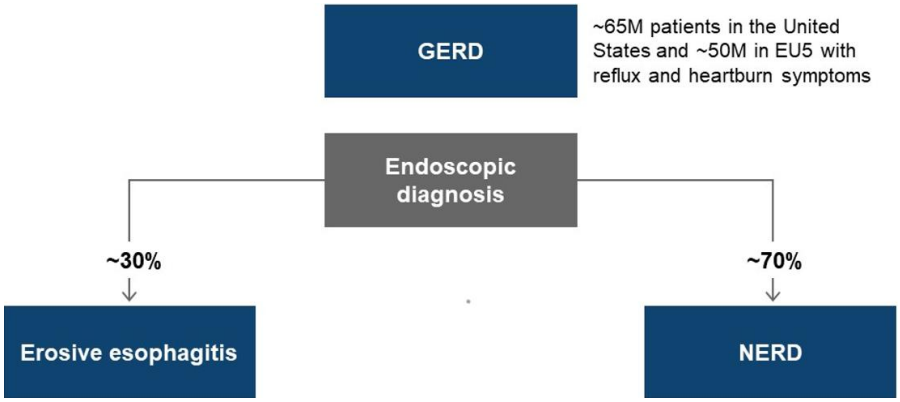
- the healing of erosive esophagitis and relief of heartburn; and
- the maintenance of healing of erosive esophagitis and relief of heartburn.

We also initiated our first Phase 3 trial for vonoprazan in symptomatic non-erosive GERD, or NERD, in February 2022.

GERD Disease Overview

GERD is one of the most prevalent diseases of any kind and is the most prevalent GI disease, affecting approximately 20% of the U.S. population and approximately 15% of the European population. We estimate there are approximately 65 million individuals with GERD in the United States and 50 million individuals with GERD in the EU5. GERD is a disease that develops when the reflux of acidic stomach contents into the esophagus causes troublesome symptoms and/or complications, and the term covers a spectrum of diseases, the main categories of which are erosive esophagitis and non-erosive reflux disease. These diseases are detailed below:

- ***Erosive esophagitis***: Approximately 30% of GERD patients have erosive esophagitis, which is classified by erosions in the gastric mucosa caused by acidic reflux of stomach contents into the esophagus. Erosive esophagitis is commonly graded by the Los Angeles classification system, which characterizes the extent of erosions in the esophagus and is graded on a scale of increasing severity from A to D, with D being the most severe. Approximately 20% to 30% of erosive esophagitis patients have the moderate to severe Los Angeles Class C or D disease. Erosive esophagitis can have serious consequences. If left untreated, esophagitis may develop into peptic stricture, Barrett’s esophagus or esophageal cancer.
- ***Non-erosive reflux disease (NERD)***: Approximately 70% of GERD patients have NERD, which is classified by an endoscopically normal esophagus, but abnormal gastric acid exposure in the esophagus and persistent symptoms.



GERD patients typically present with heartburn and reflux symptoms. Based on these symptoms, patients are typically treated first-line with PPIs prior to a diagnostic endoscopy for specific disease classification of erosive esophagitis or NERD. Clinical guidelines suggest that endoscopy be performed in patients who continue to have symptoms despite a four- to-eight-week course of daily PPIs or have alarm symptoms, including GI bleeding, anemia, weight loss, chest pain, or difficult or painful swallowing. Our market research suggests that most patients are treated empirically based on symptoms rather than based on endoscopic characterization of disease.

GERD Treatment Paradigm

Approximately 80% of GERD patients are pharmacologically treated with prescription or OTC medications. PPIs are currently the most effective anti-secretory agents available in the United States and Europe for relieving GERD symptoms and healing erosions in gastric mucosa. Our market research suggests that approximately 80% of patients who are pharmacologically treated receive PPIs, and more than 80% of PPI use is prescription rather than OTC. The majority of PPI use is chronic, with more than 70% of patients prescribed PPIs for daily use. According to IQVIA NDTI, there were approximately 7.2 billion PPI doses prescribed for the 12 months ended December 31, 2021.

There are few treatment options for GERD patients who are inadequately managed on PPI therapy. In a real world study conducted in 2020 and 2021 evaluating the perspectives and unmet needs of over 400 physicians and patients in the U.S. in the management of acid related disorders, only half of physicians reported that their patients are getting long-lasting relief from a PPI resulting in approximately 25% of patients taking a PPI more than once a day despite patients' concerns about long term side effects of PPI use. A limited number of patients proceed to a surgical procedure, such as Nissen fundoplication. However, this procedure results in postoperative morbidity of 5% to 20%, as well as a two- to six-week recovery period and a median hospital stay of two days.

Vonoprazan has the potential to be the first gastric anti-secretory agent from a novel class approved in the United States, Europe, or Canada in over 30 years. Our U.S. market research survey reported that 55% to 60% of physicians included in the survey believed that vonoprazan has demonstrated superior efficacy in the healing and maintenance of healed esophageal erosions compared to existing EE treatments, provides faster onset of action compared to existing GERD treatments, and has superior duration and magnitude of gastric pH control compared to existing GERD treatments.

Clinical Data for Vonoprazan in GERD

Five Phase 3 clinical trials have been completed comparing vonoprazan to PPIs in erosive esophagitis: our healing and maintenance of healing trial in the United States and Europe; a healing trial in Japan; a maintenance of healing trial in Japan; a healing trial in Asia (China, Taiwan, and Korea); and a maintenance of healing trial in Asia. In addition to these Phase 3 trials, several published investigator-sponsored studies have compared vonoprazan to PPIs across dosing regimens and endpoints. Results of these clinical trials are summarized below.

Healing and Maintenance of Healing of Erosive Esophagitis in the United States and Europe (PHALCON-EE)

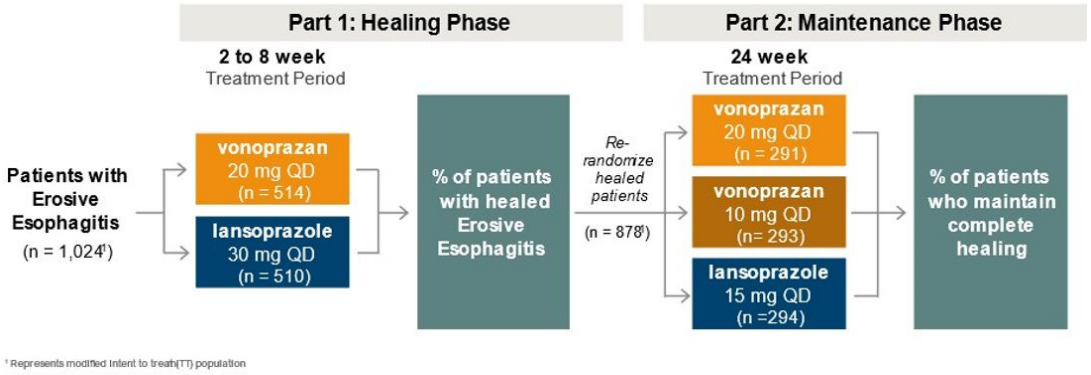
In October 2021, we announced that vonoprazan successfully met its primary endpoints and key secondary superiority endpoints in PHALCON-EE, our pivotal Phase 3 trial evaluating vonoprazan versus lansoprazole for the treatment of erosive esophagitis.

Design for PHALCON-EE Phase 3 Erosive Esophagitis Clinical Trial

PHALCON-EE was a randomized, double-blind, two-phase, multicenter, Phase 3 trial that enrolled 1,024 patients with EE in the U.S. and Europe. PHALCON-EE was modeled after the successful Phase 3 clinical trials conducted in Japan and Asia with limited differences, including the combination of the healing and maintenance phases into one single study whereas in Japan and Asia separate clinical trials were conducted for each of these indications.

The first phase of the trial, the Healing Phase, evaluated the efficacy and safety of vonoprazan 20 mg QD compared to lansoprazole 30 mg QD for the healing of EE for up to eight weeks. In the Healing Phase, patients were assessed via endoscopy to determine complete healing following 2 weeks of treatment and, if complete healing was not achieved, a second endoscopy occurred at 8 weeks of treatment. Patients who achieved complete healing were re-randomized into the second phase of the trial, the Maintenance Phase, where vonoprazan 10 mg and 20 mg were compared to lansoprazole 15 mg to assess maintenance of healing of EE via endoscopy following 24 weeks of treatment. Heartburn symptom relief was assessed via secondary endpoints in both the Healing and Maintenance Phases of the study based on twice daily e-diary data collection.

Design of US/EU Phase 3 Clinical Trial for the Healing and Maintenance of Healing of Erosive Esophagitis



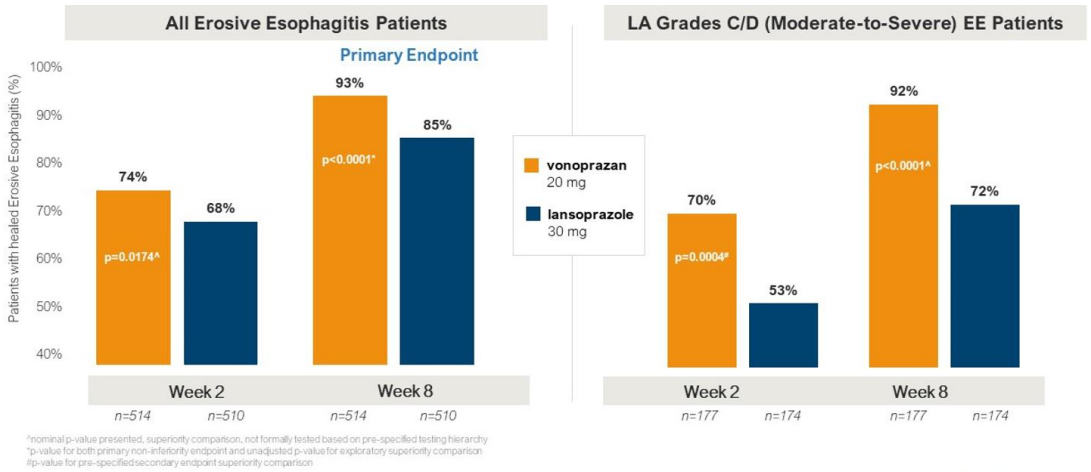
Healing Phase

The primary endpoint analysis of the Healing Phase was non-inferiority of vonoprazan 20 mg compared to lansoprazole 30 mg in the percentage of all patients who have complete healing of EE by Week 8. Vonoprazan met the non-inferiority criteria for the primary comparison with a healing rate of 93% compared to 85% for lansoprazole ($np<0.0001$). Based on a prespecified exploratory comparison test, the difference in healing rates in all patients between vonoprazan and lansoprazole was also significant (nominal $p<0.0001$). Non-inferiority analyses are conducted to evaluate whether the effect of an agent is not worse than the active control by more than a specified margin, while superiority analyses are conducted to evaluate whether an agent outperformed a comparator by a statistically significant margin.

Vonoprazan met the secondary superiority endpoint of healing in patients with moderate-to-severe disease, defined as patients with esophageal erosions classified as Grades C or D by the Los Angeles (LA) Classification System, at Week 2, demonstrating significantly faster healing than lansoprazole (70% for vonoprazan 20 mg and 53% for lansoprazole 30 mg) (p=0.0004). Vonoprazan also met the secondary endpoint of showing non-inferiority to lansoprazole 30 mg in the mean percentage of 24-hour heartburn free days over the healing period. In additional pre-specified secondary endpoint superiority comparisons, vonoprazan 20 mg healing rates were numerically greater than lansoprazole 30 mg in all patients at Week 2 (nominal p=0.0174) and in moderate-to-severe patients by Week 8 (nominal p<0.0001), although these superiority comparisons were not tested in the pre-specified testing hierarchy.

Vonoprazan 20 mg was also compared to lansoprazole 30 mg in a superiority test for onset of sustained resolution of heartburn by day 3 but did not achieve statistical significance (p=0.2196).

Results of US/EU Phase 3 Clinical Trial in the Healing of Erosive Esophagitis



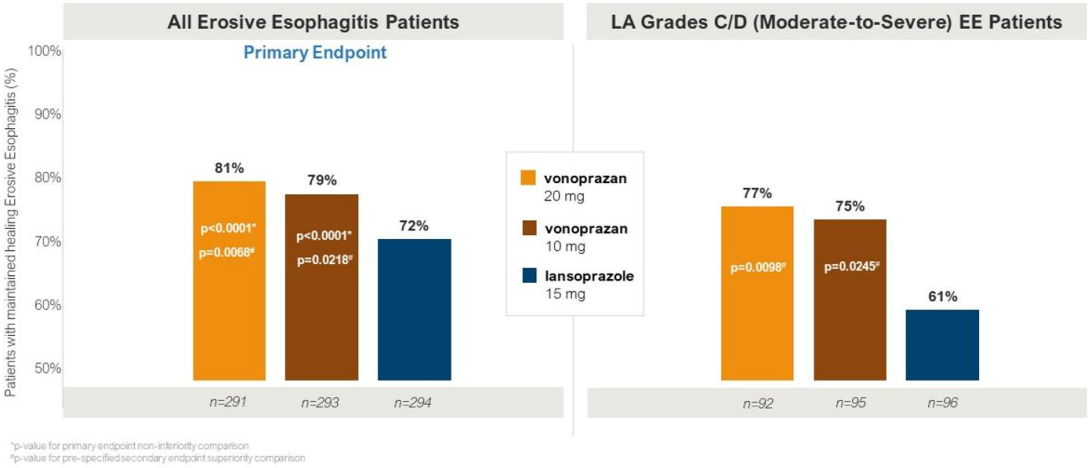
Maintenance Phase

Vonoprazan met the primary and all secondary endpoints in the Maintenance Phase. The primary endpoint of the Maintenance Phase was non-inferiority of vonoprazan 10 mg and 20 mg compared to lansoprazole 15 mg in the percentage of all patients who maintained healing of EE through Week 24.

Both vonoprazan doses met the Maintenance Phase primary endpoint of non-inferiority while also meeting the pre-specified secondary comparison demonstrating superiority of maintenance of healing versus lansoprazole (79% for vonoprazan 10 mg, 81% for vonoprazan 20 mg compared to 72% for lansoprazole 15 mg) (p<0.0001 for both non-inferiority comparisons; p=0.0218 for vonoprazan 10 mg superiority comparison; p=0.0068 for vonoprazan 20 mg superiority comparison).

Both vonoprazan doses also met the secondary endpoint of demonstrating superiority of the percentage of patients with moderate-to-severe disease who maintained healing of EE through Week 24 (75% vonoprazan 10 mg, 77% vonoprazan 20 mg v. 61% lansoprazole 15 mg) (p=0.0245 for vonoprazan 10 mg superiority comparison; p=0.0098 for vonoprazan 20 mg superiority comparison). Additionally, both vonoprazan doses also met the secondary endpoint of showing non-inferiority to lansoprazole 15 mg in the mean percentage of 24-hour heartburn free days over the maintenance period.

Results of US/EU Phase 3 Clinical Trial in Maintenance of Healing of Erosive Esophagitis



Healing and Maintenance of Healing of Erosive Esophagitis Clinical Trials in Japan and Asia

The results of PHALCON-EE were consistent with the results of earlier Phase 3 trials of vonoprazan in healing and maintenance of healing of erosive esophagitis after which it was modeled. These trials were conducted in Japan as well as other countries in Asia.

In two Phase 3 trials in healing of erosive esophagitis comparing vonoprazan 20 mg QD to lansoprazole 30 mg QD for up to eight weeks, one conducted in Japan and the other in several countries in Asia, vonoprazan achieved the primary endpoint of non-inferiority versus lansoprazole on the percent of patients with healed erosive esophagitis up to Week 8. Exploratory testing suggested higher healing rates for vonoprazan versus lansoprazole in the moderate to severe patients at Week 2 in both studies.

Similarly, in two Phase 3 trials in maintenance of healing of erosive esophagitis comparing two doses of vonoprazan (10 mg and 20 mg QD) to lansoprazole 15 mg QD for 24 weeks, one conducted in Japan and the other in several countries in Asia, both vonoprazan doses achieved the primary endpoint of non-inferiority versus lansoprazole on the percent of patients with recurrence of erosive esophagitis during the 24-week maintenance period. In both studies, exploratory testing suggested higher maintenance of healing rates for both vonoprazan doses versus lansoprazole in all patients and in the moderate to severe patients.

Our Development Program in Symptomatic Non-Erosive Reflux Disease (NERD)

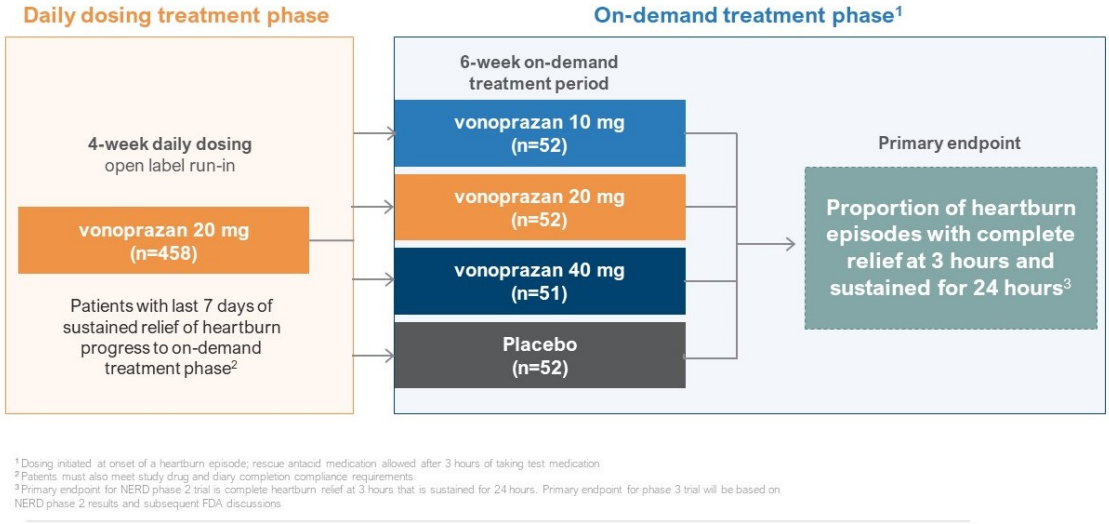
We believe that there is opportunity to broadly position vonoprazan's use in GERD with an indication in symptomatic GERD in patients without erosions, or NERD, in addition to an indication in erosive esophagitis. We are evaluating vonoprazan as a treatment for NERD with both daily and on-demand, or as-needed, dosing regimens. NERD patients do not have esophageal erosions which require chronic treatment to prevent recurrence of erosions and its potential sequelae. We believe the rapid onset of acid control of vonoprazan may enable on-demand use for the management of heartburn in NERD patients as an alternative to chronic daily treatment with PPIs.

On Demand Dosing of Vonoprazan for the Treatment of NERD

In February 2022, we announced that vonoprazan (10 mg, 20 mg and 40 mg), successfully met the primary endpoint in PHALCON-NERD, a Phase 2 trial evaluating three doses of vonoprazan versus placebo as an on-demand treatment of NERD.

Design for PHALCON-NERD Phase 2 NERD On-Demand Clinical

PHALCON-NERD was a Phase 2, randomized, double-blind, multicenter study that enrolled 458 subjects in the U.S. to evaluate the efficacy and safety of vonoprazan 10 mg, 20 mg, and 40 mg administered on demand for relief of episodic heartburn compared to placebo in subjects with symptomatic NERD (as confirmed by endoscopy). After an initial four week vonoprazan 20 mg QD dose open-label run-in period, two hundred and seven subjects with no heartburn on the last 7 days of the run-in period who also met drug and diary compliance requirements were randomized to receive vonoprazan 10 mg, 20 mg, 40 mg or placebo on-demand for six weeks. Subjects completed an electronic diary to assess presence and severity of heartburn symptoms and use of rescue antacid (if needed).

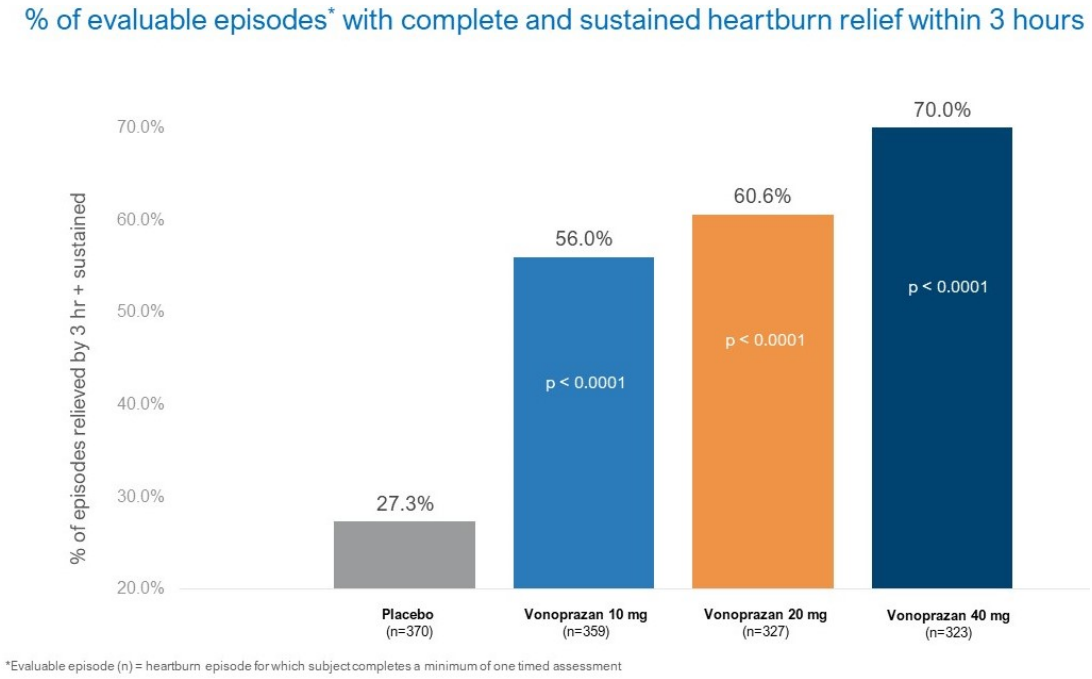


[1] Dosing initiated at onset of a heartburn episode; rescue antacid medication allowed after 3 hours of taking test medication
[2] Patients must also meet study drug and diary completion compliance requirements
[3] Primary endpoint for NERD phase 2 trial is complete heartburn relief at 3 hours that is sustained for 24 hours. Primary endpoint for phase 3 trial will be based on NERD phase 2 results and subsequent FDA discussions

In this Phase 2 proof -of-concept trial, the primary endpoint was the percentage of heartburn episodes completely relieved within 3 hours and with no further heartburn reported for 24 hours after taking study drug. Within three hours, vonoprazan 10 mg, 20 mg, and 40 mg achieved complete and sustained relief in 56.0%, 60.6% and 70.0% of evaluable heartburn episodes, respectively, as compared to 27.3% of episodes for placebo.

The PHALCON-NERD open-label daily dosing run-in phase, where all participants enrolled received vonoprazan 20 mg QD for four weeks, the mean percentage of 24-hour heartburn free days observed was 65.4% (median 76.0%) over this treatment period.

Results of Phase 2 NERD On Demand Dosing Trial

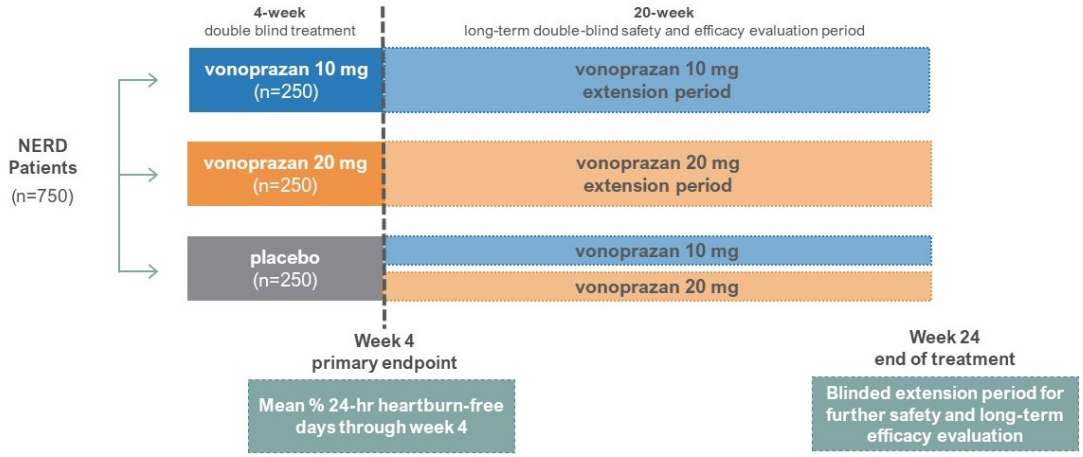


Daily Dosing of Vonoprazan for the Treatment of NERD (NERD-301)

We initiated a single Phase 3 clinical trial of vonoprazan in symptomatic NERD in February 2022. Our trial explores both vonoprazan10 mg and 20 mg doses in the Phase 3 daily dosing study. The primary endpoint of this trial is the percentage of 24-hour heartburn-free days (without daytime or nighttime heartburn as assessed by daily diary) for each vonoprazan treatment group compared to placebo. This is the same endpoint used in other Phase 3 trials for PPIs that are approved for the treatment of NERD.

Design for NERD-301 Phase 3 NERD Continuous Dosing Clinical Trial

NERD-301 is a Phase 3, multicenter, double-blind study of vonoprazan versus placebo assessing the relief of heartburn. Approximately 750 subjects with NERD (as confirmed by endoscopy) and heartburn symptoms will be randomized to receive vonoprazan 10 mg, vonoprazan 20 mg, or placebo QD for 4 weeks. Subjects will complete an electronic diary twice daily to record the presence and maximum severity of daytime and nighttime heartburn symptoms and use of study-supplied rescue antacid throughout the study. After the placebo-controlled treatment period, all subjects will receive blinded vonoprazan (10 mg or 20 mg QD) in a 20 week extension period.



We expect to report topline data from this clinical trial in 2023.

Prior Clinical Trials of Vonoprazan for the Treatment of NERD

Takeda conducted two Phase 3 multicenter, randomized, double-blind, parallel group trials with vonoprazan in Japanese patients with endoscopically confirmed NERD. In the first clinical trial, vonoprazan demonstrated a significant reduction in symptom severity versus placebo (p=0.0139), and in the second trial, vonoprazan demonstrated a faster onset of symptom relief versus placebo (p=0.0003). However, the studies did not show a statistically significant difference in the primary endpoint of proportion of days over a 4-week period without heartburn between vonoprazan and placebo (p=0.0504 and p=0.0643). We believe that the design of these trials may have contributed to their results. For example, the first trial, which studied vonoprazan 10 mg and 20 mg, included a 1-week single blind antacid run-in period where patients were instructed to take antacids after each meal, 3 times per day. Only those patients who did not respond to the antacid treatment were randomized into the double-blind portion of the trial. We believe this design unintentionally enriched the study with patients with non-acid related, or functional disease. In contrast, none of the PPI placebo-controlled continuous dosing studies that were used for U.S. registration employed an antacid run-in period. A high number of subjects suffering from functional heartburn might explain the unusually low response rates seen in this trial both for placebo (7%) and the vonoprazan test regimens (10-12%). In addition, nearly 40% of all patients in this study did not experience a single heartburn free day during the 4 weeks of the study, which in our view is suggestive of a highly prevalent functional heartburn patient population.

In the second study, the single-blind run-in period was changed to be a placebo run-in, where responders would not be eligible for double-blind period; added a specific exclusion criterion for functional heartburn; reduced the diary collection period from twice daily to once daily; and dropped the 20 mg dose choosing to study the 10 mg dose. In contrast to the first study, this study produced historically high placebo response rate (62%). Nevertheless, the data in this study show a clearer benefit of vonoprazan (73%) over placebo than the first study. While the primary endpoint of heartburn free days missed significance (p= 0.0643) due to the high placebo response, we believe this study shows that vonoprazan demonstrates improvement in NERD compared to placebo. We believe that reducing the diary to once daily may have contributed to a higher placebo response, and that not including the 20 mg dose prevented this trial from having its best chance at succeeding.

PPI NERD trials conducted in Japan have generally seen higher placebo response rates and reduced effect sizes than the U.S. PPI NERD counterpart studies. We think this is related to regional variations in identifying true heartburn over other GI related symptoms. Accordingly, we have decided to conduct our initial NERD study only at sites located in the United States.

Further, in a Phase 2 clinical trial in European patients with NERD who were partial responders to high dose PPIs, vonoprazan did not demonstrate superiority versus esomeprazole in the primary endpoint of the percentage of heartburn free days over the four-week treatment period. As was the case with the NERD trials conducted by Takeda in Japanese patients, we believe this result may have been due to inclusion of patients with GI disorders unrelated to acid.

Vonoprazan in Combination with Antibiotics for the Treatment of *H. pylori* Infection

Disease Burden and Outcomes

H. pylori is a bacterial pathogen that infects approximately 35% of the U.S. population, 45% of the EU5 population, and more than 50% of the global population. We estimate that there are approximately 115 million individuals in the United States and 145 million individuals in the EU5 infected with *H. pylori*, and we believe there are approximately 2.5 million patients treated for *H. pylori* infection in the United States each year. As a result of the chronic inflammation induced by *H. pylori* infection, approximately 20% of infected patients develop a range of pathologies including dyspepsia, peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma. Gastric cancer is the third most common cause of cancer-related death worldwide, and over 80% of gastric cancers are attributed to *H. pylori* infection. Globally there are more than one million new cases of gastric cancer and approximately 782,000 deaths each year. Eradication of *H. pylori* infection has been proven to reduce the incidence of gastric cancer, and the American College of Gastroenterologists, or ACG, guidelines recommend treatment for all patients diagnosed with *H. pylori* infection.

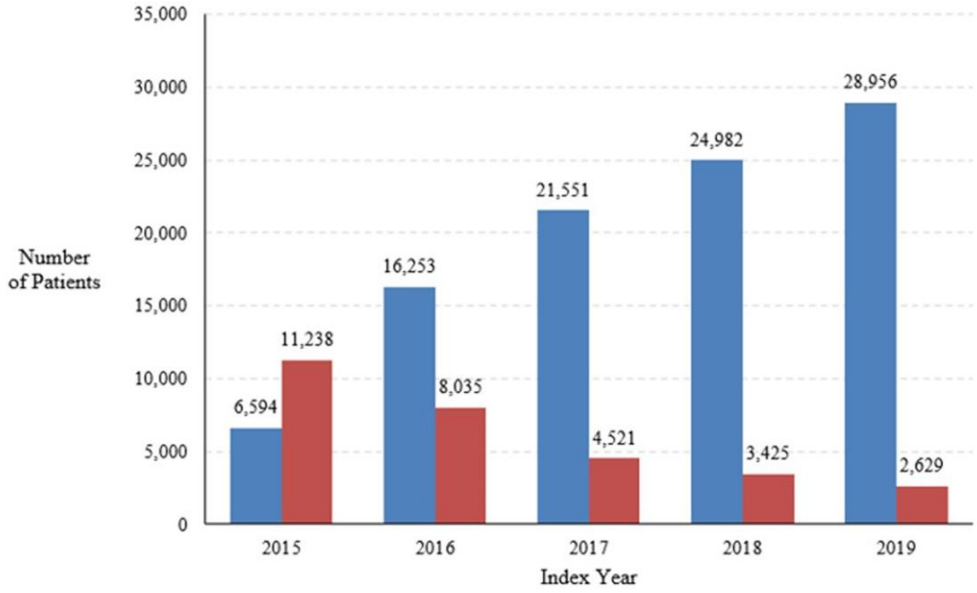
H. pylori eradication rates from the 1990s have fallen to current rates of <80% due to increasing antibiotic resistance. In 2017, the World Health Organization (WHO) listed *H. pylori* among the 16 antibiotic-resistant bacteria that pose the greatest threat to human health and designated *H. pylori* as a Class 1 carcinogen, meaning that it is a definite known cause of cancer. In 2014, the FDA added *H. pylori* to the agency's list of qualifying pathogens that have the potential to pose a serious threat to public health under the GAIN Act. We believe that vonoprazan-based treatment regimens have the potential to restore eradication rates to their original rates in the United States and Europe given the clinical and post-marketing experience in the Japanese market.

A recent study compiled real-world health insurance claims data in Japan from 2008 to 2016 for *H. pylori* eradication. Prior to vonoprazan's approval in late 2014, the *H. pylori* eradication rate across Japan fell to below 80% as shown in the figure below. Approximately one year after vonoprazan's launch, the eradication rate increased to greater than 85%. From January 2015 to March 2016, the eradication rate with PPI-containing regimens in Japan was between 78% and 82% while the eradication rate with vonoprazan-containing regimens was 91% across all patients in this analysis. Results are similar in an ongoing real-world study we are conducting using a different Japanese health insurance claims database. Among patients initiating vonoprazan or a PPI between January 2015 and January 2020 to treat *H. pylori* infection, 80% of PPI-treated patients and 93% of vonoprazan-treated patients did not receive a second line of triple therapy.

Eradication Rate of *H. pylori* Infection in Japan Before and After Launch of Vonoprazan

In Japan, vonoprazan-containing regimens have become the most common first line treatment. One-year post launch, approximately 80% of all treated *H. pylori*-infected patients received vonoprazan-based regimens. In the ongoing study of *H. pylori*-infected patients, vonoprazan-based regimens overtook PPI-based regimens as the most common first-line treatment between 2015 and 2019. Within this Japanese database, the number of patients using vonoprazan-based regimens increased from 6,594 to 28,956 patients, while the number of patients using a PPI-based regimen decreased from 11,238 to 2,629, shown in the figure below.

Uptake of Vonoprazan-Based vs. PPI-Based Therapy for First Line Treatment of *H. pylori* Infection in Japan from 2015-2019



Current Treatment Paradigm in the United States and Europe

The ACG treatment guidelines for *H. pylori* infection recommend using PPIs in conjunction with antibiotics to improve antibiotic efficacy against *H. pylori* infection. The use of anti-secretory agents enhances the effect of antibiotics in two ways. First, anti-secretory agents increase gastric pH, which in turn increases the stability of the antibiotics. For example, amoxicillin and clarithromycin are chemically unstable at the low pH typically found in the human stomach. Second, several antibiotics, including amoxicillin and clarithromycin, are most potent against *H. pylori* at the time of maximum bacterial replication, which occurs at pH 6.0 to 8.0. *H. pylori* is in a dormant state at lower pH values, which reduces the effectiveness of the antibiotics.

The table below shows the minimum inhibitory concentration of antibiotic required to eradicate 90% of *H. pylori* in vitro, or MIC90. As pH increases, the amount of antibiotic required for 90% eradication decreases substantially.

***H. pylori* MIC_{90} Values as a Function of pH**

	MIC_{90} (mg/L)		
	pH 7.5	pH 6.0	pH 5.5
Ampicillin	0.06	0.25	0.5
Clarithromycin	0.03	0.06	0.25

A triple therapy regimen (PPI, clarithromycin, and either amoxicillin or metronidazole) is the regimen most commonly used in clinical practice for the first-line treatment of *H. pylori* infection. However, *H. pylori* eradication rates with PPI triple therapy in the 1990s have fallen to current levels of <80%, primarily due to increased resistance of *H. pylori* to clarithromycin and metronidazole. A recent meta-analysis indicates that U.S. resistance rates measured from 2012 to 2016 were 20% for clarithromycin, 29% for metronidazole, and 19% for levofloxacin. Additionally, in a U.S.-based study from 2021, 65.6% of tested *H. pylori* was resistant to at least one antibiotic currently used for treatment, with resistance rates of 33% clarithromycin and approximately 30% for metronidazole and levofloxacin. These figures represent a marked increase from 2009 to 2011 for both clarithromycin and metronidazole, for which resistance was 9% for clarithromycin, 21% for metronidazole, and 11% for levofloxacin. *H. pylori* resistance to amoxicillin remains low despite its use in most triple therapy regimens; resistance is generally <2% among isolates in the United States and Europe. There is a similar trend of increasing resistance to key antibiotics in Europe.

Given the declining eradication rates for *H. pylori*, quadruple therapy is recommended as first-line treatment in areas with known high rates of clarithromycin or metronidazole resistance; however, our U.S. market research study reported that physicians prescribe quadruple therapy to only 17% of first-line patients. Due predominantly to considerations of convenience and patient compliance, approximately 75% physicians surveyed in our market research expressed a preference for convenience, or combination packs compared to individual bottles for both dual and triple therapy. Further, geographic patterns of resistance in the United States are poorly understood and treatment is largely empiric, with susceptibility testing rarely conducted prior to first-line treatment. Our U.S. market research study reported that only 8% and 16% of physicians conduct resistance testing prior to prescribing treatment for first-line and second-line *H. pylori* infection, respectively.

In our U.S. market research study, physicians highlighted the need for more effective and simpler first-line treatment options. For the treatment of *H. pylori* infection, surveyed physicians highlighted the need for improved eradication rates and more convenient dosing as key unmet needs. Over 50% of surveyed physicians agreed that vonoprazan dual or triple therapy provided a superior eradication rate in patients with clarithromycin-resistant *H. pylori*, and, on average, 48% and 47% reported a preference to use vonoprazan first line in patients with *H. pylori* infection, and patients with refractory *H. pylori* infection, respectively.

Our H. pylori Phase 3 Clinical Trial in the United States and Europe – PHALCON-HP

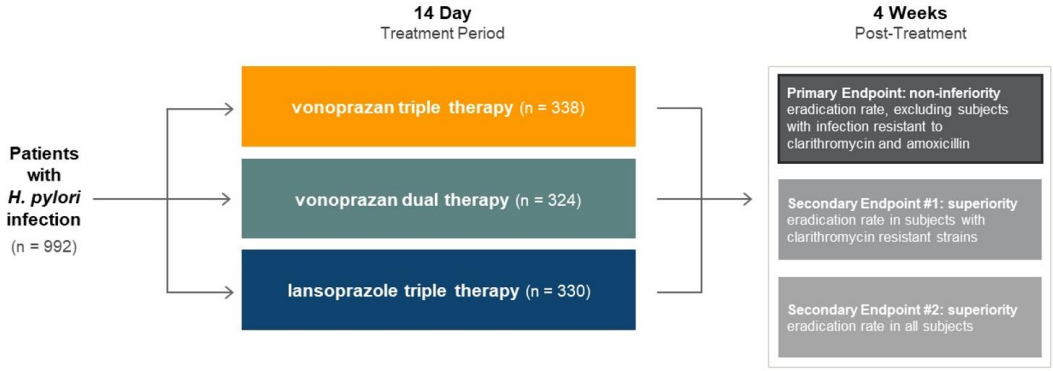
In April 2021, we announced that in PHALCON-HP, our pivotal Phase 3 clinical trial for the eradication of *H. pylori* infection, both vonoprazan-based regimens successfully met their primary endpoints and met all secondary endpoints. The trial studied vonoprazan triple therapy and vonoprazan dual therapy compared to lansoprazole triple therapy. We believe PHALCON-HP is the largest U.S. Phase 3 registration trial ever conducted in *H. pylori* infection, randomizing 992 patients with confirmed *H. pylori* infection.

PHALCON-HP was a randomized, multicenter, Phase 3 trial that enrolled 1046 patients of which 992 patients with a confirmed *H. pylori* infection were randomized to one of three arms:

- ***vonoprazan dual therapy***: vonoprazan 20 mg BID and amoxicillin 1 g TID for 14 days (n=324);
- ***vonoprazan triple therapy***: vonoprazan 20 mg BID, amoxicillin 1000 mg BID and clarithromycin 500 mg BID for 14 days (n=338); and
- ***PPI triple therapy***: lansoprazole 30 mg BID, amoxicillin 1000 mg BID and clarithromycin 500 mg BID for 14 days (n=330).

The objective of the PHALCON-HP trial was to compare eradication rates in all treated subjects as well as in two pre-identified subgroups of patients: those patients with clarithromycin resistant strains of *H. pylori*, and those patients who did not have clarithromycin or amoxicillin resistant strains of *H. pylori*. For regulatory purposes, the primary endpoint of this study was a non-inferiority comparison in the non-resistant subgroup for each of vonoprazan triple therapy and vonoprazan dual therapy compared to lansoprazole triple therapy. All endpoints measured the percentage of patients with successful eradication of *H. pylori* infection as assessed by ^{13}C-urea breath test four weeks after completion of treatment. The primary analysis in the non-resistant population assessed the non-inferiority of vonoprazan dual therapy compared to lansoprazole triple therapy and vonoprazan triple therapy compared to lansoprazole triple therapy. Secondary analyses for superiority were conducted in all patients and in the subgroup of patients with clarithromycin-resistant *H. pylori* infection. Further efficacy analyses were conducted using the pre-specified per protocol population (n=822), which is comprised of patients who were protocol compliant as defined by FDA established criteria.

Design for PHALCON-HP Phase 3 *H. pylori* Clinical Trial



Primary endpoint analysis

Both vonoprazan-based regimens successfully met their primary endpoints in the subset of patients with *H. pylori* strains that were not shown to be resistant to clarithromycin or amoxicillin. In the mITT population, *H. pylori* eradication rates were 84.7% with vonoprazan triple therapy and 78.5% for vonoprazan dual therapy compared to 78.8% with lansoprazole triple therapy ($p<0.0001$ and $p=0.0037$, respectively, for non-inferiority).

In the per protocol population, *H. pylori* eradication rates were 90.4% with vonoprazan triple therapy and 81.2% with vonoprazan dual therapy compared to 82.1% with lansoprazole triple therapy (p<0.0001 and p=0.0077, respectively, for non-inferiority).

Secondary endpoint analysis

Vonoprazan triple therapy and vonoprazan dual therapy also met all secondary endpoints, and demonstrated superior eradication rates versus lansoprazole triple therapy in all patients and patients with clarithromycin resistant strains of *H. pylori*. Patients with clarithromycin resistant strains comprised 20.3% of the PHALCON-HP study population.

Vonoprazan triple therapy

The *H. pylori* eradication rate of vonoprazan triple therapy was superior to that of lansoprazole triple therapy among all patients in both the mITT population (80.8% vs. 68.5%; p=0.0001) and the per protocol population (85.7% vs. 70.0%; p<0.0001).

The *H. pylori* eradication rate with vonoprazan triple therapy was superior to that of lansoprazole triple therapy in the subset of patients with *H. pylori* strains resistant to clarithromycin in both the mITT population (65.8% vs. 31.9%; p<0.0001) and the per protocol population (67.2% vs. 29.0%; p<0.0001).

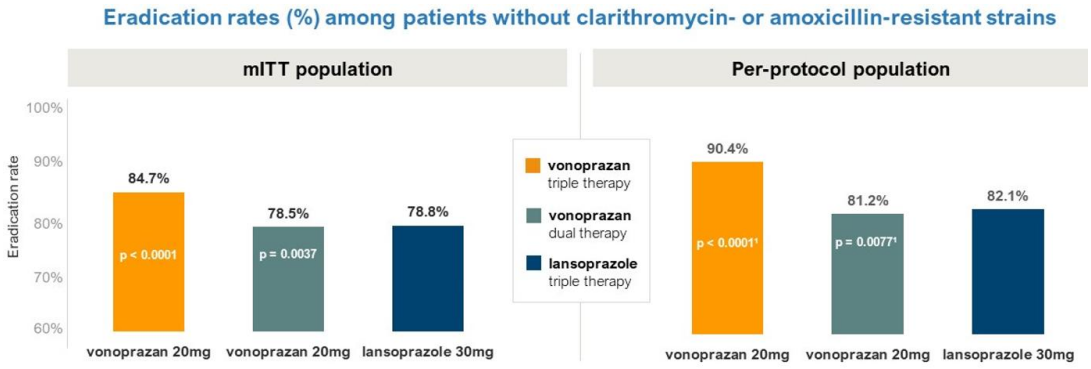
Vonoprazan dual therapy

The *H. pylori* eradication rate of vonoprazan dual therapy was superior to that of lansoprazole triple therapy among all patients in both the mITT population (77.2% vs. 68.5%; p=0.0063) and the per protocol population (81.1% vs. 70.0%; p=0.0013).

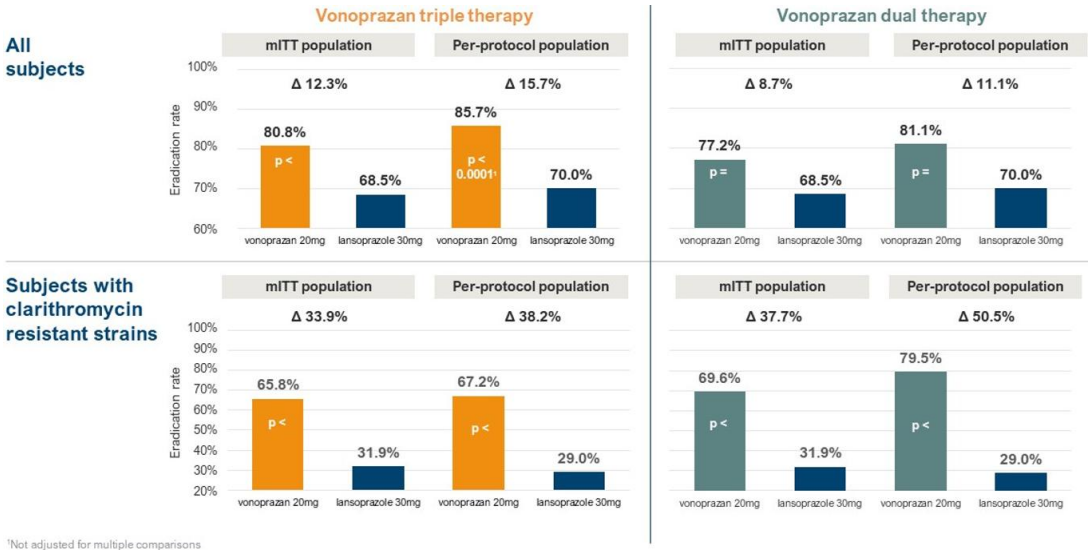
The *H. pylori* eradication rate of vonoprazan dual therapy was superior to that of lansoprazole triple therapy in the subset of patients with *H. pylori* strains resistant to clarithromycin in both the mITT population (69.6% vs. 31.9%; p<0.0001) and the per protocol population (79.5% vs. 29.0%; p<0.0001).

Results of US/EU Phase 3 Clinical Trial in *H. Pylori* Infection

Primary Endpoint Analysis –Subjects without clarithromycin or amoxicillin resistant strains



Secondary Endpoint Analyses – All subject and subjects with clarithromycin resistant strains



Antibiotic resistance and declining eradication rates are significant clinical issues, and we believe that vonoprazan triple therapy and vonoprazan dual therapy have the potential to provide improvements over PPI-based therapies in addressing each of these issues. Vonoprazan dual therapy also has potential to spare the use of clarithromycin, representing an opportunity both for effective treatment and sound antibiotic stewardship through the avoidance of an additional antibiotic. As an alternative to multi-antibiotic drug regimens, vonoprazan dual therapy might also help to limit the spread of resistance among other pathogenic bacteria within populations. In addition, the vonoprazan triple therapy and vonoprazan dual therapy will both be available in daily dosing blister cards inclusive of the appropriate antibiotic. We believe this convenience pack has the potential to enhance compliance in a category where full adherence to treatment regimen is often a challenge.

Convenience Pack for H. pylori.

In September 2021, we submitted NDAs for vonoprazan triple therapy and vonoprazan dual therapy for the treatment of *H. pylori* infection in adults, each as a pre-packaged convenience or combination pack with either clarithromycin and amoxicillin or amoxicillin alone. In November 2021, the FDA accepted our NDAs for filing and granted Priority Review with a PDUFA action date of May 3, 2022. If approved by the PDUFA date, we expect to launch convenience packs with vonoprazan dual therapy and vonoprazan triple therapy in the second half of 2022.

Convenience packs have the potential to improve patient adherence and treatment outcomes, and we believe there is a meaningful market opportunity for such a product. In the United States, PrevPac was formerly marketed as a pre-packaged convenience pack of lansoprazole, clarithromycin, and amoxicillin and achieved peak sales of $150 million. In Japan, vonoprazan is marketed both as a stand-alone medicine as well as in pre-packaged convenience packs with either clarithromycin and amoxicillin (Vonosap) or metronidazole and amoxicillin (Vonopion).

Phase 3 Clinical Trial in Japan of Vonoprazan in Combination with Antibiotics to Treat H. pylori Infection

The results of PHALCON-HP were consistent with the results of a Phase 3 clinical trial in *H. pylori*-positive patients completed in Japan. In that trial, patients were treated with either vonoprazan triple therapy (vonoprazan 20 mg BID, amoxicillin 750 mg BID, and clarithromycin (200 mg or 400 mg) BID) or lansoprazole triple therapy (lansoprazole 30 mg BID, amoxicillin 750 mg BID, and clarithromycin (200 mg or 400 mg) BID) for seven days as is customary in Japan. The primary endpoint of the clinical trial was confirmed *H. pylori* eradication determined by ^{13}C-urea breath test. The primary analysis was non-inferiority, and additional analyses in the second line eradication rate and eradication rate in antibiotic-resistant subgroups were also conducted.

Vonoprazan-based triple therapy demonstrated a non-inferior eradication rate of 93% compared to 76% for lansoprazole-based triple therapy ($p<0.0001$). Post hoc analyses suggested that vonoprazan-based triple therapy was superior to lansoprazole-based triple therapy ($p<0.0001$). Patients who were not eradicated on vonoprazan-based triple therapy or lansoprazole-based triple therapy were treated with a triple therapy regimen of vonoprazan, amoxicillin, and metronidazole. In this second-line setting, the *H. pylori* eradication rate with vonoprazan triple therapy was 98%. Exploratory analysis suggested that vonoprazan-based triple therapy had significantly higher eradication rates versus the lansoprazole-based triple therapy in the subgroup of subjects with clarithromycin resistant strains of *H. pylori*.

Summary of Vonoprazan Safety Data

Safety in Clinical Studies

As of December 2021, over 8,000 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 PHALCON-HP, both vonoprazan-based regimens were generally well tolerated with safety results comparable to patients who received lansoprazole triple therapy. The most common adverse events (≥2.0%) reported in the vonoprazan triple therapy, vonoprazan dual therapy, and lansoprazole triple therapy arms, respectively, were diarrhea (4.0%, 5.2%, and 9.6%), dysgeusia (4.3%, 0.6%, and 6.1%), abdominal pain (2.3%, 2.6% and 2.9%), headache (2.6%, 1.4%, 1.4%), vulvovaginal candidiasis (2.3%, 1.4%, 1.2%), hypertension (2.0%, 1.1%, 0.9%), and nasopharyngitis (0.3%, 2.0%, 0.9%). Overall rates of discontinuation due to adverse events were 2.3% for vonoprazan triple therapy-treated patients, 0.9% for vonoprazan dual therapy-treated patients, and 1.2% for lansoprazole triple therapy-treated patients.

Additionally, the safety results for vonoprazan observed in PHALCON-EE were consistent with the results observed in prior clinical studies. In the healing phase of the study, the most common adverse events (≥2%) were abdominal pain (2.1% for vonoprazan and 1.2% for lansoprazole), diarrhea (2.1% for vonoprazan and 2.5% for lansoprazole). Rates of discontinuation due to adverse events in the healing phase were 1% for vonoprazan 20 mg and 2.2% for lansoprazole 30 mg.

In the maintenance phase of the study, the most common adverse events (≥2%) were gastritis (2.7% vonoprazan 10 mg, 6.4% vonoprazan 20 mg, 2.7% lansoprazole), diarrhea (1.0% vonoprazan 10 mg, 2.7% vonoprazan 20 mg, 4.4% lansoprazole), abdominal pain (4.1% vonoprazan 10 mg, 5.4% vonoprazan 20 mg, 2.4% lansoprazole), dyspepsia (3.7% vonoprazan 10 mg, 4.1% vonoprazan 20 mg, 2.7% lansoprazole), gastroesophageal reflux disease (2.4% vonoprazan 10 mg, 3.7% vonoprazan 20 mg, 2.0 lansoprazole), hypertension (3.0% vonoprazan 10 mg, 3.4% vonoprazan 20 mg, 2.0% lansoprazole), liver function test (1.0% vonoprazan 10 mg, 2.0% vonoprazan 20 mg, 3.0% lansoprazole), and nausea (2.0% vonoprazan 10 mg, 1.4% vonoprazan 20 mg, 1.0% lansoprazole). Rates of discontinuation due to adverse events in the maintenance phase were 0.7% for vonoprazan10 mg, 2.7% for vonoprazan 20 mg, and 0.7% for lansoprazole.

Frequency of serious adverse events, or SAEs, in the healing phase were similar between vonoprazan 20 mg and lansoprazole 30 mg at 0.6%. In the maintenance phase, SAEs were reported in 4.7% of patients for vonoprazan 20 mg, 3.4% for vonoprazan 10 mg and 2.4% for lansoprazole 15 mg. Further, this clinical trial was conducted during the 2020-2021 global pandemic, and coronavirus infection was reported in 2.1% of the vonoprazan 20 mg-treated patients and 1.8% of the lansoprazole-treated patients in the healing phase whereas in 6.1% of the vonoprazan 10 mg-treated patients, 10.1% of the vonoprazan 20 mg-treated patients and 6.7% of the lansoprazole-treated patients in the maintenance phase. There were 2 deaths in the vonoprazan 20 mg-treated patients due to coronavirus infection. None of the coronavirus infection events reported were considered related by the investigator.

In PHALCON-NERD, vonoprazan was generally well tolerated. In both phases of the trial, no adverse event was reported in more than three percent of the participants in a treatment group. There was a total of four SAEs in the daily dosing phase and no SAEs in the on-demand phase. The safety data for all vonoprazan arms were comparable to placebo and consistent with what was reported in previous studies.

Certain earlier generation P-CABs 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 P-CAB class. It is notable that vonoprazan is based on a pyrrole chemical structure and is chemically distinct from previously discontinued P-CABs that were based on an imidazole structure. Vonoprazan has had a similar hepatic safety profile to lansoprazole across all 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, transient ALT or AST elevations 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.

Vonoprazan Post-Marketing Safety in Japan and Asia

The most recent post-marketing safety report from December 2021 includes an estimate of over 50 million patients who have received vonoprazan in Japan and other countries in Asia since its 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 believed to be idiosyncratic reactions. Post-marketing safety data, including the December 2021 post-marketing safety report, has been submitted to the PMDA.

Vonoprazan Launch in Japan

Vonoprazan Regulatory Status

Vonoprazan first received approval in Japan on December 26, 2014 as TAKECAB® for the following indications:

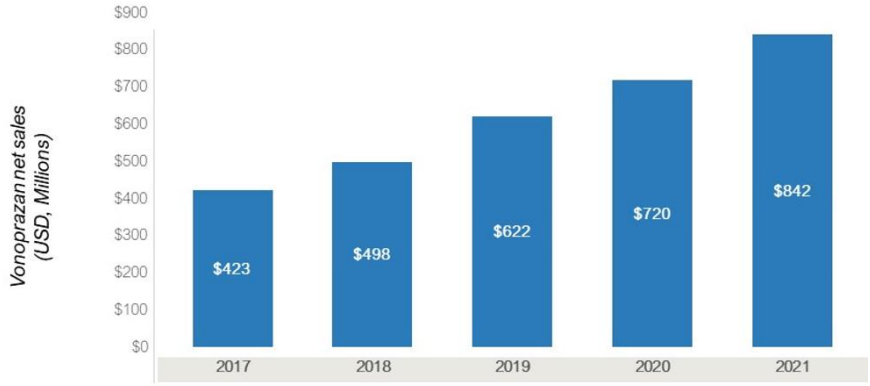
- Healing and maintenance of healing of erosive esophagitis;
- Adjunct to antibiotics in *H. pylori* treatment;
- Gastric ulcer;
- Duodenal ulcer;
- Prevention of recurrence of gastric ulcer or duodenal ulcer during low-dose aspirin administration; and
- Prevention of recurrence of gastric ulcer or duodenal ulcer during nonsteroidal anti-inflammatory drug (NSAID) administration.

Vonoprazan was subsequently approved in Japan in February 2016 for the treatment of *H. pylori* in combination packs with antibiotics (Vonosap Pack 400, Vonosap Pack 800, and Vonopion Pack), and has since been approved in numerous other countries in Asia and Latin America as well as Russia.

Vonoprazan Commercialization in Japan

Vonoprazan was approved in Japan in December 2014. In 2021, its seventh full year on the market, vonoprazan generated approximately $850 million in net sales in Japan, a 17% increase over the prior year. In addition, in the quarter ended December 31, 2021, vonoprazan generated over $249 million in net sales, a 16% increase over the corresponding quarter from the prior year.

Vonoprazan net sales in Japan (2017-2021)



*Sales for Q1 2017 reported on a gross basis
**U.S. dollars based on the conversion rate of 0.0090 dollar to one yen

We believe that the market dynamic for anti-secretory agents in Japan is similar to that in the United States. In both countries, the anti-secretory market is largely genericized. Ahead of the vonoprazan launch in Japan, all PPIs, other than Nexium, were available as generics. As of September 2020, generic drugs in Japan represent approximately 80% of the market by volume, compared to the United States where generics are currently approximately 90% of the market by volume. Although vonoprazan and Dexilant are priced at a premium to generic PPIs in Japan and the United States, respectively, both have experienced commercial success.

Vonoprazan Commercial Opportunity and Strategy

The market for prevention and treatment of acid-related GI diseases in the United States and Europe is large. There were approximately 7.2 billion PPI doses prescribed for the 12 months ended December 31, 2021. We estimate that there are approximately 65 million individuals with GERD in the United States and 50 million individuals with GERD in the EU5, of whom 15% to 45% are inadequately treated with PPIs. In addition, we estimate that there are approximately 115 million individuals in the United States infected with *H. pylori*, of which 2.5 million are treated each year, and 145 million individuals in the EU5 infected with *H. pylori*.

Over many decades of use, multiple drug classes and individual drugs have demonstrated the substantial commercial opportunity for therapies treating acid-related GI diseases. H2RAs including Axid, Pepcid, Tagamet, and Zantac provided the first significant improvement in disease management over antacids and as a class reached $3.5 billion in annual sales. After H2RAs, PPIs emerged as the new standard of care. Prior to the introduction of generic and OTC alternatives, annual PPI class sales reached approximately $12.5 billion in the United States, and peak sales for individual brands were approximately $3.7 billion for Prilosec, approximately $3.5 billion for Nexium, and $3.4 billion for Prevacid.

As recently as 2015, the last branded PPI, Dexilant, reached approximately $530 million in sales in the United States despite limited differentiation from other PPIs. As of December 31, 2021, Dexilant was priced at a significant premium to generic PPIs on the market. Even with premium pricing, Dexilant obtained broad insurance coverage and favorable access. As of December 2021, approximately 87% of commercially covered lives and 82% of Medicare covered lives had access to Dexilant. Furthermore, of those commercially covered lives, 48% had unrestricted access to the drug without prior authorization or step edits and 28% of patients had access at the lowest branded cost tier. We believe that, if approved in our markets, vonoprazan will be the first of the next generation of anti-secretory therapies to improve the standard of care for acid-related GI diseases by providing a safe and effective treatment option for the millions of patients in need of more potent, rapid, or durable acid suppression. Additionally, we believe the results of our Phase 3 clinical trials in *H. pylori* and erosive esophagitis support the potential differentiation of vonoprazan compared to a standard of care PPI, and if vonoprazan is approved, could result in attractive market access and formulary positioning.

In May 2021, we conducted a U.S. market research study with 100 gastroenterologists, 102 primary care physicians, and 40 gastroenterology advanced practice providers who treat *H. pylori* infection. These clinicians stated a preference to prescribe vonoprazan dual or triple therapy first line to 53% of their patients with *H. pylori* infection, and to 52% of their patients with refractory *H. pylori* infection. In the same study, in terms of aspects of vonoprazan that positively impacted the intention to prescribe, 69% of clinicians said mechanism of action, and 52% said the efficacy in patients with clarithromycin-resistant strains of *H. pylori*, respectively. In December 2021, we conducted a separate U.S. market research study with 151 gastroenterologists, 100 primary care physicians, and 50 advanced practice providers who treat GERD. For the treatment of erosive esophagitis, 65% - 67% of respondents believed that vonoprazan is differentiated from standard of care PPIs, has demonstrated superior efficacy in the healing and maintenance of healing of esophageal erosions compared to lansoprazole, and delivers symptom relief.

Sales and Marketing

We are in the process of building marketing, sales, and distribution capabilities. We plan to independently commercialize vonoprazan in the United States by building a leading specialty gastroenterology-focused commercial infrastructure to support the adoption of vonoprazan. We believe we can successfully launch vonoprazan in the United States with a focused sales force targeting high prescribers of PPIs, particularly gastroenterologists and primary care physicians. PPI prescribing is highly concentrated with approximately 75% of prescriptions in *H. pylori* and 65% of prescriptions in erosive esophagitis being written by 10% of the PPI prescribers (approximately 51,400 prescribers), according to IQVIA data. We believe we have an opportunity to achieve significant share of voice and exposure to physicians given the scarcity of actively marketed anti-secretory medicines.

To address the commercial opportunity for vonoprazan in Europe and Canada, we plan to seek one or more partners with existing commercial infrastructure and expertise in these markets.

Additional Vonoprazan Development Opportunities

Indications

While we are initially focused on the development of vonoprazan for the treatment of GERD and *H. pylori* infection, we believe there are opportunities to expand the use of vonoprazan to other indications in our licensed territories. For example, in Japan, vonoprazan is also approved for the treatment of gastric ulcers, treatment of duodenal ulcers, prevention of recurrence of gastric ulcer or duodenal ulcer during low-dose aspirin administration, and prevention of recurrence of gastric ulcer or duodenal ulcer during NSAID administration. Barrett’s esophagus and Zollinger Ellison syndrome are severe diseases related to acid secretion where PPIs are the current standard of care. The improved acid control of vonoprazan relative to PPIs may lead to improved results over PPIs.

Eosinophilic esophagitis is an autoimmune disease with significant unmet need. Although not approved for this indication, PPIs are prescribed for the treatment of eosinophilic esophagitis. Vonoprazan demonstrated similar efficacy to PPIs in an investigator-sponsored clinical trial in Japan. In this clinical trial, 112 patients with eosinophilic esophagitis were treated with vonoprazan, or the PPI rabeprazole or esomeprazole. Of patients treated with vonoprazan, 82% had complete relief of symptoms compared to 70% for esomeprazole and 76-78% for rabeprazole. Similarly, 35% of patients treated with vonoprazan demonstrated complete remission of eosinophilic esophagitis by histology, compared to 37% for esomeprazole and 31-38% for rabeprazole.

Formulations and Packaging

Orally Disintegrating Tablet. An orally disintegrating tablet, or ODT, formulation for vonoprazan is currently in development by Takeda. We may conduct one or more Phase 1 trials to support potential approval of the ODT formulation. We believe that the ODT represents a meaningful commercial opportunity for patients with difficulty swallowing, as estimated peak U.S. sales of the lansoprazole ODT formulation were over $450 million.

Intravenous Formulation. We are exploring the potential to develop an intravenous formulation of vonoprazan for use in acute bleeding, critically ill patients, or other in-hospital applications. Several PPIs have approved intravenous formulations.

Pediatric Formulation. We are exploring the potential to develop an oral formulation, in addition to an ODT formulation, for pediatric use.

Over the Counter Use

We believe that vonoprazan has the ideal profile for an OTC product, including the potential for on-demand symptom relief and a well-tolerated safety profile. Sales of OTC heartburn relief products in the United States are substantial, constituting a multi-billion-dollar market.

Competition

The biopharmaceutical industry is characterized by rapidly advancing technologies, intense competition and strong emphasis on proprietary products. We face potential competition from many sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and government agencies and public and private research institutions. If vonoprazan receives marketing approval in the United States, Europe or Canada, it will compete with existing therapies and new therapies that may become available in the future.

Some of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and commercializing those treatments. These same competitors may invent technology that competes with vonoprazan. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and subject recruitment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for vonoprazan, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, we expect that vonoprazan, if approved, will be priced at a premium over competitive generic products and our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

We expect that vonoprazan, if approved for the treatment of patients with erosive esophagitis and treatment of *H. pylori* infection in adults, will primarily compete with generic PPIs marketed by multiple pharmaceutical companies in both the prescription and OTC markets. Additionally, in March 2020, RedHill Biopharma Ltd. launched Talicia, a co-formulated capsule comprising generic omeprazole, amoxicillin, and rifabutin for the treatment of *H. pylori* infection.

We are aware of one other P-CAB in development in the United States, as well as a number of other P-CABs in territories outside of the United States that if developed and approved in our territories may compete with vonoprazan. In the United States, Neurogastrx intends to commence a Phase 3 erosive esophagitis trial for fexuprazan, under an exclusive license from Daewoong Pharmaceutical Co., Ltd., or Daewoong, sometime in 2022. Outside the United States, Daewoong recently received regulatory approval of, and plans for a first half of 2022 launch for fexuprazan in South Korea, 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 marketed by CJ Healthcare Corp. in South Korea and is currently in development in Japan by RaQualia Pharma, Inc. Additionally, Jeil Pharm has received authorization to conduct a Phase 3 trial in South Korea of its P-CAB candidate, JP-1366, in erosive esophagitis, and Cinclus Pharma AG's linaprazan glurate has completed a Phase 1 clinical trial in Europe and is currently in Phase 2 clinical trials. To our knowledge, none of these compounds have demonstrated superiority to PPIs on clinical endpoints.

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 in Phase 3 clinical trials in Indonesia, Sihuan Pharmaceutical's anaprazole, currently in Phase 3 clinical trials in China, Eisai's azeloprazole, currently in a Phase 2 clinical trial in Japan, and Sidem Pharma's tenatoprazole, currently in Phase 2 clinical trials in Europe and Canada.

Intellectual Property

Intellectual property, including patents, trade secrets, trademarks and copyrights, is important to our business. Our commercial success depends in part on our ability to obtain and maintain proprietary intellectual property protection for vonoprazan, as well as for future product candidates and novel discoveries, product development technologies, and know-how. Our commercial success also depends in part on our ability to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to develop and maintain protection of our proprietary position by, among other methods, licensing or filing U.S. and foreign patents and applications relating to our technology, inventions, and improvements that are important to the development and implementation of our business.

Our patent portfolio, comprising patents and patent applications exclusively licensed to us, is built with a goal of establishing broad protection that generally includes, for the product candidate compound, claims directed to composition of matter, pharmaceutical compositions or formulations, methods of synthesis, and methods of treatment using such pharmaceutical compositions or formulations. As of December 31, 2021, our patent portfolio covering vonoprazan consists solely of exclusively licensed patents and patent applications from Takeda. Subject to the terms of the license agreement we entered into with Takeda on May 7, 2019, or the Takeda License, we have licensed from Takeda exclusive rights in the United States, Europe, and Canada to patents and patent applications covering the composition of matter, formulation, use and/or manufacture of vonoprazan. Our patent portfolio comprises 11 distinct patent families protecting the technology relating to the compound vonoprazan and its synthetic intermediates, methods of synthesizing vonoprazan and related compounds, various formulations of vonoprazan products, as well as methods of treating diseases with vonoprazan and related compounds. As of December 31, 2021, our portfolio consists of approximately 22 issued U.S. patents, 5 pending U.S. applications, 13 issued European patents subsequently validated in individual European countries, 4 pending European applications, 5 issued Canadian patents, and 3 pending Canadian applications. The issued patents and pending applications have nominal expiration dates ranging from 2024 to 2038, without accounting for any available patent term adjustments or extensions. The issued U.S. patent covering the composition of matter of vonoprazan is expected to expire in August 2028, not including patent term extension. The issued U.S. patent covering the formulation of vonoprazan is expected to expire in August 2030, not including patent term extension.

The term of individual patents in our portfolio depends upon the legal term of patents in the countries in which they are obtained. In most countries in which we file, including the United States, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the term of a patent may be eligible for patent term adjustment, which permits patent term restoration as compensation for delays incurred at the USPTO during the patent prosecution process. In addition, for patents that cover an FDA-approved drug, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. While the length of the patent term extension is related to the length of time the drug is under regulatory review, 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 one patent per approved drug may be extended under the Hatch-Waxman Act. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek any available patent term extension to any issued patents we may be granted in any jurisdiction where such extensions are available; however, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. The relevant patent laws and their interpretation outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our licensed pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us or Takeda in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, issued patents do not guarantee the right to practice our technology in relation to the commercialization of our products. Issued patents only allow us to block potential competitors from practicing the claimed inventions of the issued patents.

Further, patents and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing vonoprazan and any future product candidates and practicing our proprietary technology, and any issued patents may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for vonoprazan and any future product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to vonoprazan and any future product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us, and for employees and consultants to enter into invention assignment agreements with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Where applicable, the agreements provide that all inventions to which the individual contributed as an inventor shall be assigned to Phathom, and as such, will become our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Further, we have filed for and have received trademark registrations for our company name "Phathom Pharmaceuticals" in the United States, European Union, and other foreign jurisdictions, and are pursuing trademark protection in certain other foreign jurisdictions.

License Agreement with Takeda Pharmaceutical Company Limited

On May 7, 2019, we and Takeda entered into the Takeda License, pursuant to which, Takeda granted us an exclusive, sublicensable (with Takeda's reasonable consent) license under certain patents and know how relating to vonoprazan and owned or controlled by Takeda during the term of the Takeda License to commercialize vonoprazan products using specified formulations for all human therapeutic uses in the United States, Europe and Canada, and a non-exclusive license under such patents and know how to develop and manufacture such 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. We granted Takeda a non-exclusive, royalty-free, sublicensable license under our rights in any patents and know-how that are necessary or useful to enable Takeda to develop and manufacture vonoprazan products anywhere in the world for the purposes of commercialization outside United States, Europe and Canada. We also granted Takeda an exclusive, royalty-free license under our rights in certain patents and know-how owned or controlled by us and necessary for the exploitation of vonoprazan products, in each case for Takeda to commercialize any vonoprazan product outside of the United States, Canada, and Europe and for purposes other than human therapeutic use.

During the term of the Takeda License, we and our affiliates are not permitted to commercialize any pharmaceutical product, other than vonoprazan, that treats acid-related disorders, except for certain generic and OTC competing products in specified circumstances. We will be responsible, at our cost, for the development, manufacture and commercialization of the vonoprazan products. We are required to use commercially reasonable efforts to develop and commercialize the vonoprazan products in our licensed territory.

Under the Takeda License, Takeda has the sole right and authority, with our input, to prepare, file, prosecute, and maintain all Takeda and joint patents on a worldwide basis at its own cost. We are responsible, at our cost, for preparing, filing, prosecuting, and maintaining patents on inventions made solely by us in connection with vonoprazan, subject to input from Takeda. We have the first right to enforce the licensed patent rights with respect to certain infringing products in the United States, Europe and Canada.

We paid Takeda upfront consideration consisting of a cash payment of $25.0 million, 1,084,000 shares of common stock and a warrant to purchase 7,588,000 shares of common stock, or the Takeda Warrant. We agreed to make milestone payments to Takeda upon achieving certain tiered aggregate annual net sales of licensed products in the United States, Europe and Canada up a total maximum milestone amount of $250.0 million. We also agreed to make tiered royalty payments in the low double digits to the mid-teens on net sales of licensed products, subject to specified offsets and reductions. Royalties will be payable, on a product-by-product and country-by-country basis from the first commercial sale of such product in such country, until the latest of expiration of the licensed patents covering the applicable product, expiration of regulatory exclusivity in such country, or 15 years following first commercial sale in such country.

The Takeda License will continue until the expiration of the obligation to pay royalties in all countries and on all products. We may terminate the Takeda License in its entirety without cause upon six months' prior written notice. We and Takeda may terminate the Takeda License in the case of the other party's insolvency, or upon prior written notice within a specified time period 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.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of vonoprazan. Vonoprazan is a small molecule that can be manufactured using commercially available technologies. We currently rely on Takeda to supply us with vonoprazan drug product for clinical use.

With respect to any future product candidates, we expect to continue to rely on third-party contract manufacturers to manufacture clinical supplies and commercial quantities of any approved product. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our relationships with Takeda, Sandoz and Catalent.

Takeda Commercial Supply Agreement

In April 2020, we entered into a Commercial Supply Agreement with Takeda , or the Takeda Supply Agreement, pursuant to which Takeda will supply us with commercial quantities of vonoprazan bulk drug. Pursuant to the Commercial Supply Agreement, Takeda has agreed to supply us certain quantities of vonoprazan bulk drug product according to approved specifications at a fixed price per batch of bulk drug product in order to commercialize vonoprazan in accordance with the Takeda License. The Takeda Supply Agreement sets forth a minimum and maximum number of batches of vonoprazan bulk drug product that we are required to order each year, and if we do not purchase the minimum number of batches in a year, other than as a result of Takeda's inability to supply such batches for any reason, or as a result of force majeure, we are required to pay Takeda the amount corresponding to the shortfall. Takeda has no obligation to supply bulk drug product above the maximum number of batches specified in the Takeda Supply Agreement.

In addition, under the Takeda Supply Agreement, Takeda will provide certain services and materials, including vonoprazan drug substance, to support the transfer of technology and Takeda manufacturing know-how to our contract manufacturing organizations, or CMOs, that we designate. Takeda has agreed to negotiate in good faith to provide reasonable additional support, including technical advice and supply of materials, to assist us with technology transfers to the CMOs.

The Takeda Supply Agreement will continue until the earlier of (a) two years from the date we place an order for bulk drug product for the first commercial launch of vonoprazan in any jurisdiction in the United States, Europe or Canada, and (b) December 31, 2023. The Takeda Supply Agreement may be terminated upon written notice by either party if the other party has failed to remedy a material breach within a specified cure period following written notice of such breach. The Takeda Supply Agreement will terminate immediately upon the termination of the Takeda License in accordance with its terms. We are exploring additional options for commercial supply of vonoprazan API from other third-party contract manufacturers.

Sandoz Supply and Packaging Agreement

In December 2020, we entered into a Supply and Packaging Services Agreement with Sandoz GmbH, or the Sandoz Supply Agreement, pursuant to which Sandoz has agreed to supply commercial quantities of amoxicillin capsules and clarithromycin tablets, to package these antibiotics with vonoprazan drug product in finished convenience packs, and to supply us with these convenience packs.

Pursuant to the Sandoz Supply Agreement, we agreed to purchase certain quantities of convenience packs from Sandoz at an agreed upon price per pack. The price per pack is fixed for the first two (2) years following launch of the convenience pack in the United State and may be adjusted thereafter based on Sandoz's cost increases, subject to an annual cap. The Sandoz Supply Agreement sets forth an annual minimum number of convenience packs that we must purchase each year following launch of the convenience pack product, and if we do not meet the minimum order in a given year, we are required to pay Sandoz the amount corresponding to the shortfall. Sandoz has no obligation to supply convenience packs above a maximum number of packs above a certain percentage of our forecasts. We have agreed to purchase convenience packs, amoxicillin capsules and clarithromycin tablets, in each case intended for sale in the United States, exclusively from Sandoz during the five-year period following launch.

The Sandoz Supply Agreement will continue for five years from launch of the convenience pack in the U.S. and may be terminated effective at the end of the initial five-year term upon written notice by either party prior to the end of the third year following launch. In the absence of such notice, the Sandoz Supply Agreement will extend automatically for an additional three-year period, and thereafter as mutually agreed upon by the parties. The Sandoz Supply Agreement may also be terminated at any time upon written notice by either party for uncured material breach following written notice of such breach.

Catalent Commercial Supply Agreement

In July 2021, we entered into a Commercial Supply Agreement, or the Tablet Supply Agreement, with Catalent Pharma Solutions, LLC, or Catalent, pursuant to which Catalent has agreed to supply us with commercial quantities of vonoprazan fumarate tablets.

Pursuant to the Tablet Supply Agreement, Catalent has agreed to supply us with, and the Company has agreed to purchase from Catalent, finished vonoprazan tablets at an agreed upon price per unit. The price per unit may be adjusted annually based on increases in costs incurred by Catalent. The Tablet Supply Agreement requires us to purchase a specified percentage of its requirements of finished vonoprazan tablets from Catalent, which percentage is subject to adjustment following the third anniversary of the first day of the calendar quarter during which Catalent is scheduled to deliver the initial finished vonoprazan tablets to us intended for commercial sale, excluding validation batches, or the Commencement Date.

Unless terminated earlier, the term of the Tablet Supply Agreement extends for a period of five years from the Commencement Date. The Tablet Supply Agreement will extend automatically for additional two year periods unless terminated by either party upon at least 24months prior written notice. The Tablet Supply Agreement may also be terminated at any time upon written notice by either party if the other party has failed to remedy a material breach of the terms of the Tablet Supply Agreement within a specified period following receipt of written notice of such breach.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the NDA process before it may be legally marketed in the United States.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with Good Laboratory Practice, or GLP, regulations and other applicable regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, regulations to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCPs; and

- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. Prior to beginning the first clinical trial with a product candidate in the United States, a sponsor must submit an IND to the FDA. The sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The sponsor will also include a protocol detailing, among other things, the objectives of the first phase of the clinical trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated, if the first phase lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of one or more qualified investigators in accordance with GCP regulations, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND as well as any subsequent protocol amendments, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An IRB at each institution participating in the clinical trial must review and approve each protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- ***Phase 1***: The product candidate is initially introduced into healthy human volunteers or patients with the target disease or condition. These studies test for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness.

- ***Phase 2***: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks.

- ***Phase 3***: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of the product's effectiveness for its intended use(s) and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk-benefit ratio of the product candidate and provide, if appropriate, an adequate basis for product labeling.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

While the IND is active, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or in vitro testing suggesting a significant risk to humans exposed to the drug, and any clinically important increased rate of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators and other aspects of the clinical trial is then made public as part of the disclosure.

NDA Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under current PDUFA guidelines, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted.

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

Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as additional clinical trials or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates. The FDA has a Fast Track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, product candidates are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. The sponsor of a Fast Track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. A Fast Track product candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any marketing application for a drug submitted to the FDA for approval, including a product candidate with a Fast Track designation or Breakthrough Therapy designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product candidate is eligible for priority review if it is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. The FDA will attempt to direct additional resources to the evaluation of an application designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product candidate may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA will generally require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast Track designation, Breakthrough Therapy designation, accelerated approval, and priority do not change the standards for approval but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. In addition, the FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Any drug products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the Internet. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds on post-approval clinical trials, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials.

Additionally, under the GAIN Act, the FDA may designate a product as a “qualified infectious disease product,” or QIDP. In order to receive this designation, a drug must qualify as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (2) a so-called “qualifying pathogen” found on a list of potentially dangerous, drug-resistant organisms established and maintained by the FDA under the law. The FDA interprets QIDP designation to apply to a specific drug product, including a specific dosage form of the product. A sponsor must request such designation before submitting a marketing application, and the FDA will respond to a request for QIDP designation within 60 days of the date the FDA receives the request. The GAIN Act permits the FDA to revoke a QIDP designation only if the request for such designation contained an untrue statement of material fact.

The benefits of QIDP designation include potential eligibility for priority review and Fast Track designation, and an extension by an additional five years of any non-patent marketing exclusivity period awarded, such as a five-year exclusivity period awarded for a new molecular entity. This extension is in addition to any pediatric exclusivity extension that may be awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment. The GAIN Act provisions prohibit the grant of an exclusivity extension where the application is a supplement to an application for which an extension is in effect or has expired, is a subsequent application for a specified change to an approved product, or is an application for a product that does not meet the definition of QIDP based on the uses for which it is ultimately approved.

U.S. Healthcare Fraud and Abuse Laws and Compliance Requirements

In addition to FDA regulation of pharmaceutical products, U.S. federal and state healthcare laws and regulations restrict business practices in the pharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities, and constrain the business or financial arrangements and relationships with healthcare providers and other parties. These laws include anti-kickback and false claims laws, civil monetary penalties laws, and transparency laws regarding drug pricing and payments or other items of value provided to physicians and other healthcare providers.

The federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation.

The federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws prohibit, among other things, any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the 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 civil False Claims Act.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent 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 federal Physician Payments Sunshine Act 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 specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other 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, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to 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 payors, including private insurers, or by 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; 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; and state and local laws that require the registration of pharmaceutical sales representatives.

Violation of any of such laws or any other governmental regulations that apply may result in significant criminal, civil and administrative penalties including damages, fines, imprisonment, disgorgement, 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, contractual damages, reputational harm, diminished profits and future earnings, disgorgement, exclusion from participation in government healthcare programs and the curtailment or restructuring of our operations.

U.S. Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidate for which we may seek regulatory approval. Sales in the United States will depend, in part, on the availability of sufficient coverage and adequate reimbursement from third-party payors, which include government health programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care organizations and private health insurers. Prices at which we or our customers seek reimbursement for vonoprazan and any future product candidates can be subject to challenge, reduction or denial by third-party payors.

The process for determining whether a third-party payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. In the United States, there is no uniform policy among payors for coverage or reimbursement. Decisions regarding whether to cover a product, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies, but also have their own methods and approval processes. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that can require manufacturers to provide scientific and clinical support for the use of a product to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Third-party payors may not consider vonoprazan and any future product candidates to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Additionally, decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

Medicaid is a joint federal and state program 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, 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 a manufacturer 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. 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 outpatient 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 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 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 four 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. 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

U.S. Healthcare Reform

In the United States, there has been, and continues to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the profitable sale of product candidates.

Among policy makers and payors in the United States, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, or the Affordable Care Act, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly affected the pharmaceutical industry. The Affordable Care Act, increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a 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; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; creates 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 established a Center for Medicare Innovation at the 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, or ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021, through August 15, 2021, for 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 Medicare payments to providers of 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, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several 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 pharmaceutical products. For example, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation.

The likelihood of implementation of these and other reform initiatives is uncertain. Moreover, 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. Individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and other transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing. It is possible that additional governmental action is taken in response to the COVID-19 pandemic. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union, or EU, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Regulation and Procedures Governing Marketing Authorization of Medicinal Products in the EU

Non-clinical studies and clinical trials

Similarly to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new biological substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on good clinical practices, or GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

A clinical trial application, or CTA, must be submitted to competent national health authorities and independent ethics committees, much like the FDA and IRB, respectively. Once the CTA is approved by the national health authority and the ethics committee has granted a positive opinion in relation to the conduct of the trial in the relevant member state(s), in accordance with a country's requirements, clinical study development may proceed. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation.

Currently, CTAs must be submitted to the competent authority in each EU member state in which the trial will be conducted. Under the new Clinical Trials Regulation, which will become applicable on January 31, 2022, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only limited involvement. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on the duration of the individual clinical trial from January 31, 2022 onward. If an ongoing clinical trial continues for more than three years from January 31, 2022 the Clinical Trials Regulation will begin to apply to the clinical trial as of January 31, 2025.

Medicines used in clinical trials must be manufactured in accordance with good manufacturing practice, or GMP. Other national and EU-wide regulatory requirements may also apply.

Marketing Authorizations

In the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization, or MA. To obtain regulatory approval of a product candidate in the EU, we must submit a Marketing Authorization Application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product.

There are two types of MAs:

- "Centralized MAs" are issued by the European Commission through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA and are valid throughout the EU. The centralized procedure is mandatory for certain types of products, such as (i) medicinal products derived from biotechnological processes, (ii) designated orphan medicinal products, (iii) advanced medicinal therapy products, or ATMPs, such as gene therapy, somatic cell-therapy or tissue-engineered medicines and (iv) medicinal products containing a new active substance indicated for the treatment certain diseases, such as HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for any products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or for which the granting of a MA would be in the interest of public health in the EU.

- "National MAs" are issued by the competent authorities of the EU member states, only cover their respective territory, and are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this National MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a National MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU member states make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance. Under the centralized procedure and in exceptional cases, the CHMP might perform an accelerated review of a MA in no more than 150 days (not including clock stops).

Data and marketing exclusivity

The EU also provides opportunities for market exclusivity. Upon receiving MA reference medicinal product, generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial MA of the reference product in the EU. The overall 10-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those 10 years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Pediatric investigation plan

In the EU, MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all EU member states and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another.

Outside of the United States, the pricing of pharmaceutical products and medical devices is subject to governmental control in many countries. In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products, but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products and medical devices will likely continue as countries attempt to manage healthcare expenditures. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower.

Failure to comply with the aforementioned EU and member state laws may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The aforementioned EU rules are generally applicable in the European Economic Area, or EEA, which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom, or UK, left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the United Kingdom during the transition period under the terms of the EU-UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement, or TCA, and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

EU laws which have been transposed into UK law through secondary legislation continue to be applicable as “retained EU law”. However, new legislation such as the EU Clinical Trials Regulation or in relation to orphan medicines will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ‘appropriate authority’ to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK’s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, or GB; broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019, or the Exit Regulations.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, including a 150-day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt-out. After Brexit, companies established in the UK cannot use the centralized procedure and instead must follow one of the UK national authorization procedures or one of the remaining post-Brexit international cooperation procedures to obtain an MA to commercialize products in the UK. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA’s decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein, Norway) to be granted in GB.

Data privacy and security laws

Pharmaceutical companies may be subject to federal, state and foreign data privacy, security and data breach notification laws governing the collection, use, disclosure and protection of health-related and other personal information. For example, in the U.S., HIPAA imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon "covered entities" (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, received, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HIPAA mandates the reporting of certain breaches of health information to the Department of Health and Human Services, or HHS, to affected individuals and if the breach is large enough, to the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured PHI, a complaint about privacy practices or an audit by the HHS may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission or the FTC, failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company's data security 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. Individually identifiable health information is considered sensitive data that merits stronger safeguards. In addition, certain state and non-U.S. laws, such as the California Consumer Privacy Act, or CCPA, the California Privacy Rights Act, or CPRA, and the EU General Data Protection Regulation, or GDPR, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Human Capital

As of February 24, 2022, we had 77 full-time employees, 11 of whom have a Ph.D. or M.D. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Corporate Information

We were originally incorporated under the laws of the state of Delaware on January 9, 2018 under the name North Bridge IV, Inc. On March 13, 2019, we changed our name to Phathom Pharmaceuticals, Inc. and merged YamadaCo IIA, Inc., a Delaware corporation, or YamadaCo, with and into our company, with Phathom Pharmaceuticals, Inc. as the surviving entity, or the Merger. References throughout this annual report to Phathom Pharmaceuticals, Inc. include North Bridge IV, Inc. prior to the Merger. Our principal executive offices are located at 100 Campus Drive, Suite 102, Florham Park, New Jersey 07932, and our telephone number is (877) 742-8466.

Available Information

Our internet address is www.phathompharma.com. Our investor relations website is located at https://investors.phathompharma.com.com. We make available free of charge on our investor relations website under "Financials and Filings" our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, our directors' and officers' Section 16 reports and any amendments to those reports as soon as reasonably practicable after filing or furnishing such materials to the SEC. They are also available for free on the SEC's website at www.sec.gov.

We use our investor relations website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD. Investors should monitor such website, in addition to following our press releases, SEC filings and public conference calls and webcasts, information relating to our corporate governance is also included on our investor relations website. The information in or accessible through the SEC and our website are not incorporated into, and are not considered part of, this filing.

Item 1A. Risk Factors

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 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;
- We currently depend entirely on the success of vonoprazan, which is our only product candidate. If we are unable to advance vonoprazan in clinical development, obtain regulatory approval and ultimately commercialize vonoprazan, or experience significant delays in doing so, 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 clinical trials, or receive regulatory approval on a timely basis, if at all;
- Vonoprazan 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 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 marketing and no sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may 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 regulatory approval for or commercialize vonoprazan and our business could be harmed;

- We currently engage third-party manufacturers for 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 we obtain is not sufficiently broad, if we lose any of our patent protection, or if we are unable to maintain our existing Qualified Infectious Disease Product, or QIDP, designations for vonoprazan in combination with amoxicillin and clarithromycin for the treatment of *H. pylori* infection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected;

- The successful commercialization of vonoprazan or any future product candidates, if approved, 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;

- If following commercialization of 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 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 ongoing 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, 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.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a late clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2018, and to date, we have focused primarily 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 obtain regulatory approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct 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 history of successfully obtaining regulatory approvals for and commercializing biopharmaceutical products.

We have incurred significant operating losses since our inception. If vonoprazan is not successfully developed and approved in the United States, Europe and/or Canada, we may never generate any revenue. We have incurred cumulative net losses since our inception and, as of December 31, 2021, we had an accumulated deficit of $529.4 million. Substantially all of our losses have resulted from 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. Vonoprazan will require substantial additional time and resources before we will be able to begin generating revenue from product sales, and any future product candidates will require substantial additional development time and resources before we will be able to apply for or receive regulatory approvals and 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 continue our development of, seek additional regulatory approvals for, and potentially commercialize vonoprazan and seek to identify, assess, acquire, in-license, or develop additional product candidates.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials and preclinical studies of vonoprazan and any future product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products. We are still in the early stages of a number of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. In addition, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Because of the 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 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 to commercialize vonoprazan for *H. pylori* and erosive esophagitis and progress our NERD development program. In addition, if vonoprazan receives approval and is 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 regulatory approval for vonoprazan or any future product candidate, we also expect to incur significant 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 any future product candidate. 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 million under our loan and security agreement, or the Loan Agreement, with Hercules Capital, or Hercules, will enable us to fund our operations into mid-2023. In particular, we expect that these funds will allow us to complete our Phase 3 clinical trial studying vonoprazan for NERD (daily dosing), and launch vonoprazan for *H. pylori* and erosive esophagitis. 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 sales and marketing capabilities if vonoprazan or any future product candidate is approved;
- 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;
- delays and cost increases as a result of the ongoing COVID-19 pandemic;
- 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 vonoprazan or 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 payors 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 payors;
- 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 product sales. In addition, vonoprazan and other potential product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, would initially be derived from sales of vonoprazan, which we do not expect to be commercially available in our licensed territories until 2022, if at all.

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, 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 includes, 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.

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 the Development and Regulatory Approval of Product Candidates

We currently depend entirely on the success of vonoprazan, which is our only product candidate. If we are unable to advance vonoprazan in clinical development, obtain regulatory approval and ultimately commercialize vonoprazan, or experience significant delays in doing so, our business will be materially harmed.

We currently only have one product candidate, vonoprazan, which we in-licensed from Takeda. Our business presently depends entirely on our ability to successfully develop, obtain regulatory approval for, and commercialize vonoprazan in a timely manner. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development that may be able to better sustain failure of a lead product candidate. In April 2021, we reported positive results from a pivotal Phase 3 clinical trial for vonoprazan triple therapy and vonoprazan dual therapy for the treatment of *H. pylori* infection, and in September 2021 we submitted NDAs for vonoprazan triple therapy and vonoprazan dual therapy for the treatment of *H. pylori* infection in adults to the FDA, which granted the NDAs Priority Review and set a PDUFA action date of May 3, 2022. In October 2021, we reported positive results from a pivotal Phase 3 trial for vonoprazan for the treatment of erosive esophagitis, and in March 2022, we plan to submit an NDA to the FDA for vonoprazan for healing of all grades of erosive esophagitis and relief of heartburn, and maintenance of healing of all grades of erosive esophagitis and relief of heartburn. In February 2022, we initiated a Phase 3 trial for vonoprazan using a daily dosing regimen for the treatment of NERD and expect to report topline results in 2023. Our assumptions about vonoprazan's commercial potential are based in large part on the commercial experience of vonoprazan in Japan. However, our assumptions may prove to be wrong, and we may encounter a materially and adversely different development and commercial experience. The success of vonoprazan will depend on several factors, including the following:

- acceptance by the FDA or by comparable foreign regulatory authorities of our proposed design of our clinical trials;
- successful enrollment in clinical trials and completion of clinical trials with favorable results;
- the willingness of the FDA, the European Medicines Agency, or EMA, and other comparable foreign regulatory authorities to accept the data from 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;
- demonstrating safety and efficacy to the satisfaction of applicable regulatory authorities;
- the outcome, timing and cost of meeting regulatory requirements established by the FDA, EMA, and other comparable foreign regulatory authorities;
- receipt of marketing approvals from applicable regulatory authorities, including one or more NDAs from the FDA and maintaining such approvals;
- making and/or maintaining arrangements with Takeda, Catalent, Sandoz, or any future third-party manufacturers for, or establishing, commercial manufacturing capabilities and receiving/importing commercial supplies approved by FDA and other regulators from Takeda, Catalent or any future third-party manufacturer;
- establishing sales, marketing and distribution capabilities and commercializing vonoprazan, if approved, 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
- maintaining and growing an organization of people who can develop and, if approved, commercialize, market, and sell vonoprazan to physicians, patients, healthcare payors, and others in the medical community.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful completion of clinical development, regulatory approval and commercialization of vonoprazan, which may never occur. We have not yet succeeded in obtaining marketing approval for vonoprazan. If we are unable to develop or obtain regulatory approval for, or, if approved, successfully commercialize vonoprazan, we may not be able to generate sufficient revenue to continue our business.

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 payors 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 esophagitis. 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 esophagitis. 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.

For the foregoing reasons, our clinical trials and our efforts to obtain regulatory approval for vonoprazan may not be successful. Further, any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval 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 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 approval from regulatory authorities for the sale of vonoprazan or any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of vonoprazan or 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.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. For example, in March 2020, due to global 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 for approximately three months.

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 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 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 2021, more than 8,000 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 P-CABs 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 P-CAB 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 2021 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 2021 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 and any future product candidates becomes more widespread 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.

In addition, if vonoprazan or any future product candidate receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approvals of such product, or seek an injunction against its manufacturer;
- we may be required to recall a product or change the way such product is administered to patients;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or a contraindication;
- 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;
- we may be required to change the way a product is distributed or administered, conduct additional clinical trials or change the labeling of a product or be required to conduct additional post-marketing studies or surveillance;
- we could be sued and held liable for harm caused to patients;
- sales of the product may decrease significantly or the product could become less competitive; and
- our reputation may suffer.

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, results of operations and prospects.

As a company, we have never obtained regulatory approval for a product candidate and may be unable to do so for vonoprazan or any future product candidates.

Although we have completed our pivotal Phase 3 clinical trials for vonoprazan for treatment of *H. pylori* infection and erosive esophagitis, and have submitted NDAs for the use of vonoprazan dual therapy and vonoprazan triply therapy for the treatment of *H. pylori* in adults, we still need to obtain regulatory approvals from the FDA. As a company, we have not previously obtained any regulatory approvals and consequently we may be unable to successfully obtain approval of vonoprazan or 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, 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 any future product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of vonoprazan 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 any future product candidates until we receive regulatory approval from the FDA and in the EU, we are not permitted to market vonoprazan and 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.

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 vonoprazan and 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 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, Sandoz, 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 regulatory approval to market vonoprazan and any future product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually receive approval of an NDA or foreign marketing application for vonoprazan and any future product candidates, the FDA or other comparable foreign regulatory authority may grant approval contingent on 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 regulatory approval would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

Designation of vonoprazan in combination with both amoxicillin and clarithromycin, and with amoxicillin alone as a QIDP, receipt of Fast Track designation, and the potential to receive priority review, may not actually lead to faster development or regulatory review or other benefits, and do not assure FDA approval of vonoprazan or any future product candidates which may receive such designations.

The Generating Antibiotic Incentives Now, or GAIN, Act established certain programs intended to incentivize the development of antibacterial and antifungal drugs for human use to treat serious or life-threatening infections. Specifically, pursuant to the GAIN Act, the FDA may designate certain antimicrobial products as QIDPs, which would qualify them for certain benefits. A QIDP is an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (2) a so-called "qualifying pathogen" found on a list of potentially dangerous, drug-resistant organisms established and maintained by the FDA under the GAIN Act. The FDA interprets QIDP designation to apply to a specific drug product, including a specific dosage form of the product, and the FDA does not apply the designation to the drug substance in general or beyond the specified indications identified in the designation. The benefits of QIDP designation include eligibility for Fast Track designation, eligibility for priority review, and an extension by an additional five years of any non-patent exclusivity period awarded, such as a five-year exclusivity period awarded for a new chemical entity. This extension is in addition to any pediatric exclusivity extension that may be awarded. Receipt of QIDP designation does not assure ultimate approval by the FDA or related GAIN Act exclusivity benefits. A sponsor must request such designation before submitting a marketing application, and the FDA will respond to a request for QIDP designation within 60 days of the date the FDA receives the request.

In August 2019, the FDA granted QIDP designation to vonoprazan tablets in combination with both amoxicillin tablets and clarithromycin tablets, and with amoxicillin tablets alone, for the treatment of *H. pylori* infection. Further, in May 2021, the FDA granted 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. Under the GAIN Act, the FDA may only revoke a QIDP designation if the request for such designation contained an untrue statement of material fact. While we believe that our request for our QIDP designations did not contain any untrue statement of material fact, if the FDA were to seek to revoke our QIDP designations covering our products containing vonoprazan in combination with both amoxicillin and clarithromycin, and with amoxicillin alone, and if FDA were successful in doing so, we would not obtain the GAIN Act exclusivity benefits for such products. If this were to occur, it could have a material, adverse effect on our business prospects.

Vonoprazan in combination with both amoxicillin and clarithromycin and with amoxicillin alone has received Fast Track designation for the treatment of *H. pylori* infection and the NDAs we submitted for each of these combinations have received priority review.

The Fast Track designation program is intended to expedite or facilitate the process for reviewing new drug candidates that meet certain criteria.

Specifically, new drugs are eligible for Fast Track designation if they are intended, alone or in combination with one or more drugs, to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the drug candidate and the specific indication for which it is being studied. With a Fast Track designated drug candidate, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Priority review means the FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review) following the NDA filing date. The FDA automatically grants priority review to the first application or efficacy supplement submitted for a specific drug and indication that has received the QIDP designation.

Obtaining a QIDP designation, priority review, or Fast Track designation does not change the standards for product approval but may expedite the development or approval process. Accordingly, such QIDP designations, Fast Track designations, and priority review may not actually result in faster clinical development or regulatory review or approval. Furthermore, QIDP designation, Fast Track designation, and priority review would not increase the likelihood that vonoprazan will receive marketing approval in the United States.

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. 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 vonoprazan may be suitable for use on a continuous (or daily) basis for the management of NERD and in February 2022 commenced a Phase 3 trial for vonoprazan daily-dosing for NERD. In addition, we believe the rapid onset of action of vonoprazan may enable on-demand, or as needed, use for the management of NERD. However, two Phase 3 clinical trials of vonoprazan in Japanese patients with endoscopically confirmed NERD conducted by Takeda did not demonstrate a statistically significant difference in symptom scores between vonoprazan and placebo. We believe that this result may be due to patient selection. In addition, Takeda conducted a Phase 2 clinical trial in Europe in 256 patients with NERD who were partial responders to high dose PPIs. Patients were randomized to receive vonoprazan 20 mg, vonoprazan 40 mg, or esomeprazole 40 mg for four weeks. Neither vonoprazan dose demonstrated a benefit versus esomeprazole on the primary endpoint of the percentage of heartburn free days over the treatment period. We believe this result may also be due to patient selection. Specifically, the above trials may not have been adequately designed to achieve appropriate patient selection. We may be incorrect in our beliefs regarding the results of such trials and any future clinical trials we conduct in NERD patients may not succeed for similar or other reasons, 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 esophagitis 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 esophagitis 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 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, 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, in March 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA utilized this risk-based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. More recently, 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. 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 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 regulatory approval for or commercialize vonoprazan and 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 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 Takeda for the manufacture of vonoprazan for clinical development and expect to continue to rely on Takeda, Catalent or other third parties for clinical supplies for the foreseeable future, and we will rely on Takeda, Catalent and other third parties to produce commercial supplies of vonoprazan drug substance and drug product, and on Sandoz for commercial supplies of amoxicillin and clarithromycin for our convenience packs. This reliance on third parties increases the risk that we will not have sufficient quantities of 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. Pursuant to the Takeda License, we entered into a clinical manufacturing and 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 drug product, and a commercial supply and packaging agreement with Sandoz for commercial supply of amoxicillin, clarithromycin and finished convenience packs containing vonoprazan 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 related raw materials for clinical development and commercial supply. If Takeda, Catalent 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 or Catalent 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 or Catalent 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 and Sandoz for compliance with applicable cGMP or similar requirements. If Takeda, Catalent, 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, 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 develop, obtain regulatory approval for or market 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 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. 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 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 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 vonoprazan and 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 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 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 and any products 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, Sandoz or any future manufacturers could delay clinical development or marketing approval, 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 vonoprazan and any future product candidates. If Takeda, Catalent, 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, 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 outbreak. If Takeda, Catalent, 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 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 and Catalent, 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 currently rely on Takeda and Catalent to manufacture vonoprazan 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 any future product candidates, due to capital costs required to develop or commercialize vonoprazan and 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 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 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 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 the development and commercialization of vonoprazan or 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 Candidates

Even if we receive regulatory approval for vonoprazan and any future product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, vonoprazan and any future product candidates, if approved, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with vonoprazan and any future product candidates, if approved.

Following potential approval of vonoprazan or 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 vonoprazan or any 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, if the FDA or a comparable foreign regulatory authority approves vonoprazan or any future product candidates, 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 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 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 will become applicable on 31 January 2022. The CTR will be directly applicable in all EU member states, repealing the current Clinical Trials Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new CTR becomes applicable. The extent to which ongoing clinical trials will be governed by the CTR will depend on when the CTR becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the CTR becomes applicable the CTR will at that time begin to apply to the clinical trial. 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 of regulatory exclusivity, eligibility for expedited pathways, etc.) is expected to be adopted by the European Commission by the end of 2022. The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (not expected before the end of 2024) may have a significant impact on the biopharmaceutical industry in the long term.

The commercial success of vonoprazan or any future product candidates will depend upon the degree of market acceptance of such product candidates by physicians, patients, healthcare payors and others in the medical community.

Vonoprazan and any future product candidates may not be commercially successful. The commercial success of vonoprazan 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 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 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 payors;
- 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 vonoprazan or any future product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors 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 payors regarding the benefits of our products may require significant resources and may never be successful.

With respect to vonoprazan, Takeda has the right to develop and commercialize the product outside of the United States, Europe, and Canada and has received marketing approval for vonoprazan in certain countries in Asia and Latin America. 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 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, as vonoprazan and any future product candidates would be, 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. If we receive marketing approval for a product candidate, 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 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 vonoprazan or any future product candidates, if approved, 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 payors are essential for most patients to be able to afford prescription medications such as vonoprazan or any future product candidate, if approved. Our ability to achieve coverage and acceptable levels of reimbursement for our products by third-party payors 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 payor, 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 payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors 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 payor 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 payors 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 payor coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, 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 payors 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 payors 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 payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor 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 payors 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 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.

If we successfully commercialize vonoprazan and any future product candidates, if approved, we will likely participate in governmental programs, such as Medicaid, 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, 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. 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 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 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 four 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. 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 vonoprazan, if approved for the treatment of erosive esophagitis and treatment of *H. pylori* infection, will primarily compete with generic PPIs marketed by multiple pharmaceutical companies in both the prescription and OTC markets. Additionally, in March 2020, RedHill Biopharma Ltd. launched Talicia, a co-formulated capsule comprising generic omeprazole, amoxicillin, and rifabutin for the treatment of *H. pylori* infection.

We are aware of one other P-CAB in development in the United States, as well as a number of other P-CABs in territories outside of the United States that, if developed and approved in our territories, may compete with vonoprazan. In the United States, Neurogastrx intends to commence a Phase 3 erosive esophagitis trial for fexuprazan, under an exclusive license from Daewoong Pharmaceutical Co., Ltd., or Daewoong, sometime in 2022. Outside the United States, Daewoong recently received regulatory approval of, and plans for a first half of 2022 launch for fexuprazan in South Korea, 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, tegoprazan is marketed by CJ Healthcare Corp. in South Korea and is currently in development in Japan by RaQualia Pharma, Inc. Additionally, Jeil Pharm has received authorization to conduct a Phase 3 trial in South Korea of its P-CAB candidate, JP-1366, in erosive esophagitis, and Cinclus Pharma AG's linaprazan glurate has completed a Phase 1 clinical trial in Europe and is currently in Phase 2 clinical trials. To our knowledge, none of these compounds have demonstrated superiority to PPIs on clinical endpoints.

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 in Phase 3 clinical trials in Indonesia, Sihuan Pharmaceutical's anaprazole, currently in Phase 3 clinical trials in China, Eisai's azeloprazole, currently in a Phase 2 clinical trial in Japan, and Sidem Pharma's tenatoprazole, currently in Phase 2 clinical trials in Europe and Canada.

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the 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. If we successfully obtain approval for vonoprazan or any future product candidate, 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 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 or any future products 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 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 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 and any future product candidates will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of vonoprazan 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 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 currently have a limited marketing and sales organization and have no experience as a company in commercializing products, and we may have to invest significant resources to develop these capabilities. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenue.

We have limited internal marketing, sales or distribution capabilities, and we have never commercialized a product. If vonoprazan or any future product candidates ultimately receive regulatory approval, we must build a marketing and sales organization with technical expertise and supporting distribution capabilities to commercialize each such product in major markets, which will be expensive and time consuming, or collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. We plan to independently commercialize vonoprazan in the United States by building a leading specialty gastroenterology commercial infrastructure to support the adoption of vonoprazan and we plan to seek one or more partners with existing commercial infrastructure and expertise in Europe and Canada. We have no prior experience as a company in the marketing, sale and distribution of biopharmaceutical products and there are significant risks involved in building and managing a marketing and sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team.

Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. We may not be able to enter into collaborations or hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms, or at all. In addition, our product revenues and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we are not successful in commercializing vonoprazan or any future product candidates, either on our own or through arrangements with one or more third parties, we may not be able to generate any future product revenue and we would 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 vonoprazan 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 vonoprazan 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 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 vonoprazan or any future product candidates, which may change from time to time;
- coverage and reimbursement policies with respect to vonoprazan or any future product candidates, if approved, and potential future drugs that compete with such products, if approved;
- the cost of manufacturing vonoprazan or any future product candidates, which may vary depending on the quantity of production and the terms of our agreements with Takeda, Catalent, Sandoz and any future third-party manufacturers;
- business interruptions resulting from geopolitical actions, including war 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 preclinical studies or clinical trials for vonoprazan or 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.

The COVID-19 pandemic continues to impact worldwide economic activity. A pandemic, including COVID-19 or other public health epidemic, 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 could have on our business, the continued spread of new variants of COVID-19 and the measures taken by the governments of countries affected could, in addition to disrupting our 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 vonoprazan following regulatory approval, 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 have also had an adverse impact on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed. The extent to which the COVID-19 pandemic impacts our results will depend on future developments that are highly uncertain and cannot be predicted, including new information that may emerge concerning the severity of the virus and the actions to contain its impact.

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 the Loan Agreement with Hercules. We borrowed $100.0 million at the inception of the Loan Agreement and may be eligible to borrow up to an additional $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 this 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 May 15, 2023, certain levels of trailing three-month net product revenue from the sale of vonoprazan and 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 Loan 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.

We are dependent on the services of our current management and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit 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 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 employment agreements or offer letters with each member of our senior management team, these agreements are terminable at 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 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 for qualified personnel among pharmaceutical, biotechnology and other businesses. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able 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 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 our organization from forty-seven full-time employees in December 2020 to seventy-three full-time employees as of December 31, 2021. As we continue development 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. 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 future growth effectively.

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 payors, 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 payors, 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. Among the 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 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 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 without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for 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 Medicare payments to providers of 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, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. 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. For example, the Build Back Better Act, if enacted, would introduce substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated "maximum fair price" for certain selected drugs or pay an excise tax for noncompliance, and the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D. If the Build Back Better Act is not enacted, similar or other drug pricing proposals could appear in future legislation.

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 payors 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 payors. 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 face an inherent risk of product liability as a result of the clinical trials of vonoprazan and any future product candidates and will face an even greater risk if we obtain regulatory approval for and commercialize vonoprazan or any future product candidates. For example, we may be sued if vonoprazan or any future product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or 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, negligence, strict liability and a breach of warranties. Claims may be brought against us by clinical trial participants, patients or others using, administering or selling products that 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 and any future product candidates; and
- a decline in our stock price.

We currently maintain product liability insurance coverage in connection with our clinical trials, but do not maintain such insurance coverage for commercialization of vonoprazan and any future product candidates. Insurance coverage is increasingly expensive. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of vonoprazan and any future product candidates. Although we plan to 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 have, and future policies will also have, various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may 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.

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.

If we or any of our potential future collaborators are successful in commercializing vonoprazan or any future product candidates, the FDA and foreign regulatory authorities would require that we and Takeda (with respect to vonoprazan) and any of our current or potential future collaborators, report certain information about adverse medical events 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.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements 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 state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with 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 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, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties 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 laws and regulations 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. Certain states have also adopted comparable 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, 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 handling certain personal information. It provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the CPRA recently passed in California. The CPRA will impose 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 a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security 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 in Virginia and Colorado and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our 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 and security practices that appear to be 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. The FTC expects a company's data security 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 Europe, GDPR, went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the EEA. 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 or 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 to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws. 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, or the CJEU, limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on use of the standard contractual clauses, or SCCs. While the CJEU upheld the adequacy of the SCCs, it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the SCCs must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place, however, the nature of these additional measures is currently uncertain. The CJEU went on 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, such supervisory authority is under an obligation to suspend or prohibit that transfer. 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. 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; the UK's Information Commissioner's Office launched a public consultation on its draft revised data transfers mechanisms in August 2021. 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. 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 systems, or those of any of our CROs, manufacturers, service providers, other contractors or consultants or potential future collaborators, may fail or suffer security 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 measures, our internal computer systems and those of our current and any future CROs and other service providers, contractors, consultants and collaborators are vulnerable to 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. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the increased number of our employees who are working remotely, which may create additional opportunities for cybercriminals 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 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 disclosure of or access to personally identifiable information or individually identifiable health information (violating certain privacy laws such as GDPR), 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 security breaches involving particular personally 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 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. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, 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 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 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 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 we obtain is not sufficiently broad, or if we lose any of our patent protection, 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.

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 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 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 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 and any future product candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that vonoprazan 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 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 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 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 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 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 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 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 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 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 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 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 clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us 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 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.

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 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 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 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 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 and any future product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of vonoprazan and any future product candidates, 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 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.

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 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;
- regulatory approval of vonoprazan and any future product candidates, or limitations to specific label indications or patient populations for its use, 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, 2021, up to 14,646,341 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, registering the resale of up to 14,499,416 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. As a result, Takeda and Frazier are each able to freely sell some or all of their 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 $1.07 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 Court of Chancery of the State of Delaware will be the exclusive forum for certain 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 to offset future taxable income, if any, until such unused losses expire (if at all).

Under recently enacted U.S. tax legislation, 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 Act 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 on third-party manufacturers to produce vonoprazan 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 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.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our corporate offices are located in Buffalo Grove, Illinois, and Florham Park, New Jersey. We believe that our facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

For additional information, see Note 6, Lease Commitments included in Item 15 of this Annual Report on Form 10-K.

Item 3. Legal Proceedings

We are not currently subject to any material legal proceedings. From time to time, we may be involved in legal proceedings or subject to claims incident to the ordinary course of business. Regardless of the outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol "PHAT" since our initial public offering on October 25, 2019, which was completed at a price to the public of $19.00 per share. Prior to our initial public offering, there was no public market for our common stock.

Holders of Common Stock

As of February 24, 2022, there were 31,712,742 shares of our common stock outstanding held by approximately 52 holders of record of our common stock. This number was derived from our shareholder records and does not include beneficial owners of our common stock whose shares are held in the name of various dealers, clearing agencies, banks, brokers and other fiduciaries.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments. In addition, under the terms of our Loan Agreement, we are prohibited from paying any cash dividends without the consent of the lenders.

Securities Authorized for Issuance Under Equity Compensation Plans

See Item 12 of Part III of this annual report on Form 10-K for information about our equity compensation plans which is incorporated by reference herein.

Performance Graph

Not applicable.

Unregistered Sales of Equity Securities

Use of Proceeds

On October 24, 2019, our registration statement on Form S-1 (File No. 333-234020) was declared effective by the SEC for our initial public offering. At the closing of the offering on October 29, 2019, we sold 10,997,630 shares of common stock, which included the exercise in full by the underwriters of their option to purchase 1,434,473 additional shares, at an initial public offering price of $19.00 per share and received gross proceeds of $209.0 million, which resulted in net proceeds to us of approximately $191.5 million, after deducting underwriting discounts and commissions of approximately $14.6 million and offering-related transaction costs of approximately $2.9 million. None of the expenses associated with the initial public offering were paid to directors, officers, persons owning ten percent or more of any class of equity securities, or to their associates, or to our affiliates. Goldman Sachs & Co. LLC, Jefferies LLC and Evercore Group L.L.C. acted as joint book-running managers for the offering.

As of December 31, 2021 the net proceeds from our initial public offering and follow on offering have been applied as follows: $151.7 million toward the clinical development of vonoprazan and $79.7 million towards working capital and general corporate purposes. As of December 31, 2021, we have used all of the net proceeds from our IPO of approximately $191.5 million.

Issuer Repurchases of Equity Securities

None.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes included elsewhere in this annual report. This discussion and analysis contains forward-looking statements based upon our current beliefs, plans and expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under "Risk Factors" or in other parts of this annual report.

Overview

We are a late clinical-stage biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal, or GI, diseases. Our initial product candidate, vonoprazan, is an oral small molecule P-CAB. P-CABs are a novel class of medicines that block acid secretion in the stomach. Vonoprazan has shown rapid, potent, and durable anti-secretory effects and has demonstrated clinical benefits over the current standard of care as a single agent in the treatment of gastroesophageal reflux disease, or GERD, and in combination with antibiotics for the treatment of *H. pylori* infection. Takeda developed vonoprazan and has received marketing approval in numerous countries in Asia and Latin America as well as Russia. Vonoprazan generated approximately $850 million in net sales in its seventh full year on the market since its approval in Japan in late 2014. In May 2019, we in-licensed the U.S., European, and Canadian rights to vonoprazan from Takeda.

In 2021 we reported topline data from two pivotal Phase 3 clinical trials for vonoprazan: one for the treatment of *H. pylori* infection (PHALCON-HP), and a second for the treatment of erosive GERD (PHALCON-EE), also known as erosive esophagitis, or EE. In April 2021, we reported positive topline data from PHALCON-HP, and in October 2021, we reported positive topline data from PHALCON-EE. In September 2021, we submitted two new drug applications (NDAs) for treatment regimens containing vonoprazan for the treatment of *H.* pylori, and in November 2021, the U.S. Food and Drug Administration, or FDA, accepted both NDAs for filing, granted each of them Priority Review, and assigned us a Prescription Drug User Fee Act (PDUFA) action date in May 2022. Based on the results of the PHALCON-EE trial, we expect to submit an NDA for vonoprazan for the treatment of erosive esophagitis in March 2022. In August 2019, we received Qualified Infectious Disease Product, or QIDP, and Fast Track designations from the FDA, for vonoprazan tablets in combination with amoxicillin tablets and clarithromycin tablets and with amoxicillin tablets alone for the treatment of *H. pylori* infection. In January 2021 and May 2021, respectively, we received additional Fast Track and QIDP designations to include amoxicillin capsules in addition to amoxicillin tablets. QIDP designation provides a potential extension of any regulatory exclusivity awarded, if approved. We have also initiated development of vonoprazan for the treatment of NERD. In February 2022, we commenced enrollment of patients in a Phase 3 trial studying vonoprazan, dosed on a once-daily basis, for the treatment of NERD with topline data expected in 2023. Also in February 2022, we reported positive topline data from a Phase 2 trial studying vonoprazan for on-demand treatment of NERD.

If approved, we plan to independently commercialize vonoprazan in the United States. We also plan to seek commercial partnerships for vonoprazan in Europe and Canada, expand development of vonoprazan into other indications, dosing regimens and alternative formulations and packaging, and in-license or acquire additional clinical or commercial stage product candidates for the treatment of GI diseases in a capital efficient manner.

We commenced our operations in 2018 and have devoted substantially all of our resources to date to 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. Our operations to date have been funded primarily through the issuance of convertible promissory notes, commercial bank debt, the proceeds from our initial public offering and our follow-on public offering. From our inception through December 31, 2021, we have raised aggregate gross proceeds of $90.3 million from the issuance of convertible promissory notes, $100.0 million of debt, net proceeds from our initial public offering of $191.5 million from the sale of 10,997,630 shares of common stock, which included the exercise in full by the underwriters of their option to purchase 1,434,473 additional shares at a public offering price of $19.00 per share, after deducting underwriting discounts, commissions and offering costs, and net proceeds of $88.6 million from the sale of 2,250,000 shares of common stock at a public offering price of $39.48 per share after deducting underwriting discounts and commissions, and an additional $0.2 million in offering costs. As of December 31, 2021, we had cash and cash equivalents of $183.3 million. Based on our current operating plan, and subject to the potential delays and cost increases resulting from the evolving COVID-19 pandemic, we believe that our existing cash and cash equivalents together with the drawdown of the remaining $100 million under our Loan Agreement with Hercules will be sufficient to fund our operations into the middle of 2023.

We do not have any products approved for sale and have incurred net losses since our inception. Our net losses for the years ended December 31, 2021 and 2020 were $143.9 million and $129.1 million, respectively. As of December 31, 2021, we had an accumulated deficit of $529.4 million. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical development activities, other research and development activities and pre-commercialization activities. We expect our expenses and operating losses will increase substantially as we advance vonoprazan through clinical trials, seek regulatory approval for vonoprazan, expand our clinical, regulatory, quality, manufacturing and commercialization capabilities, incur significant commercialization expenses for marketing, sales, manufacturing and distribution if we obtain marketing approval for vonoprazan, protect our intellectual property, expand our general and administrative support functions, including hiring additional personnel, and incur additional costs associated with operating as a public company.

We have never generated any revenue and do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for vonoprazan. Accordingly, until such time as we can generate significant revenue from sales of vonoprazan, if ever, we expect to finance our cash needs through equity offerings, our Loan Agreement, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all, and this risk could be exacerbated by the impact of COVID-19 on global economic conditions. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

License Agreement with Takeda

On May 7, 2019, we and Takeda entered into the Takeda License, pursuant to which we in-licensed the U.S., European, and Canadian rights to vonoprazan fumarate. During the term of the Takeda License, we and our affiliates are not permitted to commercialize any pharmaceutical product, other than vonoprazan, that treats acid-related disorders, except for certain generic and OTC competing products in specified circumstances. We will be responsible at our cost for the development, manufacture and commercialization of vonoprazan products. We are required to use commercially reasonable efforts to develop and commercialize the vonoprazan products in our licensed territory.

Under the Takeda License, Takeda has the sole right and authority, with our input, to prepare, file, prosecute, and maintain all Takeda and joint patents on a worldwide basis at its own cost. We are responsible, at our cost, for preparing, filing, prosecuting, and maintaining patents on inventions made solely by us in connection with vonoprazan, subject to input from Takeda.

We paid Takeda upfront consideration consisting of a cash fee of $25.0 million, 1,084,000 shares of our common stock, the Takeda Warrant to purchase 7,588,000 shares of our common stock at an exercise price of $0.00004613 per share, and issued Takeda a right to receive an additional common stock warrant, or the Takeda Warrant Right, if Takeda's fully-diluted ownership of the Company represented less than a certain specified percentage of the fully-diluted capitalization, including shares issuable upon conversion of then outstanding convertible promissory notes, calculated immediately prior to the closing of our IPO. The Takeda Warrant Right expired without effect since no fair value had been allocated to it upon completion of our IPO, and no additional warrant was issued. We agreed to make milestone payments to Takeda upon achieving certain tiered aggregate annual net sales of licensed products in the United States, Europe and Canada up to a total maximum milestone amount of $250.0 million. We also agreed to make tiered royalty payments at percentages in the low double digits on net sales of licensed products, subject to specified offsets and reductions. Royalties will be payable, on a product-by-product and country-by-country basis from the first commercial sale of such product in such country, until the latest of expiration of the licensed patents covering the applicable product, expiration of regulatory exclusivity in such country, or 15 years following first commercial sale in such country.

Components of Results of Operations

Operating Expenses

Research and Development

To date, our research and development expenses have related to the development of vonoprazan. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Research and development expenses include:

- salaries, payroll taxes, employee benefits, and stock-based compensation charges for those individuals involved in research and development efforts;
- external research and development expenses incurred under agreements with CROs, and consultants to conduct and support our ongoing clinical trials of vonoprazan; and
- costs related to the manufacturing of vonoprazan for our clinical trials.

We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of vonoprazan. We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future clinical trials and nonclinical studies of vonoprazan or any future product candidates due to the inherently unpredictable nature of clinical and preclinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Our future clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses evaluated in the trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the phase of development of the product candidate;
- the efficacy and safety profile of the product candidate; and
- delays and cost increases as a result of COVID-19

General and Administrative

General and administrative expenses consist of salaries and employee-related costs, including stock-based compensation, for personnel in executive, finance, accounting, legal, human resources and other administrative functions, legal fees relating to intellectual property and corporate matters, and professional fees for accounting and consulting services. We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities, pre-commercial preparation activities for vonoprazan and, if any future product candidate receives marketing approval, commercialization activities. We also anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Interest Income

Interest income consists of interest on our money market funds.

Interest Expense

Beginning on September 17, 2021, interest expense consists of (i) cash interest at a variable annual rate equal to the greater of (a) 5.50% and (b) the Prime Rate (as reported in the Wall Street Journal) plus 2.25% (the "Interest Rate"), (ii) payment-in-kind interest at a per annum rate of interest equal to 3.35%, and (iii) amortization of the Hercules Loan Agreement debt discount recorded in connection with the fair value of warrants issued to the lenders, the debt issuance costs incurred, and the obligation to make a final payment.

Prior to September 17, 2021, interest expense consisted of interest on our outstanding commercial bank debt with SVB at a variable annual rate equal to the greater of (a) 7.25% and (b) Prime Rate (as reported by the Wall Street Journal) plus 1.75% and amortization of the SVB Term Loan debt discount recorded in connection with the fair value of warrants issued to the lenders, the debt issuance costs incurred, and the obligation to make a final payment.

Change in Fair Value of Warrant Liabilities

In connection with the entry into the Loan Agreement, we issued the lenders warrants to purchase our capital stock, or the Lender Warrants. The Lender Warrants were accounted for as liabilities as they contained a holder put right under which the lenders could have required us to pay cash in exchange for the warrants. We adjusted the carrying value of the Lender Warrants to their estimated fair value at each reporting date, with any change in fair value of the warrant liabilities recorded as an increase or decrease to change in fair value of warrant liabilities in the statements of operations. The Lender Warrants were accounted for at fair value using the Black-Scholes option-pricing model with an expected term equal to the remaining contractual term of the warrants. When we drew down an additional $25.0 million, or the Term Loan B, in March 2020, the Lender put right expired, and we recorded a final fair value adjustment and reclassified the Lender Warrants balance of $0.3 million to additional paid-in-capital.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020 (in thousands):

	Years Ended December 31,		
	2021	2020	Change
Operating expenses:			
Research and development	$ 72,338	$ 98,148	$ (25,810)
General and administrative	62,742	27,517	$ 35,225
Total operating expenses	135,080	125,665	9,415
Loss from operations	(135,080)	(125,665)	(9,415)
Other income (expense):			
Interest income	41	1,091	(1,050)
Interest expense	(6,788)	(4,581)	(2,207)
Change in fair value of warrant liabilities	—	95	(95)
Other income (expense)	(2,056)	(8)	(2,048)
Total other income (expense)	(8,803)	(3,403)	(5,400)
Net loss	$ (143,883)	$ (129,068)	$ (14,815)

Research and Development Expenses. Research and development expenses were $72.3 million and $98.1 million for the years ended December 31, 2021 and 2020, respectively. The decrease of $25.8 million consisted of $41.1 million of clinical trial costs, $0.7 million of consulting expenses, and $0.9 million of other operating expenses partially offset by an increase of $6.5 million of chemistry manufacturing and controls, or CMC, costs related to vonoprazan, $6.3 million of personnel-related expenses and $4.1 million of expenses related to regulatory requirements.

General and Administrative Expenses. General and administrative expenses were $62.7 million and $27.5 million for the years ended December 31, 2021 and 2020, respectively. The increase of $35.2 million was due to increases of $17.2 million in personnel-related expenses, $15.7 million of professional services expenses for commercial, medical affairs and other services, $1.1 million in consulting fees and $1.2 million in other expenses. Due to the planned continued buildout of administrative and commercial functions, we expect General and Administrative expenses to increase in future periods.

Other Income (Expense). Other expense of $8.8 million for the year ended December 31, 2021 consisted of $6.8 million of interest expense and $2.0 million of charges related to early extinguishment of debt. Other expense of $3.4 million for the year ended December 31, 2020 consisted of $4.6 million of interest expense on outstanding commercial bank debt, partially offset by $1.1 million of interest income and $0.1 million of other income related to the decrease in the fair value of warrant liabilities.

Liquidity and Capital Resources

We have incurred net losses and negative cash flows from operations since our inception and anticipate we will continue to incur net losses for the foreseeable future. As of December 31, 2021, we had cash and cash equivalents of $183.3 million.

Loan Agreement with Hercules

On September 17, 2021, (the “Closing Date”), we entered into a Loan and Security Agreement (the “Loan Agreement”) with Hercules Capital, Inc., in its capacity as administrative agent and collateral agent and as a lender (in such capacity, the “Agent” or “Hercules”) and the other financial institutions that from time to time become parties to the Loan Agreement as lenders (collectively, the “Lenders”).

The Loan Agreement provides for term loans in an aggregate principal amount of up to $200.0 million (the “Term Loan”) under multiple tranches. The tranches consist of (i) a first tranche consisting of term loans in an aggregate principal amount of $100.0 million, all of which was funded on the Closing Date (the “First Advance”), (ii) a second tranche consisting of up to an additional $50.0 million, which became available to us upon achievement of the protocol-specified primary efficacy endpoints in our Phase 3 trial studying vonoprazan for the healing and maintenance of healing of erosive esophagitis with acceptable safety data, such that the results support the submission of a New Drug Application (“NDA”) or supplemental NDA without the need to conduct another Phase 3 study and will be available, if specified conditions are met, through December 15, 2022, (iii) a third tranche consisting of an additional $25.0 million, which will become available to us upon the achievement of (a) FDA approval of our NDA for vonoprazan and amoxicillin, or its NDA for vonoprazan, amoxicillin and clarithromycin, in each case for an indication relating to the treatment of H. pylori with an approved indication on the claim that is generally consistent with that sought in our NDA submission; and (b) filing of an NDA or supplemental NDA for vonoprazan for indications relating to the healing and maintenance of healing of erosive esophagitis (milestones (a) and (b), together, the “Second Performance Milestone”), and will be available, if specified conditions are met, through September 30, 2023, and (iv) a fourth tranche consisting of up to an additional $25.0 million, which will be available, if specified conditions are met, through March 31, 2024, upon achievement of the Second Performance Milestone. We intend to use the proceeds of the Term Loan advances for working capital and general corporate purposes. In addition, approximately $54 million of the proceeds from the First Advance was used to satisfy in full and retire our indebtedness under its previously outstanding credit facility with Silicon Valley Bank (the “SVB Term Loan”).

The Term Loan will mature on October 1, 2026 (the "Maturity Date"). The Term Loan bears (i) cash interest at a variable annual rate equal to the greater of (a) 5.50% and (b) the Prime Rate (as reported in the Wall Street Journal) plus 2.25% (the "Interest Rate") and (ii) payment-in-kind interest at a per annum rate of interest equal to 3.35%. We may make payments of interest only through October 1, 2024, which may be extended to October 1, 2025, upon the achievement of the Second Performance Milestone on or prior to September 30, 2024 and the condition that no default or event of default exists, and which is further extendable to October 1, 2026, subject to FDA approval of our NDA (or supplemental NDA) for vonoprazan for an indication relating to the healing and maintenance of healing of erosive esophagitis with an approved indication on the label that is generally consistent with that sought in our NDA submission (or supplemental NDA submission) (the "Third Performance Milestone") on or prior to September 30, 2025 and no default or event of default exists (the "interest only period"). After the interest-only period, the principal balance and related interest will be required to be repaid in equal monthly installments and continuing until the Maturity Date.

The Loan Agreement contains customary closing fees, prepayment fees and provisions, events of default, and representations, warranties and covenants, including a financial covenant requiring us to maintain certain levels of cash subject to a control agreement in favor of the Agent (minus accounts payable not paid within 120 days of invoice) ("Qualified Cash"), and commencing on May 15, 2023, trailing three-month net product revenue from the sale of vonoprazan and products containing vonoprazan. The revenue covenant will be waived at any time in which we maintain Qualified Cash equal to at least 60.0% (prior to the Third Performance Milestone), and 35% (following the Third Performance Milestone) of the total outstanding Term Loan principal amount, or our market capitalization is at least $900.0 million.

As collateral for the obligations, we granted to Hercules a senior security interest in all of our right, title, and interest in, to and under substantially all of our property, inclusive of intellectual property.

In connection with the entry into the Loan Agreement, we issued to Hercules a warrant (the "Warrant") to purchase a number of shares of our common stock equal to 2.5% of the aggregate amount of the Term Loan advances funded, and will issue to Hercules additional warrants when future Term Loan advances are funded. On the Closing Date, we issued a Warrant for 74,782 shares of common stock. The Warrant will be exercisable for a period of seven years from the date of issuance at a per-share exercise price equal to $33.43, which was the closing price of our common stock on September 16, 2021.

Commercial Bank Debt with SVB

On May 14, 2019, we entered into the Loan Agreement with SVB, as administrative and collateral agent, and lenders SVB and WestRiver Innovation Lending Fund VIII, L.P. We borrowed $25.0 million, Term Loan A, at the inception of the Loan Agreement and an additional $25.0 million, Term Loan B, in March 2020, which we collectively refer to as the Term Loans.

The SVB Term Loan bore interest at a floating rate of the higher of the Wall Street Journal Prime rate plus 1.75% or 7.25%. Under the original SVB Loan Agreement, the monthly payments consisted of interest-only through May 31, 2021. Pursuant to the first amendment to the SVB Term Loan entered into on March 11, 2020, and the second amendment to the SVB Term Loan entered into on March 11, 2021, the interest-only payment period was initially extended through July 31, 2021, and was further extended until December 31, 2021, after we received positive data from its Phase 3 clinical trial in *H. pylori* infection sufficient to file a new drug application, or NDA, with the FDA. The interest-only payment period could have been further extended until November 30, 2022, if we would receive positive data from its Phase 3 clinical trial in erosive esophagitis for vonoprazan sufficient to file an NDA with the FDA. Subsequent to the interest-only period, the Term Loans would have been payable in equal monthly installments of principal, plus accrued and unpaid interest through the maturity date of May 1, 2024.

In addition, we were obligated to pay a final payment fee of 8.25% of the original principal amount of the SVB Term Loan. We could have elected to prepay all or a portion of the SVB Term Loan prior to maturity, subject to a prepayment fee of up to 2.0% of the then outstanding principal balance and payment of a pro rata portion of the final payment fee. After repayment, no SVB Term Loan amounts could have been borrowed again. The borrowings under the SVB Term Loan were collateralized by substantially all of our assets.

The SVB Term Loan contained certain customary affirmative and negative covenants and events of default. The affirmative covenants included, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding our operating accounts. The negative covenants included, 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. Upon the occurrence of an event of default, subject to any specified cure periods, all amounts owed by us would have begun to bear interest at a rate that is 4.00% above the rate effective immediately before the event of default and could have been declared immediately due and payable by SVB, as collateral agent.

In connection with the SVB Term Loan, we issued Lender Warrants, which became exercisable when we borrowed Term Loan B in March 2020. The Lender Warrants are exercisable for 16,446 shares of common stock. The Lender Warrants expire ten years from the date of issuance. The Lender Warrants included a put option pursuant to which, in the event that we did not draw down Term Loan B on or before March 31, 2020, the warrant holders could have required us to repurchase the warrants for a total aggregate repurchase price of $0.5 million. Upon the Term Loan B draw in March 2020, the put option related to the Lender Warrants expired, at which time we recorded a final fair value adjustment and reclassified the Lender Warrants balance of $0.3 million to additional paid-in-capital.

At-the-Market-Offering

On November 10, 2020, we entered into an Open Market Sale Agreement℠, or the Sales Agreement, with Jefferies LLC, or the Sales Agent, under which we may, from time to time, sell shares of our common stock having an aggregate offering price of up to $125.0 million through the Sales Agent, or the ATM Offering. Sales of our common stock made pursuant to the Sales Agreement, if any, will be made under our shelf registration statement on Form S-3 which was filed on November 10, 2020 and declared effective by the SEC on November 16, 2020. We are not obligated to, and we cannot provide any assurances that we will, make any sales of the shares under the Sales Agreement. The Sales Agreement may be terminated by the Sales Agent or us at any time. There were no sales of our common stock under the ATM Offering for the year ended December 31, 2021.

Underwritten Public Offering

On December 16, 2020, the Company completed an underwritten public offering, in which it sold 2,250,000 shares of its common stock at a price of $42.00 per share for total gross proceeds of $94.5 million. The net purchase price after deducting underwriting discounts and commissions was $39.48 per share, which generated net proceeds of $88.8 million. We incurred an additional $0.2 million of offering expenses in connection with the public offering.

Funding Requirements

Based on our current operating plan, we believe that our existing cash and cash equivalents together with the drawdown of the remaining $100 million under our Loan Agreement with Hercules will be sufficient to fund our operations into the middle of 2023. We expect such current cash and cash equivalents, when combined with our anticipated borrowing ability, will allow us to complete our ongoing Phase 3 clinical trial studying vonoprazan for NERD (daily dosing), and, if approved, launch vonoprazan for *H. pylori* and erosive esophagitis.. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

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

- 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;
- delays and cost increases as a result of COVID-19;
- 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 vonoprazan or 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, including additional executive officers and clinical development personnel;
- the timing and amount of the milestone or other payments we must make to Takeda and any future licensors;
- the costs and timing of establishing or securing sales and marketing capabilities for vonoprazan or any future product candidate;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors 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 payors;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements; and
- costs associated with any products or technologies that we may in-license or acquire.

Until such time, if ever, as we can generate substantial product revenues to support our cost structure, we expect to finance our cash needs through equity offerings, the Loan Agreement, 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, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and 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. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Including our existing cash and cash equivalents, we believe that we have sufficient working capital on hand to fund operations such that there is no substantial doubt as to our ability to continue as a going concern at the date the financial statements were issued. There can be no assurance that we will be successful in acquiring additional funding, that our projections of future working capital needs will prove accurate, or that any additional funding would be sufficient to continue operations in future years. Based on our current operating plan, we believe that our existing cash and cash equivalents together with the drawdown of the remaining $100 million under the Loan Agreement with Hercules will be sufficient to meet our anticipated cash requirements into the middle of 2023.

Cash Flows

The following table sets forth a summary of the net cash flow activity for each of the periods indicated (in thousands):

	Years Ended December 31,		
	2021	2020	$ Change
Net cash provided by (used in):			
Operating activities	$ (148,617)	$ (69,688)	$ (78,929)
Investing activities	(328)	(1,040)	712
Financing activities	44,708	114,459	(69,751)
Net increase (decrease) in cash	$ (104,237)	$ 43,731	$ (147,968)

Operating Activities

Net cash used in operating activities was approximately $148.6 million and $69.7 million for the years ended December 31, 2021 and 2020, respectively. The net cash used in operating activities for the year ended December 31, 2021 was due to approximately $121.1 million spent on ongoing research and development and general and administrative activities and a $27.5 net change in operating assets and liabilities. The net change in operating assets and liabilities primarily related to a $28.1 million decrease in accounts payable and accrued expenses (including clinical trial expenses) in support of the growth in our operating activities, partially offset by a $0.6 million decrease in prepaid assets. The net cash used in operating activities for the year ended December 31, 2020 was due to approximately $121.4 million spent on ongoing research and development and general and administrative activities, partially offset by a $51.7 million net change in operating assets and liabilities. The net change in operating assets and liabilities primarily related to a $8.0 million decrease in prepaid clinical activities, and a $43.9 million increase in accounts payable and accrued expenses in support of the growth in our operating activities, partially offset by a $0.2 million increase in other long-term assets.

Investing Activities

Net cash used in investing activities for the years ended December 31, 2021 and 2020 was primarily due to the cash we paid for acquiring property, plant and equipment.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $44.7 million, due to $96.9 million of net proceeds from the loan agreement with Hercules and $1.9 million of proceeds related to stock option exercises partially offset by the $54.1 million repayment of the SVB Term Loan. Net cash provided by financing activities for the year ended December 31, 2020 was $114.4 million, due to $88.8 million of proceeds from our underwritten public offering, $25.0 million of proceeds from our commercial bank debt, and $0.6 million of proceeds related to stock option exercises during the year.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2021 (in thousands):

	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Total debt, including interest and final payment fee [1]	$ 146,772	$ 5,704	$ 23,208	$ 117,860	$ —
Minimum operating lease payments	$ 1,890	503	1,045	342	—
Total	$ 148,662	$ 6,207	$ 24,253	$ 118,202	$ —

(1) Our outstanding long-term debt bears interest at a variable rate. The interest amounts included herein are based on the interest rate in effect as of December 31, 2021.

In addition to the contractual obligations summarized above, on May 5, 2020, we entered into a Commercial Supply Agreement with Takeda, pursuant to which Takeda will supply commercial quantities of vonoprazan bulk drug product. We incurred $1.8 million and $0.3 million of expenses related to the Commercial Supply Agreement during the years ended December 31, 2021 and 2020, respectively. We have an estimated remaining minimum purchase obligation of approximately $0.4 million related to this agreement. As of December 31, 2021, we are unable to estimate the timing of future expenses and, therefore, any related payments are not included in the table above.

Additionally, on December 30, 2020, we entered into a Supply and Packaging Services Agreement with Sandoz, pursuant to which Sandoz has agreed to supply commercial quantities of amoxicillin capsules and clarithromycin tablets, to package these antibiotics with vonoprazan, in finished convenience packs, and to supply us with these convenience packs. The supply agreement commits the Company to a minimum purchase obligation of approximately $3.8 million during the first 24-month period following the launch of the final product. As of December 31, 2021, we are unable to estimate the timing of future expenses and, therefore, any related payments are not included in the table above. We have not incurred any expenses under the agreement during the year ended December 31, 2021.

We enter into contracts in the normal course of business for our contract research services, contract manufacturing services, professional services and other services and products for operating purposes. These contracts generally provide for termination after a notice period, and, therefore, are cancelable contracts and not included in the table above.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 1 to our financial statements, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Leases

At the inception of any contractual arrangements we may enter into, we determine whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. If both criteria are met, we record the associated lease liability and corresponding right-of-use asset upon commencement of the lease using either the implicit rate or a discount rate based on our credit-adjusted secured borrowing rate commensurate with the term of the lease. Additionally, we evaluate leases at their inception to determine if they are to be accounted for as an operating lease or a finance lease. We assess if a lease is accounted for as a finance lease if it meets one of the following five criteria: the lease has a purchase option that is reasonably certain of being exercised, the present value of the future cash flows is substantially all of the fair market value of the underlying asset, the lease term is for a significant portion of the remaining economic life of the underlying asset, the title to the underlying asset transfers at the end of the lease term, or if the underlying asset is of such a specialized nature that it is expected to have no alternative uses to the lessor at the end of the term. We account for leases that do not meet the finance lease criteria as operating leases, representing our right to use an underlying asset for the lease term. We also recognize operating lease liabilities as our obligation to make lease payments arising from the lease. We recognize operating lease liabilities with a term greater than one year and their corresponding right-of-use assets on the balance sheet at the commencement date of the lease based on the present value of lease payments over the expected lease term. As needed, we make certain adjustments to the right-of-use asset for items such as initial direct costs paid or incentives received. Because our leases do not typically provide an implicit rate, we utilize the rate of interest that we would have to pay to borrow on a collateralized basis over a similar term and in a similar economic environment. We recognize lease costs on a straight-line basis over the lease term and variable lease payments as operating expenses in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance, and other operating costs that are passed on from the lessor in proportion to the space we lease.

Stock-Based Compensation Expense

Stock-based compensation expense represents the cost of the grant date fair value of equity awards recognized over the requisite service period of the awards (generally the vesting period) on a straight-line basis with forfeitures recognized as they occur. We use the Black-Scholes valuation model to determine the fair value of our stock awards. Through December 31, 2021, our stock-based compensation expense consisted of recognized fair value related to our issuance of restricted stock awards, for which the fair value is determined based on the fair value of the underlying common stock, stock options, and ESPP awards.

Other Company Information

JOBS Act

As an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, we 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 certain accounting standards until those standards 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 intend to rely on other exemptions provided by the JOBS Act, including without limitation, not being required to comply with the auditor attestation requirements of Section 404(b) of Sarbanes-Oxley.

We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year following the fifth anniversary of the consummation of our IPO, (ii) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (iii) the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year, or (iv) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

Recent Accounting Pronouncements

The information required by this item is included in Note 1, Organization, Basis of Presentation and Summary of Significant Accounting Policies included in Item 15 of this annual report.

Off-Balance Sheet Arrangements

During the periods presented we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

Our cash and cash equivalents consist of cash in readily available checking accounts and money market funds. As a result, the fair value of our portfolio is relatively insensitive to interest rate changes. Our long-term debt bears interest at a variable rate. A 10% increase or decrease in the interest rate on our long-term debt would not have a material effect on our financial position, results of operations or cash flows.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor and research and development contract costs. We do not believe inflation has had a material effect on our results of operations during the periods presented.

Item 8. Financial Statements and Supplementary Data

The financial statements required pursuant to this item are incorporated by reference herein from the applicable information included in Item 15 of this annual report and are presented beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act as of the end of the period covered by this annual report. Based on such evaluation, our principal executive officer and principal financial officer have concluded that as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act). Internal control over financial reporting is a process designed under the supervision and with the participation of our management to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America. Management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013 Framework). Based on this assessment, our management concluded that, as of December 31, 2021, our internal control over financial reporting was effective.

Attestation Report of the Registered Public Accounting Firm

This annual report does not include an attestation report of our registered public accounting firm due to an exemption provided by the JOBS Act for "emerging growth companies."

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting during the fourth quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdiction that Prevent Inspection

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders, or the Definitive Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2021, under the headings “Election of Directors,” “Executive Officers,” and “Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference.

Code of Conduct and Ethics

We have adopted a Code of Conduct and Ethics that applies to our officers, directors and employees, which is available on our website at www.phathompharma.com. The Code of Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics and is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation

The information required by this item will be set forth in the section headed “Executive Compensation and Other Information” in our Definitive Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item will be set forth in the section headed “Security Ownership of Certain Beneficial Owners and Management” in our Definitive Proxy Statement and is incorporated herein by reference.

The information required by Item 201(d) of Regulation S-K will be set forth in the section headed “Executive Compensation” in our Definitive Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item will be set forth in the section headed “Certain Relationships and Related Person Transactions,” “Board Independence” and “Committees of the Board of Directors” in our Definitive Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item will be set forth in the section headed “Independent Registered Public Accountants’ Fees” in our Definitive Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

1. All financial statements.

The financial statements of Phathom Pharmaceuticals, Inc., together with the report thereon of Ernst & Young LLP, an independent registered public accounting firm, are included in this annual report on Form 10-K beginning on page F-1.

2. Financial statement schedules.

All schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

3. Exhibits

A list of exhibits is set forth on the Exhibit Index immediately preceding the signature page of this annual report on Form 10-K and is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

Phathom Pharmaceuticals, Inc.

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors of Phathom Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Phathom Pharmaceuticals, Inc. (the Company) as of December 31, 2021 and 2020, the related statements of operations and comprehensive loss, stockholders' equity and cash flows for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2019.

Iselin, New Jersey
March 1, 2022

PHATHOM PHARMACEUTICALS, INC.
Balance Sheets
(in thousands, except share and par value amounts)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 183,259	$ 287,496
Prepaid expenses and other current assets (including related party amounts of $0 and $82, respectively)	3,267	3,872
Total current assets	186,526	291,368
Property, plant and equipment, net	650	986
Operating lease right-of-use assets	1,914	2,373
Other long-term assets	341	384
Total assets	$ 189,431	$ 295,111
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable (including related party amounts of $1,343 and $173, respectively)	$ 5,150	$ 16,782
Accrued clinical trial expenses	1,402	19,997
Accrued expenses (including related party amounts of $2,330 and $734, respectively)	11,405	10,606
Accrued interest	477	312
Current portion of long-term debt	—	7,353
Operating lease liabilities, current	487	474
Total current liabilities	18,921	55,524
Long-term debt, net of discount	89,671	39,634
Operating lease liabilities	1,183	1,557
Other long-term liabilities	7,500	4,125
Total liabilities	117,275	100,840
Commitments and contingencies (Note 4)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; authorized shares — 40,000,000 at December 31, 2021 and 2020; no shares issued and outstanding at December 31, 2021 and 2020	—	—
Common stock, $0.0001 par value; authorized shares —400,000,000 at December 31, 2021 and 2020; issued shares— 31,656,035 and 31,262,769 at December 31, 2021 and 2020, respectively; outstanding shares— 30,511,226 and 28,516,010 at December 31, 2021 and 2020, respectively	3	3
Additional paid-in capital	601,523	579,755
Accumulated deficit	(529,370)	(385,487)
Total stockholders' equity	72,156	194,271
Total liabilities and stockholders' equity	$ 189,431	$ 295,111

See accompanying notes.

PHATHOM PHARMACEUTICALS, INC.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development (includes related party amounts of $4,933 and $2,812, respectively)	$ 72,338	$ 98,148
General and administrative (includes related party amounts of $18 and $157, respectively)	62,742	27,517
Total operating expenses	135,080	125,665
Loss from operations	(135,080)	(125,665)
Other income (expense):		
Interest income	41	1,091
Interest expense	(6,788)	(4,581)
Change in fair value of warrant liabilities	—	95
Other (expense)	(2,056)	(8)
Total other income (expense)	(8,803)	(3,403)
Net loss and comprehensive loss	$ (143,883)	$ (129,068)
Net loss per share, basic and diluted	$ (3.89)	$ (3.88)
Weighted-average shares of common stock outstanding, basic and diluted	37,002,959	33,228,158

See accompanying notes

PHATHOM PHARMACEUTICALS, INC.
Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at December 31, 2019	24,728,258	$ 2	$ 484,372	$ (256,419)	$ 227,955
Conversion of Lender Warrants into equity	—	—	318	—	318
Issuance of common stock in connection with underwritten public offering, net	2,250,000	—	88,596	—	88,596
Issuance of common stock from exercise of stock options	48,263	—	629	—	629
Vesting of restricted shares	1,489,489	1	—	—	1
Stock-based compensation	—	—	5,840	—	5,840
Net loss	—	—	—	(129,068)	(129,068)
Balance at December 31, 2020	28,516,010	$ 3	$ 579,755	$ (385,487)	$ 194,271
Issuance of common stock from exercise of stock options	107,583	—	1,944	—	1,944
Issuance of common stock from exercise of warrants	228,696	—	—	—	—
401(k) matching contribution	26,750	—	903	—	903
Vesting of restricted shares	1,601,950	—	—	—	—
Stock-based compensation	—	—	16,812	—	16,812
ESPP shares issued	30,237	—	819	—	819
Issuance of warrants	—	—	1,290	—	1,290
Net loss	—	—	—	(143,883)	(143,883)
Balance at December 31, 2021	30,511,226	$ 3	$ 601,523	$ (529,370)	$ 72,156

See accompanying notes

PHATHOM PHARMACEUTICALS, INC.
Statements of Cash Flows
(in thousands)

	Years Ended December 31,	
	2021	**2020**
Cash flows from operating activities		
Net loss	$ (143,883)	$ (129,068)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	521	323
Stock-based compensation	16,812	5,840
Issuance of PIK interest debt	990	—
Amortization of debt discount	3,595	1,273
Change in fair value of warrant liabilities	—	(95)
Other	823	322
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets (includes related party amounts of $82 and $(82), respectively)	605	7,963
Accounts payable and accrued expenses (includes related party amounts of $2,766 and $399, respectively)	(9,791)	24,009
Accrued clinical trial expenses	(18,595)	19,997
Accrued interest	165	156
Operating right-of-use asset and lease liabilities	98	(205)
Other long-term assets	43	(203)
Net cash used in operating activities	(148,617)	(69,688)
Cash flows from investing activities		
Cash paid for property, plant and equipment	(328)	(1,040)
Net cash used in investing activities	(328)	(1,040)
Cash flows from financing activities		
Proceeds from underwritten public offering, net	—	88,830
Proceeds from issuance of common stock from exercise of stock options	1,944	629
Repayment of long-term debt	(54,125)	—
Net proceeds from issuance of long-term debt	96,889	25,000
Net cash provided by financing activities	44,708	114,459
Net increase (decrease) in cash and cash equivalents	(104,237)	43,731
Cash and cash equivalents – beginning of period	287,496	243,765
Cash and cash equivalents – end of period	$ 183,259	$ 287,496
Supplemental disclosure of cash flow information		
Interest paid	$ 4,069	$ 3,464
Supplemental disclosure of noncash investing and financing activities		
Issuance of common stock warrants in connection with long-term debt	$ 1,290	$ —
Property and equipment purchases included in accounts payable and accrued expenses	$ 2	$ 145
Final interest payment fee	$ 7,500	$ 2,063
Settlement of ESPP liability in common stock	$ 819	$ —
Settlement of 401(k) liability in common stock	$ 903	$ —
Operating lease liabilities arising from obtaining right-of-use assets	$ —	$ 1,396
Conversion of Lender Warrants into Equity	$ —	$ 318
Underwritten public offering costs included in accounts payable and accrued expenses	$ —	$ 234

See accompanying notes.

1. Organization, Basis of Presentation and Summary of Significant Accounting Policies

Organization and Basis of Presentation

Phathom Pharmaceuticals, Inc., or the Company or Phathom, was incorporated in the state of Delaware in January 2018. The Company is a late clinical-stage biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal diseases. The Company's financial statements are prepared in accordance with U.S. generally accepted accounting principles, or GAAP.

Liquidity and Capital Resources

From inception to December 31, 2021, the Company has devoted substantially all of its efforts to organizing and staffing the Company, business planning, raising capital, in-licensing its initial product candidate, vonoprazan, meeting with regulatory authorities, managing the Phase 3 clinical trials of vonoprazan, and providing other general and administrative support for these operations. The Company has a limited operating history, has never generated any revenue, and the sales and income potential of its business is unproven. The Company has incurred net losses and negative cash flows from operating activities since its inception and expects to continue to incur net losses into the foreseeable future as it continues the development and preparation for commercialization of vonoprazan. From inception to December 31, 2021, the Company has funded its operations through the issuance of convertible promissory notes, commercial bank debt, the sale of 10,997,630 shares of common stock for net proceeds of approximately $191.5 million in its 2019 IPO and the sale of 2,250,000 shares of common stock for net proceeds of approximately $88.6 million in its December 2020 follow-on public offering.

The accompanying financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business, and do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or amounts and classification of liabilities. Management is required to perform a two-step analysis over the Company's ability to continue as a going concern. Management must first evaluate whether there are conditions and events that raise substantial doubt about the Company's ability to continue as a going concern (Step 1). If management concludes that substantial doubt is raised, management is also required to consider whether its plans alleviate that doubt (Step 2).

Management believes that it has sufficient working capital on hand to fund operations through at least the next twelve months from the date these financial statements were available to be issued. There can be no assurance that the Company will be successful in acquiring additional funding, if needed, that the Company's projections of its future working capital needs will prove accurate, or that any additional funding would be sufficient to continue operations in future years.

Use of Estimates

The preparation of the Company's financial statements requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. The most significant estimates in the Company's financial statements relate to accruals for research and development expenses, and the valuation of warrant liabilities and various other equity instruments. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results could differ materially from those estimates and assumptions.

Fair Value Measurements

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets.

Level 2: Inputs, other than the quoted prices in active markets that are observable either directly or indirectly.

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The carrying amounts of the Company's financial instruments, including cash and cash equivalents, are classified within the Level 1 designation discussed above, while prepaid and other current assets, accounts payable, and accrued liabilities, approximate fair value due to their short maturities. Warrant liabilities are recorded at fair value on a recurring basis.

The Company has no financial assets measured at fair value on a recurring basis. None of the Company's non-financial assets or liabilities are recorded at fair value on a non-recurring basis. No transfers between levels have occurred during the periods presented.

The warrant liabilities consist of warrants, or the Lender Warrants, issued in connection with a loan and security agreement, or the SVB Loan Agreement, for commercial bank debt (see Note 6). The Lender Warrants were accounted for as liabilities as they contained a holder put right under which the lenders could have required the Company to pay cash in exchange for the Lender Warrants. The fair value of the Lender Warrants was estimated on the date of grant using the Black-Scholes option-pricing model with an expected term equal to the remaining contractual term of the warrants. The Company estimates its expected stock volatility based on the historical volatility of a set of peer companies, which are publicly traded, and expects to continue to do so until it has adequate historical data regarding the volatility of its own publicly-traded stock price. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The Company uses an expected dividend yield of zero based on the fact that the Company has never paid cash dividends and does not expect to pay cash dividends in the foreseeable future. When the Company drew down the Term Loan B under the SVB Loan Agreement in March 2020 (see Note 6), the Lenders' put right expired, and the Company recorded a final fair value adjustment and reclassified the Lender Warrants balance of $0.3 million to additional paid-in-capital.

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs (in thousands):

	Warrant Liabilities
Balance at December 31, 2019	$ 413
Change in fair value	(95)
Reclassification of Lender Warrants into equity (Note 6)	(318)
Balance at December 31, 2020	$ —

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less when purchased to be cash equivalents. Cash and cash equivalents include cash in readily available checking accounts and money market funds.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

Property, Plant, and Equipment, Net

Property, plant and equipment are recorded at cost, less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the useful life of the asset. Computer equipment and related software are depreciated over two to three years. Furniture and fixtures are depreciated over three years. Leasehold improvements are amortized over the lesser of the lease term or the estimated useful lives of the related assets. Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation of assets disposed of are removed from the accounts and any resulting gain or loss is included in loss from operations.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property, plant and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than the carrying amount. The impairment loss, if recognized, would be based on the excess of the carrying value of the impaired asset over its respective fair value. No impairment losses have been recorded through December 31, 2021.

Leases

At the inception of a contractual arrangement, the Company determines whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. If both criteria are met, the Company records the associated lease liability and corresponding right-of-use asset upon commencement of the lease using the implicit rate or a discount rate based on a credit-adjusted secured borrowing rate commensurate with the term of the lease. The Company additionally evaluates leases at their inception to determine if they are to be accounted for as an operating lease or a finance lease. A lease is accounted for as a finance lease if it meets one of the following five criteria: the lease has a purchase option that is reasonably certain of being exercised, the present value of the future cash flows is substantially all of the fair market value of the underlying asset, the lease term is for a significant portion of the remaining economic life of the underlying asset, the title to the underlying asset transfers at the end of the lease term, or if the underlying asset is of such a specialized nature that it is expected to have no alternative uses to the lessor at the end of the term. Leases that do not meet the finance lease criteria are accounted for as an operating lease. Operating lease assets represent a right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. Operating lease liabilities with a term greater than one year and their corresponding right-of-use assets are recognized on the balance sheet at the commencement date of the lease based on the present value of lease payments over the expected lease term. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. As the Company's leases do not typically provide an implicit rate, the Company utilizes the appropriate incremental borrowing rate, determined as the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term and in a similar economic environment. Lease cost is recognized on a straight-line basis over the lease term and variable lease payments are recognized as operating expenses in the period in which the obligation for those payments is incurred. Variable lease payments primarily include common area maintenance, utilities, real estate taxes, insurance, and other operating costs that are passed on from the lessor in proportion to the space leased by the Company. The Company has elected the practical expedient to not separate between lease and non-lease components.

Research and Development Expenses and Accruals

All research and development costs are expensed in the period incurred and consist primarily of salaries, payroll taxes, employee benefits, stock-based compensation charges for those individuals involved in research and development efforts, external research and development costs incurred under agreements with contract research organizations and consultants to conduct and support the Company's ongoing clinical trials of vonoprazan, and costs related to manufacturing vonoprazan for clinical trials.

The Company has entered into various research and development contracts with clinical research organizations, clinical manufacturing organizations and other companies. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and payments made in advance of or after performance are reflected in the accompanying balance sheets as prepaid expenses or accrued liabilities, respectively. The Company records accruals for estimated costs incurred for ongoing research and development activities. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the services, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates may be made in determining the prepaid or accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

In-Process Research and Development

The Company evaluates whether acquired intangible assets are a business under applicable accounting standards. Additionally, the Company evaluates whether the acquired assets have a future alternative use. Intangible assets that do not have future alternative use are considered acquired in-process research and development. When the acquired in-process research and development assets are not part of a business combination, the value of the consideration paid is expensed on the acquisition date. Future costs to develop these assets are recorded to research and development expense as they are incurred.

General and Administrative Expenses

General and administrative expenses consist of salaries, stock-based compensation, facilities and third-party expenses. General and administrative expenses are associated with the activities of the executive, finance, accounting, information technology, legal, medical affairs and human resource functions.

Stock-Based Compensation

Stock-based compensation expense represents the cost of the grant date fair value of equity awards recognized over the requisite service period of the awards (generally the vesting period) on a straight-line basis with forfeitures recognized as they occur.

The Company also maintains an employee stock purchase program, or ESPP, under which it may issue shares. The Company estimates the fair value of stock options and shares that will be issued under the ESPP using the Black-Scholes valuation model, which requires the use of estimates. The Company recognizes stock-based compensation cost for shares that it will issue under the ESPP on a straight-line basis over the requisite service period of the award.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in the statement of operations in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (i) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (ii) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50 percent likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company’s comprehensive loss was the same as its reported net loss for all periods presented.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business as one operating segment.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. The Company included 7,588,000 shares of common stock under its warrant, or the Takeda Warrant, issued to Takeda Pharmaceutical Company Limited, or Takeda, in connection with a May 2019 license agreement (see Note 4) in the calculation of basic weighted-average common shares outstanding from the time it became exercisable at the Company's IPO because the Takeda Warrant is exercisable for little consideration. During the year ended December 31, 2021, Takeda Warrants were exercised to purchase 228,696 shares of common stock. As of December 31, 2021, Takeda Warrants to purchase 7,359,304 shares of common stock remains exercisable. For the years ended December 31, 2021 and 2020, the Company has excluded weighted-average unvested shares of 1,939,252 and 3,424,676, respectively, from the weighted-average number of common shares outstanding. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common shares and dilutive common stock equivalents outstanding for the period determined using the treasury-stock and if-converted methods. Dilutive common stock equivalents are comprised of unvested common stock, options and warrants. For the periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding as inclusion of the potentially dilutive securities (warrants, stock options, and common shares subject to repurchase) would be antidilutive.

Recently Adopted Accounting Standards

In December 2019, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, or* ASU 2019-12, which simplifies the accounting for income taxes. ASU 2019-12 is effective for annual reporting periods, and interim periods within those annual periods, beginning after December 15, 2020 on a prospective basis, and early adoption is permitted. The Company adopted this guidance effective January 1, 2021, and the adoption did not have a material impact on the Company's financial statements.

Recently Issued Accounting Pronouncements

The Company assesses the adoption impacts of recently issued accounting standards by the Financial Accounting Standards Board or other standard setting bodies on the Company's financial statements as well as material updates to previous assessments. There were no new material accounting standards issued or adopted in year of 2021 that impacted the Company.

2. Balance Sheet Details

Property, Plant and Equipment, net

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

	Years Ended December 31,	
	2021	2020
Computer equipment and software	$ 646	$ 516
Furniture and fixtures	780	747
Leasehold improvements	76	54
	1,502	1,317
Less: accumulated depreciation	(852)	(331)
Total property, plant and equipment, net	$ 650	$ 986

Depreciation and amortization expense for the years ended December 31, 2021 and 2020 was approximately $0.5 million and $0.3 million, respectively. No property, plant or equipment was disposed of during the years ended December 31, 2021 and 2020.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	Years Ended December 31,	
	2021	2020
Accrued research and development expenses	$ 3,165	$ 4,864
Accrued compensation expenses	6,344	4,587
Accrued professional & consulting expenses	1,855	1,123
Accrued other	41	32
Total accrued expenses	$ 11,405	$ 10,606

3. Related Party Transactions

Frazier is a principal stockholder of the Company. The Company has conducted operations within office space controlled by Frazier and Frazier allocated a portion of the costs associated with this office space to the Company. In addition, Frazier paid for various goods and services, such as employee wages, insurance and expense reimbursements and various administrative services associated with the operations of the Company and charged the Company for those expenses. As of December 31, 2021 and 2020, the Company had outstanding accounts payable and accrued expenses due to Frazier in the amount of $0 and $35,000, respectively, related to these shared operating expenses. For the years ended December 31, 2021 and 2020, the Company incurred $18,000 and $0.2 million, respectively, of shared operating expenses.

Frazier is a principal stockholder in PCI Pharma Services, or PCI. In the third quarter of 2019, the Company engaged PCI for clinical manufacturing services. As of December 31, 2021 and 2020, the Company had $1.7 million and $0.4 million, respectively, in outstanding accounts payable and accrued expenses related to these manufacturing services. For the years ended December 31, 2021 and 2020, the Company incurred $3.2 million and $2.3 million, respectively, of expenses related to services performed by PCI.

Takeda became a common stockholder of the Company in connection with the May 2019 license agreement (see Note 4). In conjunction with this license, Takeda provides proprietary supplies for the Company's ongoing clinical development of vonoprazan in addition to the exclusive license for the commercialization of vonoprazan in the United States, Canada and Europe. As of December 31, 2021 and 2020, the Company had $22,000 and $22,000, respectively, in outstanding accounts payable and accrued expenses related to these supply services. The Company did not have any such supply services expenses incurred for the years ended December 31, 2021 and 2020.

On May 5, 2020, the Company entered into a Commercial Supply Agreement, or the Commercial Supply Agreement, with Takeda, pursuant to which Takeda will supply commercial quantities of vonoprazan bulk drug product or drug substance. Pursuant to the Commercial Supply Agreement, Takeda has agreed to supply the Company with, and the Company has agreed to purchase from Takeda, certain quantities of vonoprazan bulk drug product according to approved specifications at a fixed price per batch of bulk drug product in order to commercialize vonoprazan in accordance with the Takeda License. Unless terminated earlier, the term of the Commercial Supply Agreement extends for a period of two years from the date the Company places an order for bulk drug product or drug substance for the first commercial launch of vonoprazan in any jurisdiction in the licensed territory, provided that this two-year period will expire no later than December 31, 2023. The Commercial Supply Agreement will terminate immediately upon the termination of the Takeda License in accordance with its terms. As of December 31, 2021 and 2020, the Company had $0.7 million and $0.2 million, respectively, in outstanding accounts payable and accrued expenses related to these product costs. For the years ended December 31, 2021 and 2020, the Company incurred $1.8 million and $0.3 million, respectively, of expenses related to the Commercial Supply Agreement. The Company has a remaining minimum purchase obligation of approximately $0.4 million related to this agreement.

In connection with the Takeda License, the Company entered into a temporary services agreement, or the Temporary Services Agreement, with Takeda on November 24, 2020. Pursuant to the Temporary Services Agreement, Takeda agreed to provide or procure the provision of services related to the ongoing clinical development of vonoprazan. The Temporary Services Agreement will terminate immediately upon termination of the Takeda License in accordance with its terms. As of December 31, 2021 and 2020, the Company had $0.2 million and $0.2 million, respectively, in outstanding accounts payable and accrued expenses related to these temporary services. For the year ended December 31, 2021 and 2020, the company incurred $0 and $0.2 million, respectively, of expenses related to the temporary services performed by Takeda.

4. Commitments and Contingencies

License Agreement

On May 7, 2019, the Company entered into a license agreement with Takeda pursuant to which it was granted an exclusive license to commercialize vonoprazan fumarate in the United States, Canada and Europe, or, the Takeda License. The Company also has the right to sublicense its rights under the agreement, subject to certain conditions. The agreement will remain in effect, on a country-by-country and product-by-product basis, until the later of (i) the expiration of the last to expire valid patent claim covering vonoprazan fumarate alone or in combination with at least one other therapeutically active ingredient, (ii) the expiration of the applicable regulatory exclusivity and (iii) 15 years from the date of first commercial sale, unless earlier terminated. The Company may terminate the Takeda License upon six months' written notice. The Company and Takeda may terminate the Takeda License in the case of the other party's insolvency or material uncured breach. Takeda may terminate the Takeda License if the Company challenges, or assists in challenging, licensed patents.

In consideration of the Takeda License, the Company (i) paid Takeda $25.0 million in cash, (ii) issued Takeda 1,084,000 shares of its common stock at a fair value of $5.9 million, (iii) issued the Takeda Warrant to purchase 7,588,000 shares of its common stock at an exercise price of $0.00004613 per share at an initial fair value of $47.9 million, and (iv) issued a right to receive an additional common stock warrant, or, the Takeda Warrant Right, should Takeda's fully-diluted ownership of the Company represent less than a certain specified percentage of the fully-diluted capitalization, including shares issuable upon conversion of then outstanding convertible promissory notes, calculated immediately before the closing of the Company's IPO, with a nominal initial fair value due to the low probability of issuance. The Takeda Warrant Right expired without effect since no fair value had been allocated to it upon completion of the IPO, and no additional warrant was issued. In addition, the Company is obligated to pay Takeda up to an aggregate of $250.0 million in sales milestones upon the achievement of specified levels of product sales, and a low double-digit royalty rate on aggregate net sales of licensed products, subject to certain adjustments. The Company incurred $0.1 million of transaction costs in connection with the Takeda License. The Takeda Warrant has an exercise price of $0.00004613 per share, expires on May 7, 2029 and became exercisable upon the consummation of the IPO. During the year ended December 31, 2021, Takeda Warrants were exercised to purchase 228,696 shares of common stock. As of December 31, 2021, Takeda Warrants to purchase 7,359,304 shares of common stock remains exercisable. Following the October 11, 2019 increase in the Company's authorized shares of common stock to 50,000,000, the Company recorded a non-cash charge related to the final fair value adjustment of the Takeda Warrants and reclassified the full balance of $144.2 million from warrant liabilities to additional paid-in capital.

Purchase Commitments

In December 2020, the Company entered into a supply agreement with Sandoz pursuant to which Sandoz will supply commercial quantities of amoxicillin capsules and clarithromycin tablets, package these antibiotics with vonoprazan, and provide in finished convenience packs. The supply agreement commits the Company to a minimum purchase obligation of approximately $3.8 million in the first 24-month period following the launch of the final product. The Company has not incurred any expenses under the agreement during the years ended December 31, 2021 and 2020.

Contingencies

In the event the Company becomes subject to claims or suits arising in the ordinary course of business, the Company would accrue a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

5. Lease Commitments

As of December 31, 2021, the Company had operating leases for office space in both Buffalo Grove, Illinois and Florham Park, New Jersey, with weighted average remaining lease terms of 3.3 years and 3.7 years, respectively. Both operating leases contain an option to extend the term for one additional five-year period, which was not considered in the determination of the right-of-use asset or lease liability as the Company did not consider it reasonably certain that it would exercise such options.

The total rent expense for the years ended December 31, 2021 and 2020 was approximately $0.7 million and $0.5 million, respectively.

The following table summarizes supplemental balance sheet information related to the operating leases as of December 31, 2021:

	As of December 31,	
	2021	2020
Assets:		
Operating lease right-of-use assets	$ 1,914	$ 2,373
Total right-of-use assets	1,914	2,373
Liabilities:		
Operating lease liabilities, current	487	474
Operating lease liabilities, non-current	1,183	1,557
Total operating lease liabilities	$ 1,670	$ 2,031

As of December 31, 2021, the future minimum annual lease payments under the operating leases were as follows (in thousands):

2022	503
2023	516
2024	529
2025	342
Total minimum lease payments	1,890
Less: amount representing interest	(220)
Present value of operating lease liabilities	1,670
Less: operating lease liabilities, current	(487)
Operating lease liabilities	$ 1,183
Weighted-average remaining lease term (in years)	3.56
Weighted-average incremental borrowing rate	7.25%

Operating cash flows for the years ended December 31, 2021 included $0.7 million in cash payments for operating leases, $0.1 million of which were prepaid lease payments. Operating cash flows for the years ended December 31, 2020 included $0.9 million in cash payments for operating leases, $0.6 million of which were prepaid lease payments.

6. Debt

Total debt consists of the following (in thousands):

	December 31, 2021
Long-term debt, current portion	$ —
Long-term debt, non-current portion	100,990
Unamortized debt discount	(11,319)
Total debt, net of debt discount	$ 89,671

On September 17, 2021, or the Closing Date, the Company entered into a Loan and Security Agreement, or, the Loan Agreement, with Hercules Capital, Inc., in its capacity as administrative agent and collateral agent and as a lender, or, in such capacity, the Agent or Hercules, and the other financial institutions that from time to time become parties to the Loan Agreement as lenders, or, collectively, the Lenders.

The Loan Agreement provides for term loans in an aggregate principal amount of up to $200.0 million, or the Term Loan, under multiple tranches. The tranches consist of (i) a first tranche consisting of term loans in an aggregate principal amount of $100.0 million, all of which was funded to the Company on the Closing Date, or First Advance, (ii) a second tranche consisting of up to an additional $50.0 million, which became available to the Company upon achievement of the protocol-specified primary efficacy endpoints in the Company's Phase 3 trial studying vonoprazan for the healing and maintenance of healing of erosive esophagitis with acceptable safety data, such that the results support the submission of a New Drug Application, or NDA, or supplemental NDA without the need to conduct another Phase 3 study and will be available, if specified conditions are met, through December 15, 2022, (iii) a third tranche consisting of an additional $25.0 million, which will become available to the Company upon the achievement of (a) FDA approval of the Company's NDA for vonoprazan and amoxicillin, or its New Drug Application for vonoprazan, amoxicillin and clarithromycin, in each case for an indication relating to the treatment of *H. pylori* with an approved indication on the claim that is generally consistent with that sought in the Company's NDA submission; and (b) filing of the Company's NDA or supplemental NDA for vonoprazan for indications relating to the healing and maintenance of healing of erosive esophagitis, or, milestones (a) and (b), together, the Second Performance Milestone, and will be available, if specified conditions are met, through September 30, 2023, and (iv) a fourth tranche consisting of up to an additional $25.0 million, which will be available, if specified conditions are met, through March 31, 2024, upon achievement of the Second Performance Milestone.

The Company paid a $1.25 million facility charge in connection with closing of the Loan Agreement and would need to pay 0.5% of any advances made under the third and fourth tranches.

The Term Loan will mature on October 1, 2026, or the Maturity Date. The Term Loan bears (i) cash interest at a variable annual rate equal to the greater of (a) 5.50% and (b) the Prime Rate (as reported in the Wall Street Journal) plus 2.25%, or the "Interest Rate", and (ii) payment-in-kind interest at a per annum rate of interest equal to 3.35%. Phathom may make payments of interest only through October 1, 2024, which may be extended to October 1, 2025, upon the achievement of the Second Performance Milestone on or prior to September 30, 2024 and the condition that no default or event of default exists, and which is further extendable to October 1, 2026, subject to FDA approval of the Company's NDA (or supplemental NDA) for vonoprazan for an indication relating to the healing and maintenance of healing of erosive esophagitis with an approved indication on the label that is generally consistent with that sought in the Company's NDA submission (or supplemental NDA submission), or the Third Performance Milestone, on or prior to September 30, 2025 and no default or event of default exists (the "interest only period"). After the interest-only period, the principal balance and related interest will be required to be repaid in equal monthly installments and continuing until the Maturity Date.

In addition, the Company is obligated to pay a final payment fee of 7.50% of the original principal amount of amounts actually advanced under the Term Loan, or, each a Term Loan Advance and together, the Term Loan Advances. As of December 31, 2021, the aggregate final payment fee for the first Term Loan Advance of $7.5 million has been recorded as an other long-term liability.

The Company may elect to prepay all or a portion of the Term Loan Advances prior to maturity, subject to a prepayment fee of up to 1.25% of the then outstanding principal balance of the Term Loan Advances being prepaid. After repayment, no Term Loan amounts may be borrowed again.

As collateral for the obligations, the Company has granted to Hercules a senior security interest in all of Company's right, title, and interest in, to and under substantially all of Company's property, inclusive of intellectual property.

The Loan Agreement contains customary closing fees, prepayment fees and provisions, events of default, and representations, warranties and covenants, including a financial covenant requiring Phathom to maintain certain levels of cash subject to a control agreement in favor of the Agent (minus accounts payable not paid within 120 days of invoice), or Qualified Cash, and commencing on May 15, 2023, trailing three-month net product revenue from the sale of vonoprazan and products containing vonoprazan. The revenue covenant will be waived at any time in which the Company maintains Qualified Cash equal to at least 60.0% (prior to the Third Performance Milestone), and 35% (following the Third Performance Milestone) of the total outstanding Term Loan principal amount, or the Company's market capitalization is at least $900.0 million. Upon the occurrence of an event of default, subject to any specified cure periods, all amounts owed by the Company may be declared immediately due and payable by Hercules, as collateral agent. As of December 31, 2021, the Company was in compliance with all applicable covenants under the Loan Agreement.

In connection with the entry into the Loan Agreement, the Company issued to Hercules a warrant, or, the Warrant, to purchase a number of shares of the Company's common stock equal to 2.5% of the aggregate amount of the Term Loan advances funded, and will issue to Hercules additional warrants when future Term Loan advances are funded. On the Closing Date, the Company issued a Warrant for 74,782 shares of common stock. The Warrant will be exercisable for a period of seven years from the date of issuance at a per-share exercise price equal to $33.43, which was the closing price of the Company's common stock on September 16, 2021. The Warrant is exercisable any time until September 17, 2028 and had an initial fair value of approximately $1.3 million.

The initial $1.3 million fair value of the Warrant, the $7.5 million final interest payment fee and $3.1 million of debt issuance costs have been recorded as debt discount and are being amortized to interest expense using the effective interest method over the term of the Term Loan.

Future minimum principal and interest payments under the Term Loan, including the final payment fee, as of December 31, 2021 are as follows (in thousands):

Year ending December 31:		
2022	$	5,704
2023		5,900
2024		17,308
2025		50,912
2026		66,948
Total principal and interest payments		146,772
Less interest and final payment fee		(46,772)
Total term loan borrowings	$	100,000

Prior to the Loan Agreement with Hercules, the Company had a loan with SVB and approximately $54.3 million of the proceeds from the First Advance was used to satisfy in full and retire the Company's indebtedness under the SVB Term Loan with SVB, including accrued interest through the payoff date.

The SVB Term Loan originated on May 14, 2019, when the Company entered into a loan and security agreement with SVB, as administrative and collateral agent, and lenders including SVB and WestRiver Innovation Lending Fund VIII, L.P. The Company borrowed $25.0 million, or Term Loan A, at the inception of the Loan Agreement and an additional $25.0 million, or Term Loan B, on March 16, 2020.

The SVB Term Loan bore interest at a floating rate of the higher of the Wall Street Journal Prime rate plus 1.75% or 7.25%. Under the original SVB Term Loan, the monthly payments consisted of interest-only through May 31, 2021. On March 11, 2020, the Company entered into the first amendment and on March 11, 2021, the Company entered into the second amendment, or together the Amendments, to the SVB Term Loan. Pursuant to the Amendments, the interest-only payment period was initially extended through July 31, 2021, and was further extended until December 31, 2021, after the Company received positive data from its Phase 3 clinical trial in *H. pylori* infection sufficient to file an NDA with the FDA. The interest-only payment period could have been further extended until November 30, 2022, if the Company would receive positive data from its Phase 3 clinical trial in erosive esophagitis for vonoprazan sufficient to file an NDA with the FDA. Subsequent to the interest-only period, the SVB Term Loan would have been payable in equal monthly installments of principal, plus accrued and unpaid interest through the maturity date of May 1, 2024.

In addition, the Company was obligated to pay a final payment fee of 8.25% of the original principal amount of the SVB Term Loan. The aggregate final payment fee for the Term Loan of $4.1 million was recorded as an other long-term liability.

The Company could have elected to prepay all or a portion of the SVB Term Loan prior to maturity, subject to a prepayment fee of up to 2.0% of the then outstanding principal balance and payment of a pro rata portion of the final payment fee. After repayment, no Term Loan amounts could have been borrowed again.

The borrowings under the SVB Term Loan were collateralized by substantially all of the Company's assets. The SVB Term Loan included affirmative and negative covenants. The affirmative covenants included, among others, covenants requiring the Company to maintain its legal existence and governmental approvals, deliver certain financial reports, maintain insurance coverage and satisfy certain requirements regarding its operating accounts. The negative covenants included, among others, limitations on the Company's 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. The SVB Term Loan also contained customary events of default, including bankruptcy, the failure to make payments when due, and a material adverse change. Upon the occurrence of an event of default, subject to any specified cure periods, all amounts owed by the Company would have begun to bear interest at a rate that is 4.00% above the rate effective immediately before the event of default and could have been declared immediately due and payable by SVB, as collateral agent.

In connection with the SVB Term Loan, the Company issued Lender Warrants to purchase stock of the Company, which expire ten years from the date of issuance. Upon completion of the IPO in 2019, the Lender Warrants became exercisable for 16,446 shares of common stock. The Lender Warrants included a put option pursuant to which, in the event that the Company did not draw down Term Loan B on or before March 31, 2020, the warrant holders could have required that the Company repurchase the warrants for a total aggregate repurchase price of $0.5 million. Upon the Term Loan B draw in March 2020, the Lender Warrants became exercisable and the put option related to the Lender Warrants expired. Accordingly, the Company recorded a final fair value adjustment and reclassified the Lender Warrants balance of $0.3 million to additional paid-in-capital.

The initial $0.4 million fair value of the Lender Warrants, the $4.1 million final payment fee and $0.2 million of debt issuance costs were recorded as debt discount and amortized to interest expense using the effective interest method over the term of the Term Loans prior to the retirement of the debt. Upon retirement of the debt any remaining unamortized amounts were recorded as an expense to Other income (expense).

During the years ended December 31, 2021 and 2020, the Company recognized $6.8 million and $4.6 million, respectively, of interest expense, including amortization of the debt discount, in connection with the Hercules Loan Agreement and SVB Term Loan. As of December 31, 2021, the Company had outstanding loan balance of $101.0 million and accrued interest of $0.5 million.

7. Stockholders' Equity

Common Stock

In March 2019, subsequent to the Merger, the Company sold 1,491,072 shares of the Company's common stock to Frazier.

In March 2019, the founders granted the Company a repurchase right for the 3,373,408 shares of common stock originally purchased in 2018. The Company has the right, but not the obligation, to repurchase unvested shares in the event the founder's relationship with the Company is terminated, subject to certain limitations, at the original purchase price of the stock. The repurchase right lapsed for 843,352 shares in March 2019 and the repurchase right for the remaining 2,530,056 shares lapses in equal monthly amounts over the following 48-month period ending in March 2023. The fair value of the founder shares at the date the repurchase right was granted is being recognized as stock-based compensation expense on a straight-line basis over the vesting period. As of December 31, 2021, 395,321 shares of common stock were subject to repurchase by the Company and the associated repurchase liability was not significant. The amount of recognized and unrecognized stock-based compensation related to the founder stock was immaterial for all periods presented.

In May 2019, the Company issued Takeda 1,084,000 shares of common stock in connection with the Takeda License.

For the period from January 1, 2019 to May 6, 2019, the Company issued 2,524,852 shares of common stock to various employees and consultants of the Company for aggregate proceeds of approximately $1,000. Upon issuance, these shares were subject to a repurchase option by the Company at the original purchase price of the shares. The repurchase rights generally lapse as to 25% of the shares on the first anniversary of the vesting commencement date, and the repurchase right lapses as to 1/48th of the shares each one-month period thereafter, subject to the purchaser remaining continuously an employee, consultant or director of the Company. In November 2019, the Company repurchased 17,560 shares at the original purchase price for an aggregate purchase price of $5.20. As of December 31, 2021, 749,488 shares remain available for repurchase by the Company and the associated repurchase liability was not significant.

On October 29, 2019, upon completion of the IPO, the Company sold 10,997,630 shares of common stock, which included the exercise in full by the underwriters of their option to purchase 1,434,473 additional shares at a public offering price of $19.00 per share. The net proceeds were approximately $191.5 million, after deducting underwriting discounts, commissions and offering costs.

In November 2020, the Company entered into an Open Market Sale Agreement, or, the Sales Agreement, with Jefferies LLC, or, the Sales Agent, under which it may, from time to time, sell shares of its common stock having an aggregate offering price of up to $125.0 million through the Sales Agent, or, the ATM Offering. Pursuant to the Sales Agreement, the Company will pay the Sales Agent a commission for its services in acting as an agent in the sale of common stock in an amount equal to 3% of the gross sales price per share sold. No shares were sold under the ATM Offering as of December 31, 2021.

On December 16, 2020, the Company completed an underwritten public offering, in which it sold 2,250,000 shares of its common stock at a price of $42.00 per share for total gross proceeds of $94.5 million. The net purchase price after deducting underwriting discounts and commissions was $39.48 per share, which generated net proceeds of $88.8 million. The Company incurred an additional $0.2 million of offering expenses in connection with this public offering.

A summary of the Company's unvested shares is as follows:

Balance at December 31, 2020	2,746,759
Share vesting	(1,601,950)
Balance at December 31, 2021	1,144,809

For accounting purposes, unvested shares of common stock are considered issued, but not outstanding until they vest.

Common stock reserved for future issuance consists of the following:

	December 31, 2021
Common stock warrants	7,450,532
Stock options and performance-based awards outstanding	4,581,029
Shares available for issuance under the 2019 Incentive Plan	1,772,744
Shares available for issuance under the ESPP Plan	842,036
Balance at December 31, 2021	14,646,341

Preferred Stock

The Company is authorized to issue up to 40 million shares of preferred stock. As of December 31, 2021, and December 31, 2020, there were no shares of preferred stock issued or outstanding.

Equity Incentive Plan

The Company's 2019 Equity Incentive Plan, or the Existing Incentive Plan, provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, and other stock awards to eligible recipients, including employees, directors or consultants of the Company. The Company had 2,231,739 shares of common stock authorized for issuance under the Existing Incentive Plan, of which, 1,400,528 stock options and 16,260 restricted stock awards were granted in 2019. As a result of the adoption of the 2019 Incentive Award Plan, or the 2019 Plan, in October 2019, no further shares are available for issuance under the Existing Incentive Plan.

2019 Incentive Award Plan

In October 2019, the board of directors adopted, and the Company's stockholders approved, the 2019 Plan, which became effective in connection with the IPO. Under the 2019 Plan, the Company may grant stock options, stock appreciation rights, restricted stock, restricted stock units and other awards to individuals who are then employees, officers, non-employee directors or consultants of the Company or its subsidiaries. The number of shares initially available for issuance will be increased by (i) the number of shares subject to stock options or similar awards granted under the Existing Incentive Plan that expire or otherwise terminate without having been exercised in full after the effective date of the 2019 Plan and unvested shares issued pursuant to awards granted under the Existing Incentive Plan that are forfeited to or repurchased by the Company after the effective date of the 2019 Plan, with the maximum number of shares to be added to the 2019 Plan pursuant to clause (i) above equal to 1,416,788 shares, and (ii) an annual increase on January 1 of each calendar year beginning in 2020 and ending in 2029, equal to the lesser of (a) 5% of the shares of common stock outstanding on the final day of the immediately preceding calendar year and (b) such smaller number of shares as determined by the board of directors. As of December 31, 2021, 1,772,744 shares remain available for issuance, which reflects 1,915,300 stock options and performance-based units ("PSU") granted, and 175,430 cancelled or forfeited, during the year ended December 31, 2021 as well as annual increases of 1,250,511 and 1,158,580 shares that were authorized on January 1, 2021 and 2020. An additional 1,582,802 shares were authorized on January 1, 2022.

Performance-based Units

During 2020, the Company granted 220,000 PSUs whereby vesting depends upon the approval by the U.S. Food and Drug Administration, or FDA, of vonoprazan for *H. pylori* and then, or concurrent with, erosive esophagitis. In 2021, the Company granted an additional 190,050 PSUs to employees. As of December 31, 2021, the PSU milestones had not been achieved. As of December 31, 2021, no related compensation cost had been recognized. The following table summarizes PSU activity under the 2019 Incentive Award Plan during the year ended December 31, 2021.

	Number of Stock Units	Weighted-Average Grant Date Fair Value Per Share
Unvested balance at December 31, 2020	220,000	$ 32.48
Granted	190,050	31.80
Vested	—	—
Forfeited	(15,750)	30.63
Unvested balance at December 31, 2021	394,300	$ 32.23

As of December 31, 2021 there was approximately $12.7 million of related unrecognized compensation cost, which will be recognized upon vesting.

Employee Stock Purchase Plan

In October 2019, the board of directors adopted, and the Company's stockholders approved, the Employee Stock Purchase Plan, or the ESPP, which became effective in connection with the IPO. The ESPP permits participants to purchase common stock through payroll deductions of up to 20% of their eligible compensation, which includes a participant's gross base compensation for services to the Company, including overtime payments and excluding sales commissions, incentive compensation, bonuses, expense reimbursements, fringe benefits and other special payments. A total of 270,000 shares of common stock was initially reserved for issuance under the ESPP. In addition, the number of shares available for issuance under the ESPP will be annually increased on January 1 of each calendar year beginning in 2020 and ending in 2029, by an amount equal to the lesser of: (i) 1% of the shares outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares as is determined by the board of directors. As of December 31, 2021, 842,036 shares of common stock remain available for issuance, which reflects 30,237 shares sold to employees during the year ended December 31, 2021 as well as the annual increases of 312,628 and 289,645 shares that were authorized on January 1, 2021 and 2020. No additional shares were authorized in January 2022.

The ESPP is considered a compensatory plan, and the Company recorded related stock-based compensation of $0.4 million and 0.3 million for the year ended December 31, 2021 and 2020, respectively. The weighted-average assumptions used to estimate the fair value of ESPP awards using the Black-Scholes option valuation model were as follows:

	Years Ended December 31,	
	2021	2020
Assumptions:		
Expected term (in years)	0.69	1.00
Expected volatility	76.25%	76.25%
Risk free interest rate	0.09%	0.15%
Dividend yield	—	—

The estimated weighted-average fair value of ESPP awards during 2021 and 2020 was $14.66 and $13.66, respectively. As of December 31, 2021, the total unrecognized compensation expense related to the ESPP was $12,000, which is expected to be recognized over a weighted-average period of approximately 0.5 months.

Stock Options

The fair value of each employee and non-employee stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The Company, prior to the IPO on October 29, 2019, was a private company and lacked company-specific historical and implied volatility information. Therefore, it estimated its expected volatility based on the historical volatility of a publicly-traded set of peer companies. Due to the lack of historical exercise history, the expected term of the Company's stock options for employees was determined utilizing the "simplified" method for awards. The expected term of stock options granted to non-employees was equal to the contractual term of the option award. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield was zero based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

A summary of the Company's stock option activity and related information is as follows:

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2020	2,728,742	$ 21.36	9.10	$ 34,432
Options granted	1,725,250	37.14		
Options exercised and shares vested	(107,583)	18.07		
Options cancelled	(159,680)	32.26		
Balance at December 31, 2021	4,186,729	$ 27.53	8.43	$ 13,973
Options exercisable as of December 31, 2021	1,127,877	19.75	7.91	6,880
Options vested and expected to vest as of December 31, 2021	4,186,729	27.53	8.43	13,973

The aggregate intrinsic value of options exercisable as of December 31, 2021 and 2020 were calculated as the difference between the exercise price of the underlying options and the closing market price of the Company's common stock on that date, which were $19.67 and $33.22 per share on December 31, 2021 and 2020, respectively. The aggregate intrinsic value of options exercised during the years ended December 31, 2021 and 2020 were approximately $1.7 million and $1.5 million, respectively.

The estimated weighted-average fair value of employee and nonemployee director stock options granted during 2021 was $22.20. As of December 31, 2021, the Company had $46.6 million of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted-average period of 2.6 years.

The weighted-average assumptions used to estimate the fair value of stock options using the Black-Scholes option valuation model were as follows:

	Years Ended December 31,	
	2021	2020
Assumptions:		
Expected term (in years)	5.93	6.06
Expected volatility	67.46%	65.07%
Risk free interest rate	0.68%	0.51%
Dividend yield	—	—

Stock-Based Compensation Expense

Stock-based compensation expense recognized for all equity awards, including founder stock, has been reported in the statements of operations as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Research and development expense	$ 3,838	$ 1,450
General and administrative expense	12,974	4,390
Total	$ 16,812	$ 5,840

8. Income Taxes

For the years ended December 31, 2021 and 2020, the Company did not record a provision for income taxes due to a full valuation against its deferred taxes. A reconciliation between the provision for income taxes and income taxes computed using the U.S. federal statutory corporate tax rate is as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Income taxes computed at the statutory rate	$ (30,216)	$ (27,105)
Permanent items	1,387	291
Change in fair value of warrants and convertible debt	—	(20)
Research and development credit	(2,950)	(3,047)
Change in valuation allowance	31,783	29,949
Other	(4)	(68)
Provision (benefit) for income taxes	$ —	$ —

Significant components of the Company's net deferred tax assets are as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 60,936	$ 33,162
Research credits	6,694	3,744
Intangible assets	13,809	14,929
Other	3,996	1,914
Gross deferred tax assets	85,435	53,749
Less valuation allowance	(85,033)	(53,250)
Deferred tax assets, net of valuation allowance	402	499
Deferred tax liabilities:		
Other	(402)	(499)
Net deferred tax assets	$ —	$ —

Based upon the Company's history of operating losses, the Company is unable to conclude that it is more likely than not that the benefit of its deferred tax assets will be realized. Accordingly, the Company has provided a full valuation allowance for its deferred tax assets as of December 31, 2021 and 2020.

As of December 31, 2021 and 2020, the Company had federal net operating loss carryforwards of approximately $290.1 million and $157.8 million, respectively, which are carried over indefinitely.

As of December 31, 2021, the Company had approximately $0.4 million of state net operating loss carryforwards that begins to expire in 2036.

As of December 31, 2021, the Company has available federal research and development credits of $7.8 million which begin to expire in 2038. The Company has $0.7 million of state research and development credits, some of which, begin to expire in 2025.

The Company has not completed a formal analysis of the potential impact of Section 382 on its deferred tax assets as of December 31, 2021. Until this analysis has been completed, the Company has not adjusted any of its deferred tax assets, including net operating losses or research and development credits. The Company will reassess the amount of net operating losses and credits subject to limitation under Section 382 when a study is complete. Due to the existence of the valuation allowance, future changes in the deferred tax assets related to these tax attributes will not impact the Company’s effective tax rate.

The Company recognizes liabilities for uncertain tax positions based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount that is more than 50% likely of being realized upon settlement. While the Company believes that it has appropriate support for the positions taken on its tax returns, the Company regularly assesses the potential outcome of examinations by tax authorities in determining the adequacy of its provision for income taxes.

The following table summarizes the activity related to the Company's gross unrecognized tax benefits:

	Years Ended December 31,	
	2021	2020
Beginning balance	$ 938	$ 176
Increases related to prior year tax positions	64	-
Increases related to current year tax positions	702	762
Ending balance	$ 1,704	$ 938

As of December 31, 2021, the Company has gross unrecognized tax benefits of $1.7 million, none of which would affect the effective tax rate due to a full valuation allowance. The Company does not anticipate any significant changes in its unrecognized tax benefits over the next 12 months. The Company's policy is to recognize the interest expense and/or penalties related to income tax matters as a component of income tax expense. The Company has no accrual for interest or penalties on its balance sheet at December 31, 2021 and has not recognized interest or penalties in its statement of operations for the year ended December 31, 2021.

The Company is subject to taxation in the United States and various states. The Company is not currently under examination by any taxing authorities. Due to the carryover of tax attributes, the statute of limitations is currently open for tax years since inception.

9. 401(k) Plan

The Company established a 401(k) savings plan during the year ended December 31, 2020. The Company’s contributions to the plan are discretionary. During the years ended December 31, 2021 and 2020, the Company incurred $0.8 million and $0.3 million, respectively, of expense related to employer contributions, which was based on a 75% match of employees' annual contributions. In January 2021, the Board of Directors approved the annual discretionary match for 2020, which was settled by contributing 8,356 shares. In August 2021, the Board of Directors approved a semi-annual discretionary match for 2021, which was settled by contributing 18,394 shares. In January 2022, the Board of Directors approved a second semi-annual discretionary match for 2021, which was settled by contributing 16,756 shares.

10. Subsequent Events

In February 2022, the Company entered into an operating lease for 6,250 rentable square feet of office space in Florham Park, New Jersey. The lease liability and the corresponding right-of-use asset associated with this lease obligation will be recorded upon the commencement of the lease, or the date in which the underlying asset is made available for use to the Company, which is expected to occur later in 2022.

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation	8-K	10-29-19	3.1	
3.2	Amended and Restated Bylaws	8-K	9-25-2020	3.1	
4.1	Form of Common Stock Certificate	S-1/A	10-15-2019	4.1	
4.2	Warrant to purchase shares of common stock issued to Takeda Company Limited, dated May 7, 2019	S-1	9-30-2019	4.2	
4.3	Warrant to purchase stock issued to Silicon Valley Bank, dated May 14, 2019	S-1	9-30-2019	4.3	
4.4	Warrant to purchase stock issued to WestRiver Innovation Lending Fund VIII, L.P., dated May 14, 2019	S-1	9-30-2019	4.4	
4.5	Note Purchase Agreement, dated May 7, 2019, by and among the Registrant and the other parties party thereto, as amended	S-1/A	10-15-2019	4.5	
4.6	Description of Registered Securities				X
10.1#	Phathom Pharmaceuticals, Inc. 2019 Equity Incentive Plan	S-1	9-30-2019	10.1	
10.2#	Form of Stock Option Grant Notice and Stock Option Agreement under the Phathom Pharmaceuticals, Inc. 2019 Equity Incentive Plan	S-1	9-30-2019	10.2	
10.3#	Form of Restricted Stock Grant Notice and Restricted Stock Agreement under Phathom Pharmaceuticals, Inc. 2019 Equity Incentive Plan	S-1	9-30-2019	10.3	
10.4#	Phathom Pharmaceuticals, Inc. 2019 Incentive Award Plan and form of stock option grant notice and stock option agreement thereunder	S-1/A	10-15-2019	10.4	
10.5#	Form of Stock Option Grant Notice and Stock Option Agreement under the Phathom Pharmaceuticals, Inc. 2019 Incentive Award Plan	10-Q	8-6-2020	10.3	
10.6#	Form of Performance Share Unit Grant Notice and Performance Share Unit Agreement under Phathom Pharmaceuticals, Inc. 2019 Incentive Award Plan	10-Q	8-6-2020	10.4	
10.7#	Phathom Pharmaceuticals, Inc. 2019 Employee Stock Purchase Plan	S-1/A	10-15-2019	10.5	
10.8#	Non-Employee Director Compensation Policy	S-1/A	10-15-2019	10.6	
10.9#	Phathom Pharmaceuticals 2020 Bonus Plan	10-Q	5-12-2020	10.1	
10.10#	Letter Agreement, dated May 7, 2019, by and between Tadataka Yamada, M.D. and the Registrant	S-1	9-30-2019	10.7	

10.11#	Employment Letter Agreement, dated July 21, 2019, by and between David Socks and the Registrant	S-1	9-30-2019	10.8
10.12#	Amended and Restated Employment Letter Agreement, dated September 25, 2019, by and between Azmi Nabulsi, M.D., M.P.H. and the Registrant	S-1	9-30-2019	10.9
10.13#	Employment Letter Agreement, dated June 25, 2020, by and between Todd Branning and the Registrant	8-K	7-13-2020	10.1
10.14#	Form of Indemnification Agreement for Directors and Officers	S-1	9-30-2019	10.11
10.15†	License Agreement, dated May 7, 2019, by and between Takeda Pharmaceuticals Company Limited and the Registrant	S-1	9-30-2019	10.12
10.16	Loan and Security Agreement, dated May 14, 2019, by and among Silicon Valley Bank, WestRiver Innovation Lending Fund VIII, L.P. and the Registrant	S-1	9-30-2019	10.13
10.17	Amendment to the Loan and Security Agreement, dated March 11, 2020, by and among Silicon Valley Bank, WestRiver Innovation Lending Fund VIII, L.P. and the Registrant	10-Q	5-12-2020	10.2
10.18#	Employment Letter Agreement, dated August 29, 2019, by and between Terrie Curran and the Registrant	S-1	9-30-2019	10.14
10.19†	Commercial Supply Agreement, by and between Takeda Pharmaceuticals Company Limited and the Registrant, dated as of April 30, 2020	10-Q	8-6-2020	10.1
10.20†	Amendment No. 1 to Takeda License Agreement, dated September 21, 2020	10-K	3-30-2021	10.20
10.21†	Supply and Packaging Services Agreement, by and between Sandoz GmbH and the Registrant, dated December 30, 2020	10-K	3-30-2021	10.21
10.22	Amendment No. 1 to Commercial Supply Agreement by and between Takeda Pharmaceuticals Company Limited and the Registrant, dated as of December 1, 2020	10-K	3-30-2021	10.22
10.23	Second Amendment to the Loan and Security Agreement, dated March 11, 2021, by and among Silicon Valley Bank, SVB Innovation Credit Fund VIII, L.P. and the Registrant	10-Q	5-11-2021	10.1
10.24	Third Amendment to the Loan and Security Agreement, dated May 26, 2021, by and among Silicon Valley Bank, SVB Innovation Credit Fund VIII, L.P. and the Registrant	10-Q	8-10-2021	10.2

10.25#	Separation and Release Agreement dated June 4, 2021, between the Registrant and Todd Branning	10-Q	8-10-2021	10.3	
10.26†	Commercial Supply Agreement with Catalent Pharma Solutions, LLC entered into on July 2, 2021	10-Q	8-10-2021	10.4	
10.27#	Amended and Restated Non-Employee Director Compensation Policy	10-Q	8-10-2021	10.5	
10.28	Loan and Security Agreement, dated September 17, 2021, by and among Hercules Capital and the Registrant	10-Q	11-8-2021	10.1	
10.29	Warrant to purchase stock issued to Hercules Capital, dated September 17, 2021	10-Q	11-8-2021	10.2	
10.30†	First Amendment to the Supply and Packaging Services Agreement, by and between Sandoz GmbH and the Registrant, dated December 4, 2021				X
23.1	Consent of independent registered public accounting firm				X
24.1	Power of Attorney				X
31.1	Certification of Chief Executive Officer of Phathom Pharmaceuticals, Inc., as required by Rule 13a-14(a) or Rule 15d-14(a) under the Securities Exchange Act of 1934, as amended				X
31.2	Certification of Principal Financial Officer of Phathom Pharmaceuticals, Inc., as required by Rule 13a-14(a) or Rule 15d-14(a) under the Securities Exchange Act of 1934, as amended				X
32.1*	Certification of Chief Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
32.2*	Certification of Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
101.CAL	Inline XBRL Taxonomy Calculation Linkbase Document.				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	Inline XBRL Taxonomy Label Linkbase Document				X
101.PRE	Inline XBRL Presentation Linkbase Document				X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				X

# Indicates management contract or compensatory plan.

† Portions of this exhibit have been omitted for confidentiality purposes.

* These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this annual report to be signed on its behalf by the undersigned, thereunto duly authorized.

PHATHOM PHARMACEUTICALS, INC.

/s/ Terrie Curran
Terrie Curran
Chief Executive Officer

Date: March 1, 2022

Pursuant to the requirements of the Securities Exchange Act of 1934, this annual report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Terrie Curran **Terrie Curran**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2022
/s/ Anthony Guzzo **Anthony Guzzo**	Vice President and Chief Accounting Officer (acting Principal Financial Officer)	March 1, 2022
* **Michael F. Cola**	Director	March 1, 2022
* **Heidi Kunz**	Director	March 1, 2022
* **Asit Parikh, M.D., Ph.D.**	Director	March 1, 2022
* **David Socks**	Director	March 1, 2022
* **Mark Stenhouse**	Director	March 1, 2022

*By: /s/ Terrie Curran
Terrie Curran, Attorney-in-fact

Exhibit 4.6

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2021, Phathom Pharmaceuticals, Inc. ("we," "us" and "our") had one class of securities registered pursuant to Section 12 of the Securities Exchange Act of 1934, as amended: our common stock.

Description of Common Stock

General

The following description summarizes some of the terms of our common stock. Because it is only a summary, it does not contain all the information that may be important to you and is subject to and qualified in its entirety by reference to our amended and restated certificate of incorporation (the "certificate of incorporation"), and amended and restated Bylaws ("bylaws"), which are filed as exhibits to our most recent Annual Report on Form 10-K and are incorporated by reference herein. We encourage you to read our certificate of incorporation and our bylaws for additional information.

As of December 31, 2021, our authorized capital stock consisted of 400,000,000 shares of common stock, $0.0001 par value per share, and 40,000,000 shares of preferred stock, $0.0001 par value per share.

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we may issue may be entitled to elect. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our amended and restated certificate of incorporation and amended and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our amended and restated certificate of incorporation.

Dividend Rights

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared by the board of directors out of legally available funds.

Liquidation Rights

In the event of our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding.

Rights and Preferences

Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock.

Fully paid and nonassessable

The outstanding shares of common stock are duly authorized, validly issued, fully paid and nonassessable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

The Nasdaq Global Market Listing

Our common stock is listed and traded on the Nasdaq Global Select Market under the ticker symbol “PHAT.”

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares. These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids.

These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 40,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board of directors, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our amended and restated certificate of incorporation provides that no member of our board of directors may be removed from office except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our amended and restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum under Delaware statutory or common law for: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders, creditors or other constituents; (iii) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our amended and restated certificate of incorporation or amended and restated bylaws; (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (v) any action asserting a claim governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934 (the "Exchange Act"), or any other claim for which the federal courts have exclusive jurisdiction.

In addition, our bylaws provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended (the "Securities Act"). Our certificate of incorporation and bylaws each provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision.

While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. We note that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least two thirds of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board of directors and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THIS EXHIBIT BECAUSE IT IS NOT MATERIAL AND WOULD LIKELY CAUSE COMPETITIVE HARM TO THE REGISTRANT IF PUBLICLY DISCLOSED. THE OMISSIONS HAVE BEEN INDICATED BY "[***]."

Exhibit 10.30

1st AMENDMENT
TO THE SUPPLY AND PACKAGING SERVICES AGREEMENT DATED DECEMBER 30, 2020

This first addendum (the "**First Amendment**") is made on the date of the last signature of the Parties below (the "**First Amendment Effective Date**")

BETWEEN

(1) **Sandoz GmbH**, a limited liability company organized and existing under the laws of Austria, registered with the commercial register of the district court (*Landesgericht*) Innsbruck under FN 50587v, with its registered address at Biochemiestrasse 10, 6250 Kundl, Austria ("**Supplier**"); and

(2) **Phathom Pharmaceuticals, Inc,** a corporation validly existing under the laws of the State of Delaware, located at 2150 E. Lake Cook Road, Suite 800, Buffalo Grove, IL 60089, U.S. ("**Customer**").

WHEREAS:

(A) Supplier and Customer have entered into a Supply and Packaging Services Agreement on December 30, 2020 (the "**Agreement**"), by which Customer has entrusted Supplier to supply certain bulk products and to perform certain packaging services relating to certain proprietary pharmaceutical products. Capitalized terms used and not otherwise defined herein shall have the meaning given to them in the Agreement.

(B) The Parties now desire to extend the scope of the agreement to the Additional Product (as defined below), as foreseen in Section 1.7 of the Agreement.

NOW, THEREFORE, in consideration of the mutual covenants and agreements set forth herein the Parties hereby agree as follows:

1. CHANGES TO THE MAIN BODY OF THE AGREEMENT

The main body of the Agreement is hereby amended as follows (changed or new wording in italics):

1.1 The last sentence of **Clause 1.2** is changed as follows:

Supplier Bulk Supply and Packaging Services shall be subject to one single ordering and invoicing mechanism for *each* Final Product.

1.2 The first paragraph of **Clause 1.3** is changed as follows:

Bulk Products. The bulk products to be packaged under this agreement are

- *For the Original Product:* Clarithromycin 500 mg FCT, Amoxicillin 500 mg HGC and Vonoprazan 20 mg FCT*; and*
- *For the Additional Product: Vonoprazan 20 mg FCT and Amoxicillin 500 mg HGC*

(jointly referred to as "Bulk Products" and each of them a "Bulk Product").

1.3 The first sentence of **Clause 1.6** is hereby changed as follows:

Phases of Cooperation. The cooperation of the Parties hereunder shall go through two (2) phases *for each the Original Product and the Additional Product:*

1.4 **Clause 1.7** is changed as follows:

Extension of Scope. The cooperation of the Parties shall in the first instance be limited to Packaging Services and other services related to the Final Products to be marketed in the Territory. However, Customer intends potentially to launch the Final Products in other regions. In case of such additional launches the scope of this Agreement shall be extended, and the terms modified, solely to the extent necessary to address such expanded scope.

1.5 The first sentence of **Clause 2.3** is changed as follows:

Further Implementation Services. In addition to the Set-up Activities covered by the LoI, Supplier shall provide the following services, as further specified in **Annex 3 (Further Im-plementation Services)**, *in relation to the Original Product* (the "**Further Implementation Services**"):

1.6 The following **new Clause 2.5** is added to the Agreement:

Additional Implementation Services. *In addition to the Set-up Activities covered by the LoI and the Further Implementation Services, Supplier shall provide the following services, as further specified in* ***Annex 3a (Additional Implementation Services)****, in relation to the Additional Product (the "****Additional Implementation Services****"):*

a) Procurement of Additional Equipment for Packaging Line and the Additional Product;

b) Installation & Operational Qualification Dual Pack and Sample Manufacturing; and

c) Sample Manufacturing Triple Pack.

1.7 The following **new Clause 2.6** is added to the Agreement:

Additional Implementation Fees. *For the performance of the Additional Implementation Services, Customer shall pay to Supplier the following service fees (the "****Additional Implementation Fees****" and each of them an "****Additional Implementation Fee****"):*

Work Package	***Fee***	***Invoice Date***
Procurement of Additional Equipment for Packaging Line and the Additional Product	**[***]**	**[***]**
Installation & Operational Qualification Dual Pack and Sample Manufacturing *Sample Manufacturing Triple Pack*	**[***]**	**[***]**

Upon **[***]**, *Supplier shall issue invoices for the Additional Implementation Fees. Clauses 6.3-6.7 shall apply mutatis mutandis.*

1.8 **Existing Clause 2.5** is now changed to **Clause 2.7** and changed as follows:

Timeline. The Parties intend that all Set-up Activities *relating to the Original Product and the Additional Product* shall be completed by end of **[***]**, except for *(i)* the *validation of the packaging*

process which shall be completed no later than **[***]**, *and (ii)* stability study which shall have an overall duration of **[***]**. In the event that any Set-up Activities cannot be successfully performed and completed in such timeline, the Parties shall promptly meet to discuss, *in good faith*, a path forward.

1.9 The first sentence of **Clause 3.1** is changed as follows:

Commencement. Upon completion of the Set-up Activities (except for the stability study) *for the Original Product and the Additional Product, respectively,* and subject to payment of the Implementation Fees *or the Additional Implementation Fees*, Supplier shall provide the Packaging Services and Deliver *the relevant* Final Products to Customer and its Affiliates throughout the remaining Term.

1.10 Clause 3.7 is changed as follows:

Purchase Obligation. Unless this Agreement is terminated or expires earlier, Customer shall source its and its Affiliates' entire demands for *each* Final Product and for Supplier Provided Bulk Products, in each case for sale during the Exclusive Purchase Period in the Territory, exclusively from Supplier and/or Supplier-designated Affiliate for a period of **[***]** (the "**Exclusive Purchase Period**") and Customer shall not, either directly or indirectly, during the Exclusive Purchase Period in the Territory, sell Final Product and/or Supplier Provided Bulk Products sourced from any party other than Supplier.

1.11 The first sentence of **Clause 5.1** is changed as follows:

Rolling Monthly Forecasts. Within the first **[***]** of each calendar month during the Term of this Agreement, Customer shall provide Supplier with a **[***]** rolling forecast (the "**Forecast**") of its requirements of *each Final* Product.

1.12 Clause 5.5 is changed as follows:

Minimum Capacity. Supplier shall at all times during the Manufacturing Phase maintain an annual minimum capacity for the provision of Packaging Services, *depending on the applicable cumulative Forecast volume for the Final Products (Original Product plus Additional Products)*, as specified in the following chart:

Forecast Volume	Minimum Capacity (as a % of Forecast)
[***]	**[***]**
[***]	**[***]**

1.13 Sentences 1 and 2 of **Clause 5.6** are changed as follows:

Order Quantities. Each Order shall be for full batches of *each* Final Product, and Supplier shall not be required to accept Orders for lesser quantities than specified in **Annex 5 (Packaging Process)**. In the event that Customer wishes to order a quantity of *a* Final Product of less than the Minimum Order Quantities or minimum batch sizes, Customer shall specify such quantity in an Order and Supplier shall notify Customer within **[***]** of receipt of any such Order of the revised price for the Final Product to reflect the increased costs to Supplier of producing smaller quantities.

1.14 Clause 5.7 is changed as follows:

Minimum Purchase Quantity. Customer shall, during each of **[***]**, place Orders for at least the following volumes of the Final Products (the "**Minimum Purchase Quantities**" and each of them a "**Minimum Purchase Quantity"**):

Calendar Year of Delivery	**Minimum Purchase Quantity**
[***]	**[***]**
[***]	**[***]**
[***]	

The Minimum Purchase Quantities for later Launch Years shall be mutually agreed by the Parties at least **[***]** prior to the end of **[***]**. In case the Parties fail to reach an agreement by such date, each Party may terminate this Agreement on **[***]** prior written notice.

In case Customer fails to order the agreed Minimum Purchase Quantity in a given Launch Year, Customer shall pay to Supplier the difference between the respective aggregated Price (plus VAT) of (i) the quantity of Final Products actually ordered by Customer from Supplier during such Launch Year and (ii) the respective Minimum Purchase Quantity, unless such failure is directly caused by an act or omission solely attributable to Supplier. **[***].**

1.15 **Clause 7.2(c)** is changed as follows:

The artwork, advertising and packaging information relating to *each* Final Product; and

1.16 **Clause 10.5** is changed as follows:

Product Recalls. The rules on recalls of *Final* Products are set out in the Quality Agreement.

1.17 The first sentence of **Clause 13.**1 is changed as follows:

Term. This Agreement shall come into effect on the Effective Date *(for the Original Product) and the First Amendment Effective Date (for the Additional Product)* and shall continue in force for a fixed term of five (5) years following Launch *for the first Final Product*, unless terminated earlier in accordance with its terms (the "**Initial Term**").

1.18 **Clause 13.**2 is changed as follows:

Termination due to Material Breach. Upon failure of any Party to remedy its material breach of any of its obligations under this Agreement (where remediable) on or before **[***]** after receipt of written notice of said breach from the other Party the Par-ty giving such notice shall have the right but not the obligation to terminate this Agreement *, on a product-by-product basis for the affected Final Product(s)*, immediately (or such longer period of time as such Party shall determine) by written notice. In respect of a material breach which is not capable of remedy, the non-defaulting Party shall have the right, but not the obligation, to terminate this Agreement, *on a product-by-product basis for the affected Final Product(s)*, immediately by written notice on the defaulting Party.

2. CHANGES TO ANNEXES

2.1 The following definitions are hereby added or amended in **Annex 1 – Definitions and Interpretation** (new wording in italics):

"Additional Implementation Fees" *has the meaning given to such term in Clause 2.6.*

"Additional Implementation Services" *has the meaning given to such term in Clause 2.5.*

"Additional Product" means *the* pharmaceutical product in final packaged form (including with package leaflet and instructions for use) containing Customer Provided Bulk Products and Amoxicillin 500 mg HGC, and meeting *the specifications laid down in Annex 5 and/or* other specifications mutually agreed upon by the Parties *in writing.*

"Agreement" means *the* Supply and Packaging Services Agreement *between the Parties dated December 30, 2020 as amended by the First Amendment*.

"Final Product" means *the Original Product and/or the Additional Product*.

***"First Amendment"** means the first amendment of the Agreement, by which the scope of the Agreement is essentially extended to the Additional Product.*

***"First Amendment Effective Date"** means the date of the last signature of the Parties of the First Amendment.*

"Launch" means, *on a product by product basis*, the first *delivery* of the *respective* Final Product in the Territory *by Supplier* to *Customer*.

"Launch Year" means, *on a product by product basis*, each twelve (12) month period commencing upon Launch of the *respective* Final Product. The first 12-month period following Launch shall be referred to as **"Launch Year 1",** the second 12-month period following Launch shall be referred to as **"Launch Year 2",** etc.

***"Original Product"** means the pharmaceutical product in final packaged form (including with package leaflet and instructions for use) containing Customer Provided Bulk Products, Clarithromycin 500 mg FCTs and Amoxicillin 500 mg HGC, and meeting the specifications laid down in Annex 5 and/or other specifications mutually agreed upon by the Parties in writing.*

2.2 A new **Annex 3a (Additional Implementation Services**) as attached hereto is added to the Agreement.

2.3 In **Annex 4 (Bulk Specifications)** the term "Finished Product" is replaced by the term "Final Product".

2.4 **Annex 5 (Packaging Process) and Annex 6 (Prices)** are amended as indicated in the changed versions of this Agreement as attached hereto (changed or added wording in italics).

3. MISCELLANEOUS

3.1 The Parties agree that the Quality Agreement will be amended to reflect the extension of the Agreement to the Additional Product.

3.2 This First Amendment shall be effective as of the First Amendment Effective Date. It shall become an integral part of the Agreement, to which it shall be incorporated for all purposes. Except as otherwise expressly modified by this Amendment, the Agreement shall remain in full force and effect in accordance with its terms.

3.3 Both Parties hereby warrant that they have the full and necessary legal capacity to enter into and execute this Amendment. The signatories of this amendment expressly declare and confirm that they have sufficient representation rights to enter into and execute this Amendment on behalf of the Party which they represent.

3.4 No modifications, amendments or supplements to the Agreement and/or this First Amendment shall be effective for any purpose unless in writing signed by both Parties, whereby electronic signatures, whether digital or encrypted, of the Parties are intended to fulfil this writing requirement and to have the same force and effect as manual signatures.

3.5 For simplicity, a consolidated version of the Agreement, incorporating all changes under this First Amendment, is attached hereto as **Schedule 1** (changed or added wording in italics).

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Parties have signed this Agreement on the dates set out below:

For and on behalf of **Sandoz GmbH**	**For and on behalf of** **Phathom Pharmaceuticals, Inc**
Signature:_____	**Signature: /s/ Jay Buchanan**
Name: [***]	**Name: Jay Buchanan**
Title: [***]	**Title: Vice President, Manufacturing and Supply Chain**
Date: [***]	**Date: December 4, 2021**

For and on behalf of **Sandoz GmbH**	**For and on behalf of** **Phathom Pharmaceuticals, Inc**
Signature:_____	**Signature: /s/ Larry Miller**
Name: [***]	**Name: Larry Miller**
Title: [***]	**Title: General Counsel**
Date: [***]	**Date: December 4, 2021**

Attachments:

- Annex 3a – Additional Implementation Services (new)
- Annex 5 – Packaging Process (amended)
- Annex 6 – Prices
- Schedule 1 – Consolidated Version of the Agreement

Annex 3a

ADDITIONAL IMPLEMENTATION SERVICES

[***]

Annex 5

PACKAGING PROCESS

Original Product - Specifications:

[***]

Additional Product - Specifications:

[***]

Process Flow Chart: *Original Product*

[***]

Process Flow Chart: Additional Product:

[***]

Annex 6

PRICES

Product Price and MOQ – *Original Product:*

[***]

Product Price and MOQ – Additional Product:

[***]

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-234357) pertaining to the 2019 Equity Incentive Plan, 2019 Incentive Award Plan, and 2019 Employee Stock Purchase Plan of Phathom Pharmaceuticals, Inc., and

(2) Registration Statement (Form S-3 No. 333-250014) of Phathom Pharmaceuticals, Inc.;

of our report dated March 1, 2022, with respect to the financial statements of Phathom Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Phathom Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young

Iselin, New Jersey
March 1, 2022

Exhibit 24.1

LIMITED POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person or entity whose signature appears below constitutes, designates and appoints each of Terrie Curran and Larry Miller, each of whom are officers of Phathom Pharmaceuticals, Inc. (the "Company"), as its true and lawful attorneys-in-fact and agent, each with power of substitution, with full power to act without the other and on behalf of and as attorney for me, for the purpose of executing and filing with the Securities and Exchange Commission the Company's Annual Report on Form 10-K for the year ended December 31, 2021, and any and all amendments thereto, and to do all such other acts and execute all such other instruments which said attorney may deem necessary or desirable in connection therewith.

Signature	**Title**	**Date**
/s/ Michael Cola Michael Cola	Director	February 25, 2022
/s/ Heidi Kunz Heidi Kunz	Director	February 24, 2022
/s/ Asit Parikh Asit Parikh	Director	February 24, 2022
/s/ David Socks David Socks	Director	February 24, 2022
/s/ Mark Stenhouse Mark Stenhouse	Director	February 24, 2022

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Terrie Curran, certify that:

1. I have reviewed this Annual Report on Form 10-K of Phathom Pharmaceuticals, Inc.

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in exchange act rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

/s/ Terrie Curran
Terrie Curran
Chief Executive Officer and President
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Anthony Guzzo, certify that:

1. I have reviewed this Annual Report on Form 10-K of Phathom Pharmaceuticals, Inc.

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in exchange act rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

/s/ Anthony Guzzo

Anthony Guzzo

Vice President and Chief Accounting Officer (acting Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO

18 U.S.C. SECTION 1350

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Phathom Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Terrie Curran, as Chief Executive Officer of the company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 1, 2022

/s/ Terrie Curran
Terrie Curran
Chief Executive Officer and President

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.

Exhibit 32.2

CERTIFICATION PURSUANT TO

18 U.S.C. SECTION 1350

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Phathom Pharmaceuticals, Inc. (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Anthony Guzzo, as Principal Financial Officer of the company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to my knowledge, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 1, 2022

/s/ Anthony Guzzo

Anthony Guzzo
Vice President and Chief Accounting Officer (acting Principal Financial Officer)

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.