Phathom Pharmaceuticals Announces Positive Topline Results from Phase 2 Trial Evaluating Vonoprazan for Non-Erosive Gastroesophageal Reflux Disease (NERD)

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- *Vonoprazan met the primary endpoint for all three dose levels (10 mg, 20 mg, 40 mg) taken on-demand, demonstrating faster and sustained relief of episodic heartburn as compared to placebo (p<0.0001)*
- *Phathom has commenced a Phase 3 NERD development program with the initiation of a pivotal Phase 3 vonoprazan daily dosing trial and will discuss with FDA a pivotal Phase 3 vonoprazan on-demand trial*

FLORHAM PARK, N.J., Feb. 09, 2022 (GLOBE NEWSWIRE) -- Phathom Pharmaceuticals, Inc. (Nasdaq: PHAT), a biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal diseases, today reported positive topline results from PHALCON-NERD, a Phase 2 study evaluating three dose levels of vonoprazan (10 mg, 20 mg, and 40 mg) as an on-demand therapy for relief of episodic heartburn in subjects with non-erosive gastroesophageal reflux disease (NERD). In this double-blind, placebo-controlled study, all three vonoprazan dose levels successfully met the primary endpoint and were statistically significant (p<0.0001) when compared to placebo.

The primary endpoint evaluated the percentage of heartburn episodes completely relieved within three hours ("complete relief") with relief sustained for over 24 hours ("sustained relief"). 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[1], respectively, as compared to 27.3% of episodes for placebo.

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

"We believe the data from this Phase 2 study are very encouraging for the treatment of NERD, a highly prevalent gastroesophageal disease which often presents itself with episodic heartburn," said Azmi Nabulsi, MD, Phathom's Chief Operating Officer. "These results support the potential of vonoprazan to transform the treatment of patients with NERD by offering much needed flexibility in the management of their NERD heartburn symptoms via preventative daily dosing or on-demand dosing."

Vonoprazan was generally well tolerated in the trial. In both phases of the trial, no adverse event was reported in more than three percent of the participants in a treatment group. There were total of four serious adverse events (SAEs) observed in the daily dosing phase and none 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.

Based upon these encouraging results, today Phathom announced that it has initiated NERD-301, a Phase 3 study evaluating vonoprazan 10 mg and 20 mg as daily dosing (QD) therapy for the treatment of NERD. Phathom expects to report topline results from NERD-301 in 2023. In addition, based on the positive Phase 2 on-demand data, Phathom also plans to discuss with the U.S. Food and Drug Administration (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 proton pump inhibitors (PPIs).

"We are incredibly excited about the PHALCON-NERD results that further highlight vonoprazan's rapid, potent and durable clinical profile. We believe today's results support the potential of vonoprazan to provide patients with two effective options to treat NERD – as preventative therapy when taken daily and as a rapid relief agent when dosed on-demand," said Terrie Curran, Phathom's President and CEO. "Patients with NERD represent approximately 70% of the estimated 65 million people living with GERD in the U.S. If successful, our Phase 3 NERD development program will provide a much-needed novel therapy and treatment options for a disease that has not seen therapeutic innovation in over 30 years."

Phathom plans to present the full results from this Phase 2 study at a future medical meeting.

PHALCON-NERD-201 study design

In this Phase 2 multi-site study conducted in the U.S., there were two separate phases. The daily dosing phase consisted of a four-week open-label run-in period where 458 participants with symptomatic NERD received vonoprazan 20 mg once daily ("QD") for up to four weeks. Participants recorded their heartburn symptoms during the run-in period using a twice daily electronic diary. Participants who had no heartburn on the last seven days of the run-in period and had complied with study drug and diary completion compliance requirements were randomized 1:1:1:1 to the on-demand phase of the trial.

The six-week on-demand phase consisted of four blinded study arms (n=207): vonoprazan 10 mg, vonoprazan 20 mg, vonoprazan 40 mg, and placebo comparator. Participants in the on-demand phase were instructed to take test medication at the onset of a heartburn episode and record their symptoms in an electronic diary over the following three hours. Participants were advised to refrain from taking rescue medication during the first three hours. Any additional heartburn episodes occurring up to 24 hours after study drug administration were also captured.

Data Table

Primary Endpoint – Complete and sustained relief within three hours

Dose	Number of evaluable heartburn episodes	% with complete and sustained heartburn relief within three hours	P-value

Placebo	370	27.3%	NA
Vonoprazan 10 mg	359	56.0%	p<0.0001
Vonoprazan 20 mg	327	60.6%	p<0.0001
Vonoprazan 40 mg	323	70.0%	p<0.0001

About Non-Erosive Gastroesophageal Reflux Disease (NERD)

NERD is the largest subcategory of gastroesophageal reflux disease (GERD) and is characterized by reflux-related symptoms in the absence of esophageal mucosal erosions. There are over 65 million U.S. patients living with GERD, and it is estimated that approximately seventy percent (70%) of this population have NERD. Symptoms of NERD impact overall quality of life and can include episodic heartburn, especially at night, regurgitation, problems swallowing, and chest pain.

About Vonoprazan

Vonoprazan is an investigational, oral small molecule potassium-competitive acid blocker (P-CAB). P-CABs are a novel class of medicines that block acid secretion in the stomach. Vonoprazan has shown the potential to have rapid, potent, and durable anti-secretory effects as a single agent in the treatment of gastroesophageal reflux disease (GERD) and in combination with antibiotics for the treatment of Helicobacter pylori (*H. pylori*) infection. The FDA has awarded qualified infection disease product (QIDP) status and granted Fast Track designation to vonoprazan in combination with both amoxicillin and clarithromycin and with amoxicillin alone for the treatment of *H. pylori* infection. Phathom submitted new drug applications in September 2021 to the U.S. FDA for vonoprazan-based regimens for the treatment of *H. pylori* infection. Phathom in-licensed the U.S., European, and Canadian rights to vonoprazan from Takeda, which completed 19 Phase 3 trials for vonoprazan and received marketing approval in Japan and numerous other countries in Asia and Latin America.

About Phathom

Phathom Pharmaceuticals is a biopharmaceutical company focused on the development and commercialization of novel treatments for gastrointestinal diseases and disorders. Phathom has in-licensed the exclusive rights in the United States, Europe, and Canada to vonoprazan, a novel potassium competitive acid blocker (P-CAB) in late-stage development for the treatment of acid-related disorders. For more information about Phathom, visit the Company's website at www.phathompharma.com or follow the Company on social media: LinkedIn at www.linkedin.com/company/phathompharma and Twitter @PhathomPharma.

Forward Looking Statement

Phathom cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. These statements are based on the Company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding the date of topline data from the Company's Phase 3 trial evaluating vonoprazan as daily dosing therapy for the treatment of NERD. The inclusion of forward-looking statements should not be regarded as a representation by Phathom that any of its plans will be achieved. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in Phathom's business, including, without limitation: reported top-line data is based on preliminary analysis of key efficacy and safety data is subject to more audit and verification procedures that could result in material changes in the final data; we may experience delays submitting the NDA including in the event that the FDA does not agree with the Company's interpretation of the data or feedback from the FDA that may be inconsistent with feedback received at prior meetings with the FDA; Phathom's ability to access additional capital under the term loan facility is subject to certain conditions including verification by the lender that the clinical milestone has been met; Phathom's dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of vonoprazan that may limit its development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; Phathom's QIDP and Fast Track designations may be withdrawn or not actually lead to a faster development or regulatory review or extended exclusivity, and would not assure FDA approval of vonoprazan; Phathom's ability to obtain and maintain intellectual property protection for vonoprazan; Phathom's ability to comply with its license agreement with Takeda; Phathom's ability to maintain undisrupted business operations due to the ongoing spread of the COVID-19 coronavirus, including delaying or otherwise disrupting its clinical trials, manufacturing and supply chain, and other risks described in the Company's prior press releases and the Company's filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in the Company's Annual Report on Form 10-K and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Phathom undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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[1] Evaluable heartburn episode is a heartburn episode for which the participant completes a minimum of one timed assessment after taking study medication.