Phathom Pharmaceuticals Announces Positive Topline Results from Pivotal Phase 3 Trial of Vonoprazan in Helicobacter pylori (H. pylori) Infection; Study Met All Primary and Secondary Endpoints

April 29, 2021

- Both vonoprazan-based treatment regimens demonstrated superior eradication rates vs. a standard of care proton pump inhibitor (PPI)-based triple therapy
- New Drug Application (NDA) submissions targeted for Q4 2021
- Phathom to host conference call and live webcast today, April 29, 2021 at 4:30 pm ET

FLORHAM PARK, N.J., April 29, 2021 (GLOBE NEWSWIRE) -- Phathom Pharmaceuticals, Inc. (Nasdaq: PHAT), a late clinical-stage biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal diseases, announced today that in PHALCON-HP, its 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 in combination with amoxicillin and clarithromycin ("vonoprazan triple therapy") and vonoprazan in combination with amoxicillin ("vonoprazan dual therapy") compared to lansoprazole in combination with amoxicillin and clarithromycin ("lansoprazole triple therapy"). PHALCON-HP is the largest Phase 3 registration trial ever conducted in *H. pylori* infection, randomizing 992 patients with confirmed *H. pylori* infection.

Phase 3 Topline Results

Primary endpoint analysis
The primary endpoints in the PHALCON-HP study were non-inferiority of the *H. pylori* eradication rate for each of vonoprazan triple and dual therapy compared to lansoprazole triple therapy. Based on U.S. Food and Drug Administration (FDA) feedback, the primary endpoint excluded patients with amoxicillin or clarithromycin resistant strains of *H. pylori*.

Both vonoprazan-based regimens successfully met their primary endpoints. In the modified intent-to-treat (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).

Additional efficacy analyses were conducted using the pre-specified per protocol population, a subset of the mITT population comprised of patients who were protocol compliant as defined by FDA draft Guidance for Industry[1]. 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, demonstrating 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%; $p<0.0001$).

"Acid suppression is a key factor in addressing shortcomings associated with currently available *H. pylori* treatments, especially in light of increased resistance to antibiotics, including clarithromycin," said Professor William D. Chey, M.D., AGAF, FACG, FACP, Professor of Medicine and Director of the GI Physiology Laboratory at the University of Michigan. "I am very impressed with the results of PHALCON-HP which demonstrate that replacing a PPI with vonoprazan in *H. pylori* treatment regimens has the potential to meaningfully enhance eradication rates that have been declining over the last two decades. Further, the potential to limit the use of clarithromycin with a dual therapy regimen has the potential to transform clinical practice."

Safety profile
Both vonoprazan-based regimens were generally well tolerated with a safety profile comparable to 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%), nausea (1.7%, 1.7% and 2.6%), headache (2.6%, 1.4%, 1.4%) and vaginal infections (2.3%, 0.9%, 0.3%). 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 1.4% for lansoprazole triple therapy-treated patients.

Full results from the PHALCON-HP study will be presented at a future medical meeting and submitted for publication in a peer-reviewed journal.

"We believe the topline results of our PHALCON-HP study support the potential of vonoprazan-based therapies to change *H. pylori* treatment," said Terrie Curran, Phathom's President and Chief Executive Officer. "There are estimated to be over 200 million people infected with *H. pylori* in the United States and Europe, and our market research among patients and physicians show antibiotic resistance, coupled with complexity of treatment, as leading causes of eradication failure. Based on these results, which further build on the robust data previously reported from clinical studies of vonoprazan-based regimens in Japan, we plan to submit NDAs with the FDA for vonoprazan dual and triple therapy in *H. pylori* before the end of the year. Phathom thanks all the patients, physicians, and clinical sites for their role in the PHALCON-HP trial and for helping in our efforts to advance the treatment landscape for the millions of patients suffering with *H. pylori* infection."

Conference call on the PHALCON-HP trial results
Phathom will host a webcasted conference call today, Thursday, April 29, 2021 at 4:30 pm ET to discuss the PHALCON-HP study results.

To view the live webcast, visit https://investors.phathompharma.com/news-events/events-and-presentations. Please join approximately 10 minutes prior to the scheduled start time.

A replay of the webcast and the slide presentation will be available after the meeting on the News & Events section of the Phathom website at https://investors.phathompharma.com/news-events/events-and-presentations.

About Helicobacter pylori (*H. pylori*) infection
H. pylori is a bacterial pathogen that is estimated to infect over 200 million individuals in the United States and Europe. Approximately 50% of the world and 36% of the US population are infected with the bacterium.[2] In many cases, *H. pylori* is acquired in childhood and through intrafamilial transmission.[3] As a result of the chronic inflammation induced by *H. pylori* infection, infected patients develop a range of pathologies including dyspepsia, peptic ulcer disease, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma.[4] Studies have found that roughly 1 in 5 patients treated for *H. pylori* will fail first line therapy when using standard clarithromycin triple therapy.[2,5]

About PHALCON-HP
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 20 mg administered twice a day (BID) and amoxicillin 1g administered three times a day (TID) (n=324); vonoprazan 20 mg BID, amoxicillin 1g BID and clarithromycin 500 mg BID (n=338); and lansoprazole 30 mg BID, amoxicillin 1g BID and clarithromycin 500 mg BID (n=330). Each treatment regimen was administered for 14 days. Diagnoses of infection and test of cure were confirmed by 13C-urea breath test. Additional efficacy analyses were conducted using the pre-specified per protocol population (n=822), a subset of the mITT population comprised of patients who were protocol compliant.

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 Fast Track designation to vonoprazan in combination with both amoxicillin and clarithromycin and with amoxicillin alone 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 Statements
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 expected submission of New Drug Applications for the eradication of *H. pylori* infection; and the potential for vonoprazan-based therapies to meaningfully enhance *H. pylori* eradication rates, limit the use of clarithromycin, and address shortcomings associated with currently available treatments. 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 NDAs 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 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 pending qualified infectious disease product (QIDP) requests may not be granted and previously granted 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] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/helicobacter-pylori-associated-duodenal-ulcer-disease-adults-developing-drugs-treatment

[2] Hooi et al. Gastroenterology. 2017;153:420.

[3] Chey et al. Am J Gastroenterol.2017;112:212.

[4] Malfertheiner et al. Gut. 2017;66:6.

[5] Alsamman et al. Dig Dis Sci. 2019;64:2893.