Phathom Pharmaceuticals Announces Positive Topline Results from PHALCON-EE Pivotal Phase 3 Erosive Esophagitis Trial

October 18, 2021

- Vonoprazan met its primary non-inferiority endpoints in both healing and maintenance phases
- Vonoprazan demonstrated superior healing rates in patients with moderate-to-severe disease at Week 2 versus lansoprazole (PREVACID®), a proton pump inhibitor (PPI)
- Vonoprazan demonstrated superior maintenance of healing in all patients and patients with moderate-to-severe disease versus lansoprazole at Week 24
- New Drug Application (NDA) submission planned for H1 2022 targeting the following indications: healing of all grades of erosive esophagitis (EE) and relief of heartburn, and maintenance of healing of all grades of EE and relief of heartburn
- Phathom to host conference call today, October 18, 2021, at 8:30 am ET

FLORHAM PARK, N.J., Oct. 18, 2021 (GLOBE NEWSWIRE) -- Phathom Pharmaceuticals, Inc. (Nasdaq: PHAT), a late clinical-stage biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal diseases, today announced that vonoprazan successfully met its primary endpoints and key secondary superiority endpoints in PHALCON-EE, a pivotal phase 3 trial evaluating vonoprazan versus lansoprazole for the treatment of erosive esophagitis. Based on the positive PHALCON-EE data, Phathom plans to submit an NDA to the U.S. Food and Drug Administration seeking the following indications: healing of all grades of EE and relief of heartburn, and maintenance of healing of all grades of EE and relief of heartburn.

“The PHALCON-EE results are a major milestone for Phathom and for the 20 million Americans suffering from erosive esophagitis. The results further solidify vonoprazan’s potential to be the first major innovation in the U.S. and European GERD market in more than 30 years,” said Terrie Curran, Phathom’s President and Chief Executive Officer. “The results demonstrated that vonoprazan is superior to a standard of care PPI across a broad range of clinically relevant endpoints in the study, importantly including the maintenance of healing erosions at 24 weeks for all EE patients. We are excited about the potential for vonoprazan to satisfy the large unmet needs of so many patients and set a new treatment paradigm in EE. We thank the patients, physicians, and clinical sites who participated in the PHALCON-EE study during the height of the COVID-19 pandemic, and we look forward to submitting an NDA and, if approved, making this treatment available for EE patients.”

Study Design

PHALCON-EE was a trial with two phases. In the first phase, vonoprazan 20 mg was compared to lansoprazole 30 mg in the healing of EE after up to 8 weeks of treatment (Healing Phase). 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, where vonoprazan 10 mg and 20 mg were compared to lansoprazole 15 mg to assess maintenance of healing via endoscopy following 24 weeks of treatment (Maintenance Phase). 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.

Study Results

Healing Phase

The primary endpoint 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 Healing Phase primary endpoint with a healing rate of 93% compared to 85% for lansoprazole ($p<0.0001$). In a preplanned exploratory superiority test, the difference between vonoprazan and lansoprazole was also significant ($p<0.0001$).[1]

Vonoprazan met the secondary superiority endpoint of healing in patients with moderate-to-severe disease[2] at Week 2, demonstrating significantly faster healing than lansoprazole (70% for vonoprazan 20 mg and 53% for lansoprazole 30 mg) ($p=0.0004$). 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 ($p=0.2196$). In additional secondary endpoint superiority

comparisons, vonoprazan 20 mg healing rates were numerically greater than lansoprazole 30 mg in all patients at Week 2 (p=0.0174)[3] and in moderate-to-severe patients[2] by Week 8 (p<0.0001)[3] although deemed nominally significant due to the sequential testing method.

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.

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 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[4] 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.

Safety profile
Overall, the safety results for vonoprazan observed in PHALCON-EE were consistent with the results observed in prior clinical studies.

The most common reported adverse event in the Healing Phase was diarrhea (2.1% for vonoprazan 20 mg and 2.5% for lansoprazole 30 mg). The most commonly reported adverse events in the Maintenance Phase (>5%) were COVID-19 infection (10.1% vonoprazan 20 mg, 6.1% vonoprazan 10 mg, 6.7% lansoprazole 15 mg), gastritis (2.7% vonoprazan 20 mg, 6.4% vonoprazan 10 mg, 2.7% lansoprazole 15 mg), and abdominal pain (5.4% vonoprazan 20 mg, 4.1% vonoprazan 10 mg, 2.4% lansoprazole 15 mg).

Frequency of serious adverse events (SAEs) in the Healing Phase were the same 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. COVID-19 infection was the only SAE reported in more than one patient per group. There were 7 COVID-19 SAEs across both phases of the study (5 on vonoprazan 20 mg and 2 on vonoprazan 10 mg). Two deaths occurred among the reported COVID-19 SAE cases. None of the COVID-19 SAEs were deemed related to the study drug by the investigator.

“Today’s results indicate an advancement in the treatment of erosive esophagitis,” said Loren Laine, M.D., Professor of Medicine and Chief, Digestive Diseases at Yale School of Medicine, and lead investigator of the PHALCON-EE study. “The PHALCON-EE data support vonoprazan as a novel potential alternative to PPIs to improve healing and reduce recurrence of erosions in patients with erosive esophagitis.”

Phathom plans to present the full results from the PHALCON-EE study at a medical meeting next year and submit them for publication in a peer-reviewed journal.

The positive PHALCON-EE data provides Phathom with access to an additional $50 million from its term loan facility with Hercules Capital. As of September 30, 2021, Phathom had approximately $225 million in available cash and cash equivalents, exclusive of the additional $50 million available from the term loan facility.

Detailed PHALCON-EE Topline Data

PHALCON-EE Topline Data					
Endpoints (Healing Phase) (n=1024*)		**Vonoprazan 20 mg (n=514)**	**Lansoprazole 30 mg (n=510)**	**P-Value (95%CI)**	
A	**% of all patients healed by Week 8**	93%	85%	p<0.0001[1] [p<0.0001][2]	
	Mean % of 24-hour heartburn free days over the healing period	67%	64%	-1.60, 7.03[5]	
	% of Grades C/D patients healed at Week 2	70%	53%	p=0.0004[3]	
	% of all patients with onset of sustained resolution of heartburn by Day 3	34%	32%	p=0.2196[3]	
	% of Grades C/D patients healed by Week 8	92%	72%	[p<0.0001][4]	
	% of all patients healed at Week 2	74%	68%	[p=0.0174][4]	
Endpoints (Maintenance of Healing)		**Vonoprazan 20 mg (n=291)**	**Vonoprazan 10 mg (n=293)**	**Lansoprazole 15 mg (n=294)**	**P-Value (95%CI) vono 20 mg v. lanso 15 mg**	**P-Value (95%CI) vono 10 mg v. lanso 15 mg**
A	**% of all patients maintained through Week 24**	81%	79%	72%	p<0.0001[1] p=0.0068[3]	p<0.0001[1] p=0.0218[3]
	% of Grades C/D patients maintained through Week 24	77%	75%	61%	p=0.0098[3]	p=0.0245[3]
	Mean % of 24-hour heartburn free days through Week 24	81%	81%	79%	-2.63, 6.72[5]	-2.27, 6.84[5]

A primary endpoint
[1] non-inferiority comparison for primary endpoints
[2] exploratory superiority comparison, nominal p value presented
[3] superiority comparison
[4] superiority comparison, not significant based on pre-specified testing hierarchy, nominal p value presented
[5] non-inferiority comparison, non-inferiority margin 15%

*****34.3% of the 1024 patients were classified as having LA Grades C/D erosions

Conference call on the PHALCON-EE trial results
Phathom will host a webcasted conference call today, October 18, 2021, at 8:30 am ET to discuss the PHALCON-EE study results.

To view the live webcast, visit https://investors.phathompharma.com/news-events/events-and-presentations. Please log in 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.

About Erosive Esophagitis
Erosive Esophagitis (EE) is a major type of gastroesophageal reflux disease (GERD) characterized by erosions in the gastric mucosa caused by acidic reflux of stomach contents into the esophagus. There are estimated to be over 65 million individuals with GERD in the U.S., of which approximately 30% have EE. In addition to experiencing troubling heartburn symptoms, patients with inadequately treated EE may progress to more severe diseases including Barrett's esophagus and esophageal cancer.

About PHALCON-EE
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. The first phase of the trial evaluated the efficacy and safety of vonoprazan 20 mg administered once-daily (QD) compared to lansoprazole 30 mg QD for the healing of EE for up to eight weeks. The second phase of the trial evaluated the efficacy and safety of vonoprazan 10 mg QD and 20 mg QD compared to lansoprazole 15 mg QD for the maintenance of healing of EE for 24 weeks. Both phases also evaluated heartburn symptoms.

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 infectious 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 NDAs in September 2021 to the 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 and follow the Company on LinkedIn and Twitter.

Forward Looking Statement
The financial results included in this press release are unaudited and preliminary estimates that (i) represent the most current information available to management as of the date of this press release, (ii) are subject to completion of financial closing and procedures that could result in significant changes to the estimated amounts, and (iii) do not present all information necessary for an understanding of Phathom's financial condition as of, or its results of operations for the quarter ended, September 30, 2021. Accordingly, undue reliance should not be placed on such preliminary estimates.

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 an NDA for healing and maintenance of healing of erosive esophagitis and heartburn symptom relief and the Company' ability to access capital under its term loan facility. 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] Exploratory superiority comparison, nominal p value presented

[2] Patients with moderate-to-severe disease relates to patients with esophageal erosions classified as Grades C or D by the Los Angeles (LA) Classification System

[3] Superiority comparison, not tested due to the pre-specified testing hierarchy, nominal p value presented

[4] Patients with moderate-to-severe disease in the Maintenance Phase refers to patients who entered the Healing Phase of PHALCON-EE with esophageal erosions classified as Grades C or D by the LA Classification System