Phathom Pharmaceuticals Presents Data on Novel Potassium-Competitive Acid Blocker (PCAB) Vonoprazan from a Range of Studies at Digestive Disease Week® (DDW) 2022

May 24, 2022

- Results from an investigational Phase 3 PHALCON-EE trial demonstrating superior healing at week 2 in patients with LA Grade C/D (moderate-to-severe) erosive esophagitis and superior maintenance of healing at week 24 in all patients with vonoprazan versus lansoprazole shared in oral presentation[1]
- Additional data showed greater acid suppression with vonoprazan than lansoprazole in healthy U.S. subjects[2]
- Insights from a claims database analysis of insured U.S. patients tested or treated for *Helicobacter pylori* (*H. pylori)* found sub-optimal diagnostic and treatment patterns despite guidelines[3]

FLORHAM PARK, N.J., May 24, 2022 (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 results from multiple studies evaluating the efficacy of vonoprazan were presented at Digestive Disease Week® (DDW) 2022, being held May 21-24 in person in San Diego, CA and virtually.

PHALCON-EE Study

In an oral presentation session, results from the PHALCON-EE study, an investigational Phase 3 registration trial evaluating vonoprazan compared to the proton pump inhibitor (PPI) lansoprazole in patients with erosive esophagitis (EE), will be shared by Loren Laine, M.D., Professor of Medicine, and Chief, Digestive Diseases at Yale School of Medicine, and lead investigator of the PHALCON-EE study.

Results of PHALCON-EE showed that vonoprazan, a novel potassium-competitive acid blocker (PCAB), demonstrated non-inferiority to the PPI lansoprazole in complete healing by week 8, the study's primary endpoint, and showed superiority in a prespecified, exploratory analysis. [1] In addition, vonoprazan demonstrated superior healing at week 2 in patients with Los Angeles (LA) Grade C/D EE and superior maintenance of healing in all patients with EE versus lansoprazole.[1] Patients with this classification are typically more difficult to treat and current available treatments may not provide complete resolution of esophageal erosions. The LA Classification categorizes EE from Grades A through D based on disease severity.[4]

"These data provide further insights from the PHALCON-EE study for the novel PCAB vonoprazan in a Western patient population, which had not been assessed previously," said Stuart J. Spechler, M.D., AGAF, FACG, co-director of the Center for Esophageal Diseases at Baylor University Medical Center in Dallas, Texas. "A significant proportion of patients with EE do not have complete resolution of erosion in the esophageal tissue with PPI therapy. The study's results demonstrate the potential of this new treatment class for all patients with EE and are particularly impressive in those with moderate-to-severe disease, who are at risk for serious complications if left untreated."

PHALCON-EE evaluated 1,024 *Helicobacter pylori* (*H. pylori)*-negative adults in the U.S. and Europe with EE who were randomized to receive vonoprazan 20 mg or lansoprazole 30 mg for up to eight weeks. The study's primary endpoints were percent healed by week 8 in the healing phase, and percent who maintained healing at week 24 in the maintenance phase.[1]

- *Healing phase*: vonoprazan was non-inferior to lansoprazole (92.9% vs. 84.6%, difference=8.3% [95% CI 4.5-12.2%]) by week 8.[1]
  - Vonoprazan was noninferior to lansoprazole in mean heartburn-free days, and superior in healing at week 2 in patients with Grade C/D esophagitis (p=0.0004).[1]
  - Higher rates of healing with vonoprazan were achieved at week 2 (difference=6.1% [95% CI 0.5-11.6%]) and in Grade C/D esophagitis by week 8 (difference=19.6% [11.8-27.6%]).[1]
- *Maintenance phase*: At week 24, both 20 mg and 10 mg doses of vonoprazan were non-inferior in maintenance of healing to lansoprazole 15 mg (80.7% vonoprazan 20 mg; 79.2% vonoprazan 10 mg; 72.0% lansoprazole 15 mg), (p=0.007 20 mg; p=0.022 10 mg).[1]
  - In a secondary endpoint, vonoprazan was superior to lansoprazole in patients with LA Grade C/D esophagitis; maintenance of

healing for Grade C/D esophagitis was greater with vonoprazan 20 mg (p=0.010) and 10 mg (p=0.025).[1]
- Mean heartburn-free days were non-inferior for vonoprazan vs. lansoprazole.[1]

“As the first head-to-head study of vonoprazan versus a traditional PPI therapy in Western patients, PHALCON-EE provides important confirmation about the potential of the PCAB treatment class for gastroenterologists and their patients,” said Azmi Nabulsi, M.D., Chief Operating Officer at Phathom. “Phathom recently submitted its new drug application in the U.S. for vonoprazan in EE based on the strength of the results from PHALCON-EE, and we’re optimistic that vonoprazan has the potential to be an important treatment option in the future for GERD patients.”

PK/PD Study
During the meeting, Dr. Laine also presented a poster on a Phase 1 study evaluating the pharmacodynamics (PD) and pharmacokinetics (PK) of vonoprazan and the PPI lansoprazole in 44 healthy U.S. subjects, which was selected as a Poster of Distinction by the American Gastroenterological Association (AGA) Institute. The primary PD endpoint was the mean 24-hour holding-time ratio for pH>4 (pH>4 HTR) on day 7. Other PD parameters included 24-hour HTR for pH>4 on day 1 and 24-hour mean intragastric pH on days 1 and 7.

- Vonoprazan had higher 24-hour HTR for pH>4 than lansoprazole on day 1 (62.4% vs. 22.6%, p<0.0001) and day 7 (87.8% vs. 42.3%, p<0.0001).[2]
- Mean 24-hour intragastric pH for vonoprazan was 4.6 vs. 2.8 for lansoprazole on day one, and 5.9 and 3.8, respectively, on day 7 (p<0.0001).[2]
  - Intragastric pH from 12-24 hours also was higher with vonoprazan than lansoprazole on day 1 (4.6 vs. 2.5, respectively) and day 7 (5.6 vs. 3.4, respectively). [2]
- The half-life was longer with vonoprazan than lansoprazole (7.9 vs. 1.4 hours) as measured on day one.[2]

Vonoprazan provided greater suppression of intragastric acidity than lansoprazole in the study.[2] This is the first study to evaluate PD and PK parameters for vonoprazan in Western subjects. Previously this data has been limited to patient populations primarily in Japan.

U.S. Claims Database Study
Also, during DDW, Dr. Shailja Shah, M.D., M.P.H., from the University of California San Diego presented a poster highlighting findings from an analysis of *Helicobacter pylori* (*H. pylori*) testing and treatment patterns in the U.S., which showed suboptimal treatment selection and post-treatment eradication testing, as well as inconsistent overall management of the disease compared to clinical guidelines; factors that could contribute to declining eradication rates.[3]

Researchers used the Veradigm Health Insights electronic medical record (EMR) database linked to Komodo claims data to evaluate *H. pylori*-coded diagnostic and treatment records over a four-year period from January 1, 2016 to December 31, 2019 for 60,593 insured patients. The analysis focused on 68.2% of patients who had one or more guideline-recommended *H. pylori* Eradication Regimens (HPER). Contrary to current guidelines, most patients (80.2%) received clarithromycin-based triple therapy as their first HPER and only 6.6% received bismuth-based quadruple therapy.[3] In addition, 88.9% of patients did not receive a second HPER.[3] Among patients with a second HPER, 53.4% received the same regimen as the first HPER.[3] Moreover, researchers found that only 67.4% of patients received a diagnostic *H. pylori* lab test after first-line therapy to confirm eradication.[3]

Following the conclusion of DDW 2022, the abstracts will be posted to Phathom’s publications and scientific section of the company website.

About VOQUEZNA TRIPLE and DUAL PAKs
VOQUEZNA TRIPLE PAK (vonoprazan, amoxicillin, clarithromycin) and VOQUEZNA DUAL PAK (vonoprazan, amoxicillin) contain vonoprazan, an oral small molecule potassium-competitive acid blocker (PCAB) co-packaged with antibiotics. PCABs are a novel class of medicines that block acid secretion in the stomach. Vonoprazan has shown the potential to provide acid suppression that can achieve pH levels that are important in enhancing antibiotic effectiveness. 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.

Indication and Important Safety Information
INDICATIONS AND USAGE
VOQUEZNA™ TRIPLE PAK™ is a co-packaged product containing vonoprazan, a potassium-competitive acid blocker (PCAB), amoxicillin, a penicillin-class antibacterial, and clarithromycin, a macrolide antimicrobial. VOQUEZNA™ DUAL PAK™ is a co-packaged product containing vonoprazan and amoxicillin. Both products are indicated for the treatment of *Helicobacter pylori* infection in adults.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of VOQUEZNA TRIPLE PAK, VOQUEZNA DUAL PAK and other antibacterial drugs, both products should be used only to treat or prevent infections that are proven or strongly suspected of being caused by bacteria.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK are contraindicated in patients with known hypersensitivity to vonoprazan or amoxicillin, any other components of the formulation, any other beta-lactams, or in patients receiving rilpivirine-containing products.

Due to the clarithromycin component, VOQUEZNA TRIPLE PAK is also contraindicated in patients with any known hypersensitivity to clarithromycin or any macrolide antibiotic, in patients receiving pimozide, lomitapide, lovastatin, simvastatin, ergotamine, dihydroergotamine, colchicine in patients with renal or hepatic impairment, or those with a history of cholestatic jaundice/hepatic dysfunction.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions: Serious and occasionally fatal reactions (e.g., anaphylaxis) have been reported with components of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK. If hypersensitivity reactions occur, discontinue use and institute immediate therapy (e.g., anaphylaxis management).

Severe Cutaneous Adverse Reactions (SCAR): Discontinue use of VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK at first signs or symptoms of SCAR or other signs of hypersensitivity and consider further evaluation. SCAR, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported with the components of both products. In addition, drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported with amoxicillin and clarithromycin.

Clostridioides difficile-associated diarrhea (CDAD): Evaluate if diarrhea occurs with VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK. CDAD has been reported with use of acid suppressing therapies and nearly all antibacterial agents, and may range in severity from mild diarrhea to fatal colitis. If CDAD is confirmed, discontinue therapy and treat appropriately.

VOQUEZNA TRIPLE PAK Warnings or Precautions Due to the Clarithromycin Component:
QT Prolongation: Avoid VOQUEZNA TRIPLE PAK in patients with known QT prolongation or receiving drugs known to prolong the QT interval, ventricular arrhythmia

(*torsades de pointes*), hypokalemia/hypomagnesemia, significant bradycardia, or taking Class IA or III antiarrhythmics.

Hepatotoxicity: Discontinue use of VOQUEZNA TRIPLE PAK if signs and symptoms of hepatitis occur.

Serious adverse reactions due to concomitant use with other drugs: Serious adverse reactions can occur with VOQUEZNA TRIPLE PAK due to drug interactions of clarithromycin with colchicine, some lipid lowering agents, some calcium channel blockers, hypoglycemic agents including insulin, quetiapine, warfarin, benzodiazepines, and other drugs.

Embryo-Fetal Toxicity: VOQUEZNA TRIPLE PAK is not recommended for use in pregnancy as clarithromycin may cause fetal harm.

Myasthenia Gravis: Exacerbation of myasthenia gravis can occur with VOQUEZNA TRIPLE PAK since it has been reported in patients receiving clarithromycin tablets.

ADVERSE REACTIONS
The most common adverse reactions (≥2%) include diarrhea, dysgeusia, vulvovaginal candidiasis, abdominal pain, headache, hypertension, and nasopharyngitis.

DRUG INTERACTIONS
Components of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK have the potential for clinically important drug interactions. See full Prescribing Information for important drug interactions.

USE IN SPECIFIC POPULATIONS
Lactation: Breastfeeding not recommended during treatment, but a lactating woman can pump and discard breast milk during treatment and for 2 days after VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK administration.

Geriatrics: VOQUEZNA TRIPLE PAK increased risk of *torsades de pointes* due to clarithromycin.

Renal and Hepatic Impairment: Avoid use in patients with severe renal impairment and avoid use in patients with moderate to severe hepatic impairment.

You are encouraged to report suspected adverse reactions by contacting Phathom Pharmaceuticals at 1-888-775-PHAT (7428) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information for VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK.

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.[5] There are estimated to be over 65 million individuals with GERD in the U.S., of which approximately 30% have EE.[6,7,8] 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.[5]

About DDW
Digestive Disease Week® (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW is an in-person and virtual meeting from May 21-24, 2022. The meeting showcases more than 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at www.ddw.org.

About Phathom Pharmaceuticals, Inc.
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 first-in-class potassium-competitive acid blocker (PCAB). Vonoprazan-based regimens are approved in the U.S. as part of a co-packaged product in combination with antibiotics for the treatment of *H. pylori* infection in adults, marketed as VOQUEZNA™ TRIPLE PAK™ (vonoprazan, amoxicillin, clarithromycin) and VOQUEZNA™ DUAL PAK™ (vonoprazan, amoxicillin). Phatho has submitted a New Drug Application to the FDA for vonoprazan in erosive esophagitis (EE) and is studying the use of vonoprazan for the treatment of non-erosive reflux disease (NERD). For more information about Phathom, visit the Company's website at www.phathompharma.com and follow the Company on LinkedIn and Twitter.

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 vonoprazan as monotherapy for the treatment of erosive esophagitis. 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: Phathom's ability to access additional capital under the term loan facility is subject to certain conditions; the inherent risks of clinical development of vonoprazan; 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 designations may not actually lead to extended exclusivity; 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.

MEDIA AND INVESTOR CONTACT
Nick Benedetto
1-877-742-8466
media@phathompharma.com
ir@phathompharma.com

---

1 Laine L et al. Double-Blind Randomized Trial of the Potassium-Competitive Acid Blocker Vonoprazan vs. the Proton Pump Inhibitor Lansoprazole in U.S. and European Patients with Erosive Esophagitis. Abstract presented at Digestive Disease Week 2022, May 21-24, 2022, San Diego, CA.

2 Laine L et al. Pharmacodynamics and Pharmacokinetics of the Potassium-Competitive Acid Blocker Vonoprazan and the Proton Pump Inhibitor Lansoprazole in Healthy U.S. Subjects. Abstract presented at Digestive Disease Week 2022, May 21-24, 2022, San Diego, CA.

3 Shah S et al. Diagnosis and treatment patterns among patients with helicobacter pylori infection in the United States: a linked EMR-claims database analysis. Abstract presented at Digestive Disease Week 2022, May 21-24, 2022, San Diego, CA.
4 Armstrong D, Bennett J R, Blum A L et al. The endoscopic assessment of esophagitis: a progress report on observer agreement.
Gastroenterology 1996; 111: 85–92.
5 Savarino E et al. The Natural History of Gastro-Esophageal Reflux Disease: A Comprehensive Review. *Dis Esophagus.* 2017;30(2):1-9. doi:10.1111/dote.12511.
6 El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut*. 2014;63(6):871-880. doi:10.1136/gutjnl-2012-304269.
7 Machicado J.D., Greer J.B., Yadav D. (2020) Epidemiology of Gastrointestinal Diseases. In: Pitchumoni C., Dharmarajan T. (eds) *Geriatric Gastroenterology*. Springer, Cham. https://doi.org/10.1007/978-3-319-90761-1_7-1.
8 U.S. Census Bureau. U.S. and World Population Clock. Accessed May 2022. https://www.census.gov/popclock.