Phathom Pharmaceuticals Presents New Data Evaluating First-in-Class Potassium-Competitive Acid Blocker (PCAB) Vonoprazan as Novel On-Demand Treatment in NERD at American College of Gastroenterology (ACG) 2022 Annual Scientific Meeting

October 23, 2022

FLORHAM PARK, N.J., Oct. 23, 2022 (GLOBE NEWSWIRE) -- Phathom Pharmaceuticals, Inc. (Nasdaq: PHAT), a biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal diseases and disorders, announced today that detailed results from an investigational Phase 2 study evaluating the efficacy of vonoprazan in non-erosive gastroesophageal reflux disease (NERD) and other data will be presented at the American College of Gastroenterology (ACG) 2022 Annual Scientific Meeting, being held October 21-26 in Charlotte, NC.

PHALCON-NERD On-Demand

In an oral plenary session during ACG, detailed results from the Phase 2 PHALCON-NERD trial studying vonoprazan as a daily dosing and on-demand therapy for relief of episodic heartburn in patients with NERD will be presented by Ronnie Fass, M.D., director of the Division of Gastroenterology and Hepatology and medical director of the Digestive Health Center at MetroHealth in Cleveland, Ohio and lead investigator of the PHALCON-NERD trial. This presentation is the first release of secondary and exploratory endpoint analyses since Phathom shared topline data from the study in February 2022.

The double-blind, placebo-controlled PHALCON-NERD study randomized 207 patients who were eligible for on-demand (“as needed”) treatment following a 4-week daily dosing run-in period in which patients received vonoprazan 20 mg once-daily. Patients without heartburn in the last seven days of the run-in period were evenly randomized to receive 10 mg, 20 mg or 40 mg of vonoprazan or placebo for six weeks.

Key results include:

- The primary endpoint was met for all three doses of vonoprazan, demonstrating complete and sustained relief in 56% (10 mg), 60.6% (20 mg) and 70% (40 mg) of heartburn episodes was achieved within three hours with no further heartburn reported for 24 hours in the on-demand period, compared to placebo (27.3%, $p<0.0001$).
- In exploratory endpoints, the onset of complete and sustained relief of heartburn episodes was also evaluated at intervals of 30 minutes, 1 hour, 1.5 hours, 2 hours, and 3 hours after taking vonoprazan to determine the earliest point of complete symptom relief.
- Significant differences in complete and sustained relief occurred across all doses of vonoprazan in as early as one hour after dosing in the on-demand period and was maintained for over 24 hours.
- In the on-demand period, vonoprazan had no treatment-emergent adverse events (AEs) reported by >1 patient per treatment group. Additionally, 16.3%, 18.4%, and 16.7% of patients treated with vonoprazan 10, 20, and 40 mg, respectively reported a treatment-emergent adverse event (TEAE) compared to 21.3% of patients receiving placebo.

“These results from the Phase 2 PHALCON-NERD study are very encouraging and demonstrate the potential of vonoprazan to be taken as-needed by patients with NERD who experience episodic heartburn symptoms and require rapid and sustained relief,” said Ronnie Fass, M.D. “NERD is a common cause of reflux-related symptoms and some patients with NERD fail to respond adequately to PPI therapy. This study suggests that the rapid suppression of gastric acid by vonoprazan translates into clinical benefits for patients with NERD when taken on demand.”

In addition, Phathom is actively conducting a Phase 3 PHALCON-NERD Daily Dosing trial to evaluate vonoprazan as a daily dosing treatment of heartburn associated with NERD. Topline data for the primary endpoint are expected in early 2023, with full results expected in late 2023.

“The data being presented at this year’s ACG further highlights Phathom’s commitment to its mission to transform treatment for patients with gastrointestinal diseases and disorders,” said Azmi Nabulsi, M.D., Chief Operating Officer at Phathom. “We are excited to share more detailed results of our Phase 2 on-demand trial and look forward to generating additional insights about vonoprazan as a potential daily preventative therapy in patients with NERD in our ongoing Phase 3 trial. Our continued research program demonstrates the promise of a new mechanism of action to provide more effective acid control with the potential to address unmet needs in the treatment of NERD and other acid-related GI conditions.”

PK/PD Model Study

Also during ACG, Dr. Carmelo Scarpignato, Professor of Medicine & Clinical Pharmacology at the United Campus of Malta, and General Secretary, World Organization for Esophageal Diseases (OESO), will present a poster (Presentation #: E0193) on a pharmacokinetics (PK) and pharmacodynamics (PD) study. Pooled data from five Phase 1 studies were used to develop a PK/PD model to investigate the relationship between vonoprazan treatment and pH HTR. The pooled data included pH measurements for 245 participants from Japan and Western countries.

Key results include:

- Simulations showed that vonoprazan 20 mg once-daily (QD) and 20 mg twice-daily (BID) are predicted to give pH>4 HTRs of 89.7% and 98.1%, respectively, by Day 7.
- HTRs for pH>6 were 53.1% for vonoprazan 20 mg QD and 75.3% for BID.

The study found vonoprazan provided high, dose-dependent pH holding time ratios (HTR) consistent with dose-dependent control of 24-hour intragastric acidity. The extent of gastric acid suppression has been shown to be an important factor in the treatment of acid-related gastrointestinal disorders, suggesting vonoprazan could have potential utility for a range of acid-related gastrointestinal disorders.

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

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 a New Drug Application under review by 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.

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.[1,2] There are estimated to be over 65 million individuals with GERD in the U.S., and it is estimated that 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.[3,4]

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.

Rash in Patients with Mononucleosis: A high percentage of patients with mononucleosis who receive amoxicillin (a component of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK) develop an erythematous skin rash. Avoid use of both products in patients with mononucleosis.

Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Assess CgA levels at least 14 days after VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK treatment and consider repeating the test if initial CgA levels are high.

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
VOQUEZNA TRIPLE PAK: The most common adverse reactions (≥2%) include dysgeusia (4.6%), diarrhea (4.0%), vulvovaginal candidiasis (3.2%), headache (2.6%), abdominal pain (2.3%), and hypertension (2.0%).

VOQUEZNA DUAL PAK: The most common adverse reactions (≥2%) include diarrhea (5.2%), abdominal pain (2.6%), vulvovaginal candidiasis (2.0%), and nasopharyngitis (2.0%).

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.

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. 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: 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; Phathom's ability to successfully launch and commercialize vonoprazan; 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 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 impact of the COVID-19 coronavirus, including delaying or otherwise disrupting its clinical trials, manufacturing and supply chain and launch and commercialization efforts; Phathom's ability to achieve and maintain adequate levels of coverage and reimbursement for vonoprazan; Phathom's ability to access additional capital under its term loan facility is subject to certain conditions, 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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10/22 US-VPZ-22-0274

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