Phathom Pharmaceuticals Announces FDA Approval of VOQUEZNA™ TRIPLE PAK™ (vonoprazan amoxicillin, clarithromycin) and VOQUEZNA™ DUAL PAK™ (vonoprazan, amoxicillin) for the Treatment of H. pylori Infection in Adults

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- VOQUEZNA TRIPLE and DUAL PAKs each contain vonoprazan, a novel, first-in-class potassium-competitive acid blocker (PCAB), and have demonstrated superior eradication rates vs. lansoprazole-based triple therapy in the overall patient population of the pivotal Phase 3 trial[1]
- VOQUEZNA treatment regimens are supplied in blister packs to help promote treatment compliance
- VOQUEZNA TRIPLE and DUAL PAKs offer physicians the flexibility of two different treatment options including a regimen without clarithromycin
- U.S. commercial launch anticipated in the third quarter of 2022

FLORHAM PARK, N.J., May 03, 2022 (GLOBE NEWSWIRE) -- Phathom Pharmaceuticals, Inc. (Nasdaq: PHAT), a biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal diseases, announced today the U.S. Food and Drug Administration (FDA) approved both VOQUEZNA™ TRIPLE PAK™ (vonoprazan tablets, amoxicillin capsules, clarithromycin tablets) and VOQUEZNA™ DUAL PAK™ (vonoprazan tablets, amoxicillin capsules), for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults. VOQUEZNA treatment regimens contain antibiotics conveniently packaged with vonoprazan, a novel potassium-competitive acid blocker (PCAB) and the first innovative acid suppressant from a new drug class approved in the U.S. in over 30 years. The two New Drug Applications for these products were given priority review designation by the FDA and previously granted as qualified infectious disease products (QIDP).

"The approval of VOQUEZNA treatment regimens offers physicians and patients two therapeutic options that showed superior eradication rates compared to proton pump inhibitor-based (PPI) lansoprazole triple therapy in the overall patient population in a pivotal trial[1]," said Terrie Curran, President and Chief Executive Officer at Phathom. "*H. pylori* eradication rates continue to decline in part due to antibiotic resistance, inadequate acid suppression, and complex treatment regimens,[2,3] resulting in treatment failures and complications for patients. New therapies that have the potential to address the limitations of current treatments are needed[2,3] and we look forward to bringing these innovative vonoprazan-based treatment options to the millions of *H. pylori* sufferers in the U.S."

Helicobacter pylori is a bacterial pathogen estimated to affect nearly 115 million people in the U.S.,[4] and over the last few decades, eradication rates have dropped to below 80%.[4] If left untreated, *H. pylori* infection can lead to serious complications, such as peptic ulcer disease and non-cardia gastric cancer.[5] Acid suppressant therapy has long been established as a backbone for *H. pylori* treatment regimens to enhance antibiotic effectiveness.[3] It was hypothesized that a more potent acid suppressant agent such as vonoprazan may help improve eradication rates of current regimens.[2,3]

"As a practicing physician, I am excited about the potential of two novel first-line *H. pylori* treatment options," said William D. Chey, M.D., AGAF, FACG, FACP, Professor of Medicine and Chief of Gastroenterology & Hepatology at the University of Michigan. "I believe the added flexibility of having two additional effective therapies, including a dual therapy option that does not contain clarithromycin, offers the potential to improve clinical outcomes in patients with *H. pylori* infection."

These approvals were based on safety and efficacy data from the Phase 3 PHALCON-HP trial, the largest U.S. registrational trial ever conducted in *H. pylori*, randomizing 1,046 patients.[1] In the modified intent-to-treat population, both VOQUEZNA treatment regimens demonstrated non-inferiority to lansoprazole triple therapy in patients without a clarithromycin or amoxicillin resistant strain of *H. pylori* at baseline. The *H. pylori* eradication rate was 84.7% with VOQUEZNA TRIPLE PAK compared to 78.8% with lansoprazole triple therapy [95% CI: -0.8, 12.6] and 78.5% for VOQUEZNA DUAL PAK compared to 78.8% with lansoprazole triple therapy [95% CI: -7.4, 6.8]. VOQUEZNA TRIPLE PAK and DUAL PAK demonstrated superior eradication rates compared to PPI-based triple therapy (lansoprazole with amoxicillin and clarithromycin) among all patients, including in patients with clarithromycin resistant strains of *H. pylori*.[1] The *H. pylori* eradication rate with VOQUEZNA TRIPLE PAK was 80.8% versus 68.5% with lansoprazole triple therapy in the overall study population [95% CI: 5.7, 18.8] and in patients who had a clarithromycin-resistant strain of *H. pylori,* 65.8% vs. 31.9%, respectively [95% CI: 17.7, 48.1].[1] *H. pylori* eradication rates for VOQUEZNA DUAL PAK were 77.2% versus 68.5% with lansoprazole triple therapy in the overall study population [95% CI: 1.9, 15.4] and in patients who had a clarithromycin-resistant strain of *H. pylori,* 69.6% vs. 31.9%, respectively [95% CI: 20.5, 52.6].[1]

Adverse event (AE) rates for the vonoprazan-based regimens were comparable to lansoprazole triple therapy in the trial.[1] The most common AEs (≥2.0%) reported in the VOQUEZNA TRIPLE PAK, VOQUEZNA DUAL PAK, and lansoprazole triple therapy arms, respectively, were diarrhea (4.0%, 5.2%, 9.6%), dysgeusia (4.6%, 0.6%, 6.1%), vulvovaginal candidiasis (3.2%, 2.0%, 1.4%), abdominal pain (2.3%, 2.6%, 2.9%), headache (2.6%, 1.4%, 1.4%), hypertension (2.0%, 1.1%, 0.9%) and nasopharyngitis (0.3%, 2.0%, 0.9%).[1]

The full prescribing information can be found here.

VOQUEZNA TRIPLE and DUAL PAKs are expected to be available in the U.S. in the third quarter of 2022 and marketed exclusively by Phathom Pharmaceuticals, Inc.

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 *Helicobacter pylori* (*H. pylori*) infection

H. pylori is a bacterial pathogen that is estimated to infect nearly 115 million individuals in the United States.[4] Approximately 50% of the world and 36% of the U.S. population is estimated to be infected with the bacterium.[4] As a result of the chronic inflammation induced by *H. pylori* infection, infected patients may develop a range of pathologies including dyspepsia, peptic ulcer disease, non-cardia gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma.[6] Studies have found that roughly 1 in 4 patients treated for *H. pylori* will fail first-line therapy when using PPI-based clarithromycin triple therapy.[6]

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.

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). Phathom 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 our plans to launch vonoprazan-based therapies for treatment of *H. pylori* infection in the third quarter of 2022 and the ability of vonoprazan-based treatments to address declining *H. pylori* eradication rates and improve clinical outcomes. 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.

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[1] VOQUEZNA TRIPLE PAK and VOQUENZA DUAL PAK Prescribing Information, Phathom Pharmaceuticals, 2022.

[2] Saleem and Howden. Update on the Management of Helicobacter pylori Infection. Curr Treat Options Gastro. 2020;18:476–487.

[3] Scott et al. The Role of Acid Inhibition in Helicobacter Pylori Eradication. 19 Jul 2016, (F1000 Faculty Rev):1747.

[4] Chey et al. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection. Am J Gastroenterol. 2017;112:212.

[5] Malfertheiner et al. Management of *Helicobacter Pylori* Infection—the Maastricht V/Florence Consensus Report. Gut. 2017;66-6.

[6] Mertz et al. Helicobacter pylori Treatment & Eradication Rates in Department of Defense Patients from 2016-2018. Am J Gastroenterol. 2020;115:S664.