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

October 30, 2023

- **Planning for a December 2023 U.S. launch for *H. pylori*, together with the U.S. launch of vonoprazan for Erosive GERD, if approved**

FLORHAM PARK, N.J., Oct. 30, 2023 (GLOBE NEWSWIRE) -- Phathom Pharmaceuticals, Inc. (Nasdaq: PHAT), a biopharmaceutical company focused on developing and commercializing novel treatments for gastrointestinal (GI) diseases, announced that the U.S. Food and Drug Administration (FDA) has approved the Prior Approval Supplement (PAS) for the reformulation of vonoprazan tablets for 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.

"We are very pleased with the FDA approval of our reformulated vonoprazan tablets for both VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, enabling Phathom to market two new first-line treatment options that offer strong *H. pylori* eradication rates," said Terrie Curran, President and Chief Executive Officer at Phathom. "*H. pylori* eradication failures are due to rising antibiotic resistance, inadequate acid suppression, and complex treatment regimens. We are excited about VOQUEZNA TRIPLE and DUAL PAKs, a new class of acid suppression therapy, that has the potential to address these issues and enhance *H. pylori* eradication. Our teams are making the final preparations for a combined December 2023 U.S. commercial launch for *H. pylori* along with the anticipated launch of vonoprazan for Erosive GERD, if approved. Thank you to Phathom employees and our manufacturing partners, Catalent and Evonik, who contributed to today's PAS approval."

These initial product 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]

VOQUEZNA TRIPLE and DUAL PAKs are expected to be available in the U.S. in December 2023 and marketed exclusively by Phathom Pharmaceuticals, Inc. Phathom is planning for a combined U.S. commercial launch of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK, together with vonoprazan for Erosive GERD, if approved.

Phathom plans to host an investor conference call in November 2023, following FDA action on the pending Erosive GERD New Drug Application, which has a PDUFA target action date of November 17, to discuss the Company's U.S. commercial launch plans.

The full Prescribing Information for VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK can be found here.

INDICATION AND IMPORTANT SAFETY INFORMATION

What are VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK?

- VOQUEZNA® TRIPLE PAK® (vonoprazan tablets, amoxicillin capsules, clarithromycin tablets) and VOQUEZNA® DUAL PAK® (vonoprazan tablets, amoxicillin capsules) are co-packaged prescription medicines for the treatment of a *Helicobacter pylori (H. pylori)* bacterial infection in adults.
- It is not known if VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK are safe and effective in children.
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of VOQUEZNA TRIPLE PAK, VOQUEZNA DUAL PAK and other antibacterial drugs, these products should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

Do not take VOQUEZNA TRIPLE PAK if you

- are known to have an allergy or be sensitive to the components of VOQUEZNA TRIPLE PAK (vonoprazan, amoxicillin, clarithromycin), macrolide antibiotics (such as azithromycin and erythromycin), or penicillin.
- are taking:
  - medicines that contain rilpivirine (Edurant, Complera, Odefsey)
  - pimozide
  - colchicine, if you have kidney or liver problems
  - lomitapide, lovastatin, and simvastatin
  - ergot alkaloids (ergotamine or dihydroergotamine)
  - lurasidone
- have a history of yellowing of the skin (jaundice) or liver problems when taking clarithromycin.

Do not take VOQUEZNA DUAL PAK if you

- are known to have an allergy or be sensitive to the components of VOQUEZNA DUAL PAK (vonoprazan, amoxicillin) or penicillin.
- are taking medicines that contain rilpivirine (Edurant, Complera, Odefsey).

Before you take VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK, tell your healthcare provider about all of your medical conditions, including if you

- are breastfeeding. If breastfeeding, pump and discard breast milk during treatment and for 2 days after treatment.
- have severe kidney disease.
- have moderate to severe liver disease.
- have myasthenia gravis.

Additionally, do not take VOQUEZNA TRIPLE PAK if:

- you are pregnant or plan to become pregnant. Clarithromycin, a medicine in VOQUEZNA TRIPLE PAK may harm your unborn baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. There can be serious side effects when some are used in combination with this product. 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, and other drugs.

What are the possible side effects of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK?
VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK can cause serious side effects including:

- **Allergic reactions (hypersensitivity):** Call your doctor right away if you have rash, hives, or other skin changes, face swelling or difficulty breathing.
- **A type of kidney problem (acute tubulointerstitial nephritis)**: Some people who take VOQUEZNA may develop a kidney problem called acute tubulointerstitial nephritis. Call your healthcare provider right away if you have a decrease in the amount that you urinate or if you notice blood in your urine.
- **Severe skin reactions:** VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK can cause severe skin reactions, such as skin rash or allergic reaction on or in any part of your body. Symptoms can also include, but are not limited to, fever, chills, body aches or shortness of breath. If you experience any of these symptoms, stop taking VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK immediately and call your doctor right away.
- **Severe diarrhea:** Call your doctor right away if you have watery stool, stomach pain, and fever that does not go away while taking VOQUEZNA DUAL PAK or VOQUEZNA TRIPLE PAK or after therapy is completed.
- **Rash in patients with mononucleosis:** Amoxicillin (a component of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK) may cause a rash in patients who have mononucleosis. Stop taking VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK if you are diagnosed with mononucleosis and call your doctor right away.
- **Altered test results for some tumors:** VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK lower stomach acid which can cause increased levels of a certain protein (CgA) in your blood. When this level is increased it may alter test results for detecting some tumors. Notify your doctor of the use of VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK prior to blood tests.

Additionally, VOQUEZNA TRIPLE PAK can cause:

- **Irregular heartbeats:** Clarithromycin may cause irregular heartbeats. Call your doctor right away if you feel faint, light-headed, or feel your heart beating irregularly.
- **Liver problems:** Call your doctor right away if you have any of the following symptoms: weight loss, yellowing of the skin

and eyes (jaundice), dark urine, rash, or pain on the right side of your abdomen.

The most common side effects may include:

- diarrhea
- temporary changes in sense of taste
- vaginal yeast infection
- stomach pain
- headache
- high blood pressure and
- cold-like symptoms

These are not all of the possible side effects of VOQUEZNA TRIPLE PAK and VOQUEZNA DUAL PAK. Call your healthcare provider for medical advice about side effects.

General information about the safe and effective use of VOQUEZNA.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK for a condition for which it was not prescribed. Do not give VOQUEZNA TRIPLE PAK or VOQUEZNA DUAL PAK to other people, even if they have the same symptoms you have. It may harm them.

For more information, ask your healthcare provider or pharmacist.

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.[1] If left untreated, *H. pylori* infection can lead to serious complications, such as peptic ulcer disease and non-cardia gastric cancer.[2] Approximately 50% of the world and 36% of the U.S. population is estimated to be infected with the bacterium. 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. 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.[3]

About VOQUEZNA® TRIPLE PAK® and VOQUEZNA® DUAL PAK®
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 markets the product 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. 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). 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
This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about the timing of the commercial launch of convenience packs containing vonoprazan for *H. pylori* infection, the potential of vonoprazan-based therapies to address declining *H. pylori* eradication rates in the U.S., and statements regarding the PDUFA goal date and the timing of a U.S. commercial launch for vonoprazan for Erosive GERD. 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: future data generated from our stability program may be different from the data submitted to the FDA to date and may not demonstrate that our mitigation efforts will continue to maintain the level of the nitrosamine impurity below the acceptable intake (AI) level throughout the shelf life of products containing vonoprazan, which could result in market action or shelf life reduction; risks associated with product manufacturing or formulation changes required to be made in connection with achieving the AI; the FDA may disagree that the existing safety and efficacy data, together with additional data, is sufficient to approve the Erosive GERD NDA; 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 ability to access additional capital under its term loan facility and royalty interest finance agreements is subject to certain conditions; Phathom's ability to obtain and maintain intellectual property protection for vonoprazan; Phathom's ability to comply with its license agreement with Takeda; 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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[2] Malfertheiner et al. Management of Helicobacter Pylori Infection—the Maastricht V/Florence Consensus Report. Gut. 2017;66-6.

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