United Therapeutics Announces FREEDOM-EV Study Of Orenitram Meets Primary Endpoint

August 8, 2018

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., Aug. 8, 2018 /PRNewswire/ -- United Therapeutics Corporation (NASDAQ: UTHR) today announced that preliminary analysis indicates that the FREEDOM-EV clinical study of Orenitram® (treprostinil) extended-release tablets in patients suffering from pulmonary arterial hypertension (PAH) has met its primary endpoint of delayed time to first clinical worsening event.

Orenitram, when taken with an oral PAH background therapy, decreased the risk of a morbidity/mortality event versus placebo by 26% (p=0.0391). Efficacy was observed across the following key subgroups: age, gender, World Health Organization (WHO) functional class, PAH etiology and background PAH therapy.

Secondary endpoints included change from baseline in six-minute walk distance (6MWD), N-terminal pro-brain natriuretic peptide levels, combined 6MWD and Borg dyspnea score (shortness of breath test) at week 24. Analysis of these secondary endpoints is ongoing.

"We are ecstatic with these results and the potential benefit to PAH patients," said Martine Rothblatt, Ph.D., Chairman and Chief Executive Officer of United Therapeutics. "Orenitram is already indicated to improve exercise capacity and has been an important part of the PAH treatment armamentarium since 2014. FREEDOM-EV expands on these benefits by demonstrating that Orenitram also delays disease progression. We are so grateful for the patient volunteers, investigative sites and research collaborators that participated in the FREEDOM-EV study. Based on these positive results, we look forward to sharing the final study data with the PAH community and working with the FDA to update the product labeling for Orenitram."

"We are excited about the opportunity these results provide for more PAH patients to benefit from prostacyclin therapy," added Michael Benkowitz, President and Chief Operating Officer of United Therapeutics. "With the FREEDOM-EV results, we believe more physicians and payers will value Orenitram as a clinically-effective oral prostacyclin analogue that is dose-titratable over the course of a patient's disease."

United Therapeutics plans to submit the results to the U.S. Food and Drug Administration in support of a label amendment to reflect the FREEDOM-EV results, and is evaluating whether the results could support marketing applications for Orenitram outside the United States.

About FREEDOM-EV

FREEDOM-EV was a phase 3, international, multi-center, randomized, double-blind, placebo-controlled, clinical worsening study of Orenitram in patients with PAH receiving background oral monotherapy (a phosphodiesterase type 5 inhibitor, an endothelin receptor antagonist or a soluble guanylate cyclase stimulator). Global enrollment was completed in December 2017 with a total of 690 patients. Patients were randomized 1:1 to receive three daily doses of Orenitram or placebo. This event-driven study was conducted in 152 centers from 23 countries in North and Latin America, Europe, and Asia-Pacific, with 214 patients having an adjudicated clinical worsening (morbidity or mortality) event (defined as death, hospitalization due to worsening of PAH, initiation of inhaled or infused prostacyclin treatment for PAH, disease progression or unsatisfactory long-term clinical response). The majority of patients had either WHO functional class II (63%) or class III (34%) PAH symptoms. Treatment with Orenitram in the FREEDOM-EV study was generally well tolerated and the safety profile was consistent with previous studies and known prostacyclin-related adverse events (see the discussion of adverse events below under "About Orenitram"). Dosing in FREEDOM-EV was initiated at 0.125 mg three times daily (TID) and increased to a maximum of 12 mg TID. This event-driven study was designed to demonstrate a prolongation of time to the first morbidity/mortality event for Orenitram compared with placebo and to evaluate the safety of Orenitram in PAH patients. All investigator reported morbidity and mortality events were adjudicated by an independent adjudication committee blinded to the study treatment.

Detailed study results will be made available through scientific disclosure at upcoming medical society meetings and in peer reviewed publications.

About Orenitram

Indication

Orenitram is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%).

When used as the sole vasodilator, the effect of Orenitram on exercise is about 10% of the deficit, and the effect, if any, on a background of another vasodilator is probably less than this.

Important Safety Information for Orenitram

CONTRAINDICATIONS

- Orenitram is contraindicated in patients with severe hepatic impairment (Child Pugh Class C)
- WARNINGS AND PRECAUTIONS
- Abrupt discontinuation or sudden large reductions in dosage of Orenitram may result in worsening of PAH symptoms
- Orenitram inhibits platelet aggregation and increases the risk of bleeding
- The Orenitram tablet shell does not dissolve. In patients with diverticulosis, Orenitram tablets can lodge in a diverticulum

DRUG INTERACTIONS / SPECIFIC POPULATIONS

- Concomitant administration of Orenitram with diuretics, antihypertensive agents, or other vasodilators increases the risk of symptomatic hypotension
- Orenitram inhibits platelet aggregation; there is an increased risk of bleeding, particularly among patients receiving anticoagulants
- Co-administration of Orenitram and the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to treprostinil; therefore, Orenitram dosage reduction may be necessary in these patients
- Pregnancy Category C. Animal reproductive studies with Orenitram have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans
- It is not known whether treprostinil is excreted in human milk or absorbed systemically after ingestion. Because many drugs are excreted in human milk, choose Orenitram or breastfeeding
- Safety and effectiveness in patients under 18 years of age have not been established
- There is a marked increase in the systemic exposure to treprostinil in hepatically impaired patients

ADVERSE REACTIONS

- In the 12-week placebo-controlled monotherapy study, adverse reactions that occurred at rates at least 5% higher on Orenitram than on placebo included headache, diarrhea, nausea, flushing, pain in jaw, pain in extremity, hypokalemia, and abdominal discomfort.

Please see Full Prescribing Information and Patient Information for Orenitram. For additional information about Orenitram, visit www.orenitram.com or call 1-877-UNITHER (1-877-864-8437).

About United Therapeutics

United Therapeutics Corporation is a biotechnology company focused on the development and commercialization of innovative products to address the unmet medical needs of patients with chronic and life-threatening conditions. [uthr-g]

Forward-looking Statements

Statements included in this press release that are not historical in nature are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among others, statements regarding the impact of the FREEDOM-EV results on physicians, payers and patients, our plans to submit the FREEDOM-EV results to the FDA to update the product's label, and the potential for the FREEDOM-EV results to support marketing applications for Orenitram outside the U.S. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic and other reports filed with the Securities and Exchange Commission that could cause actual results to differ materially from anticipated results. In particular, we note that analysis of the full FREEDOM-EV study results is ongoing, including analysis of secondary endpoints. These further analyses could have a material impact on how useful the full results will be to healthcare providers and payers, and how they will be viewed by the FDA and other regulators. In addition, the forward-looking statements in this press release are qualified by the cautionary statements, cautionary language and risk factors set forth in our periodic reports and documents filed with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. We claim the protection of the safe harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. We are providing this information as of August 8, 2018, and assume no obligation to update or revise the information contained in this press release whether as a result of new information, future events or any other reason.

View original content:http://www.prnewswire.com/news-releases/united-therapeutics-announces-freedom-ev-study-of-orenitram-meets-primary-endpoint-300693668.html

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