United Therapeutics Announces FREEDOM-EV Study Of Orenitram® To Continue As Planned Following Interim Analysis

September 7, 2017

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., Sept. 7, 2017 /PRNewswire/ -- United Therapeutics Corporation (NASDAQ: UTHR) today announced that the independent data monitoring committee (DMC) for the FREEDOM-EV study of Orenitram (treprostinil) extended-release tablets had completed a pre-specified interim safety and efficacy analysis. The DMC did not identify any new safety concerns associated with Orenitram therapy, and recommended that the trial be continued as planned without modification.

FREEDOM-EV is a Phase 3, international, multi-center, randomized, double-blind, placebo-controlled, clinical worsening study of Orenitram in patients with pulmonary arterial hypertension (PAH) receiving background oral monotherapy study (a phosphodiesterase type 5 inhibitor or an endothelin receptor antagonist). In accordance with the study protocol and DMC charter, previous interim safety analyses were performed at scheduled intervals throughout the study and this interim safety and efficacy analysis was performed after approximately 75% of the target 205 adjudicated clinical worsening (morbidity or mortality) events occurred within the study. United Therapeutics is intentionally blinded to the interim analysis data and will remain blinded to results of the study until after the study is completed.

The threshold for stopping the trial early for overwhelming efficacy was intentionally set high with the understanding that a more robust result, based on a larger number of clinical worsening (morbidity or mortality) events, could be obtained by the study continuing to completion.

The DMC's recommendation to continue as planned reflects its review of all available safety and efficacy data, and was made independently. Neither United Therapeutics nor the U.S. Food and Drug Administration (FDA) has reviewed the interim clinical trial results and neither participated in the DMC's closed session deliberation.

"We had stringent criteria for this interim analysis, and look forward to receiving the full results of the FREEDOM-EV study during the second half of 2018," said Martine Rothblatt, Ph.D., Chairman and Chief Executive Officer of United Therapeutics. "We remain optimistic that the FREEDOM-EV study is positioned for success based on our extensive review of the existing and continually increasing body of data from clinical and real-world evidence studies, and we are preparing for the study's conclusion in accordance with its statistical analysis plan."

About Orenitram

Orenitram is an extended-release, oral tablet form of treprostinil, which was launched commercially in the United States during the second quarter of 2014. Orenitram is the only FDA approved, orally administered prostacyclin analogue, and is the only oral PAH prostacyclin class therapy approved in the United States that is titratable to tolerability, without a dose ceiling. Orenitram was approved by the FDA in December 2013 for treatment of PAH patients to improve exercise capacity. Orenitram is not approved in major markets outside the United States. The primary study that established efficacy included predominately patients with functional class II-III symptoms and etiologies of idiopathic or heritable PAH (75%) or PAH associated with connective tissue disease (19%).

Orenitram is contraindicated in patients with severe hepatic impairment. 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.

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.

Orenitram is in 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, patients should 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.

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.

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 timing and outcome of the final FREEDOM-EV results and any related regulatory filings. 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. Such forward-looking statements 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 September 7, 2017, 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.

ORENITRAM is a registered trademark of United Therapeutics Corporation.

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