United Therapeutics Announces FDA Approval Of Third Generation Nebulizer For The Tyvaso® Inhalation System

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SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., Oct. 23, 2017 /PRNewswire/ -- United Therapeutics Corporation (NASDAQ: UTHR) today announced approval by the U.S. Food and Drug Administration (FDA) of a new inhalation device, called the TD-300/A, for use with Tyvaso® (treprostinil) Inhalation Solution (Tyvaso).

Tyvaso was originally approved by the FDA for the treatment of pulmonary arterial hypertension (PAH) in 2009, under a New Drug Application covering a drug-device combination product consisting of Tyvaso drug product, as well as an ultrasonic nebulizer and accessories referred to as the Tyvaso Inhalation System. Tyvaso is the most-prescribed inhalation therapy for PAH in the United States, and since its launch, United Therapeutics has been working on improvements to the Tyvaso Inhalation System to aid patient compliance and enhance ease of use.

The TD-300/A is a significant step forward on that front. Designed based on patient and physician feedback, the new device has a cleaner, more ergonomic design that includes single button operation, an intuitive user interface for adjusting breath counts, a color, graphical display that leads patients through the inhalation process and displays time since last treatment, and an internal, rechargeable battery.

"We are extremely proud of this new device, which is just one example of our commitment to improving the ease of administration of treprostinil therapy so that more patients can benefit from our medicine," said Martine Rothblatt, Ph.D., Chairman and Chief Executive Officer of United Therapeutics. "We are not resting on our laurels with this device, however. We recently launched a new program to develop a small, metered dose inhalation device for treprostinil, and are planning to study the administration of inhaled treprostinil on a *pro re nata* 'as needed' basis, to provide more flexibility for patients to use inhaled treprostinil where they need it, when they need it. And of course, we are continuing the development of our advanced delivery devices for Remodulin®, such as our RemUnity™ subcutaneous pump, and RemoPro™, a prodrug formulation of treprostinil.'

"Tyvaso is an important element of our continuum of care, which provides a range of treprostinil therapy options across a spectrum of PAH patients," said Michael Benkowitz, President and Chief Operating Officer. "The launch of the TD-300/A, planned for mid-2018, will further optimize Tyvaso therapy for patients and, we believe, reduce the rate of therapy discontinuation associated with the current nebulizer."

About Tyvaso

Tyvaso is a prostacyclin vasodilator indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with New York Heart Association (NYHA) Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%). The effects diminish over the minimum recommended dosing interval of 4 hours; treatment timing can be adjusted for planned activities.

While there are long-term data on use of treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.

The efficacy of Tyvaso has not been established in patients with significant underlying lung disease (such as asthma or chronic obstructive pulmonary disease). Patients with acute pulmonary infections should be carefully monitored to detect any worsening of lung disease and loss of drug effect.

Tyvaso is a pulmonary and systemic vasodilator. In patients with low systemic arterial pressure, Tyvaso may cause symptomatic hypotension. Tyvaso dosage should be titrated slowly in patients with hepatic or renal insufficiency, as exposure to treprostinil may be increased in these patients. Tyvaso inhibits platelet aggregation and increases the risk of bleeding.

Co-administration of a cytochrome P450 (CYP) 2C8 enzyme inhibitor, such as gemfibrozil, may increase exposure to treprostinil. Co-administration of a CYP2C8 enzyme inducer, such as rifampin, may decrease exposure to treprostinil. Increased exposure is likely to increase adverse events, whereas decreased exposure is likely to reduce clinical effectiveness.

Co-administration of the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to oral treprostinil. Co-administration of the CYP2C8 enzyme inducer rifampin decreases exposure to oral treprostinil. It is unclear if the safety and efficacy of treprostinil by the inhalation route are altered by inhibitors or inducers of CYP2C8.

Limited case reports of treprostinil use in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. However, there are risks to the mother and the fetus associated with pulmonary arterial hypertension. It is not known whether treprostinil is excreted in human milk.

The most common adverse events seen with Tyvaso in ≥4% of PAH patients and more than 3% greater than placebo in the placebo-controlled clinical study were cough (54% vs 29%), headache (41% vs 23%), throat irritation/ pharyngolaryngeal pain (25% vs 14%), nausea (19% vs 11%), flushing (15% vs <1%), and syncope (6% vs <1%).

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 of the anticipated launch of the TD-300/A device, and its impact on the rate of therapy discontinuation for Tyvaso, as well as further research and development efforts into new devices for Tyvaso and Remodulin, into a prodrug formulation of treprostinil and into the administration of inhaled treprostinil on a pro re nata basis. 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 October 23, 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.

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