United Therapeutics Announces Additional Six Months Of Regulatory Exclusivity For Adcirca®

November 20, 2017

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., Nov. 20, 2017 /PRNewswire/ -- United Therapeutics Corporation (NASDAQ: UTHR) today announced that the U.S. Food and Drug Administration (FDA) has granted pediatric exclusivity for Adcirca® (tadalafil) tablets through May 21, 2018, based on study results submitted by Eli Lilly and Company (Lilly) in response to a written request by the FDA to investigate the use of tadalafil in pediatric patients with Duchenne muscular dystrophy.

United Therapeutics markets and sells Adcirca for treatment of pulmonary arterial hypertension (PAH) in the United States under a license agreement with Lilly. A U.S. patent for Adcirca will expire November 21, 2017, and FDA's decision provides an additional six months of regulatory exclusivity running from this date, providing an additional six months before FDA can approve a generic version of Adcirca.

Under a previously-announced amendment to its license agreement with Lilly, effective December 1, 2017, United Therapeutics' royalty rate on net product sales of Adcirca will increase from five percent to ten percent, and the company will also be required to make milestone payments to Lilly equal to $325,000 for each $1,000,000 in net product sales.

Because the data submitted by Lilly to FDA does not include PAH patients, United Therapeutics does not anticipate any resulting expansion of the indication for Adcirca to include pediatric patients.

About Adcirca

Adcirca is a phosphodiesterase 5 inhibitor (PDE5i) indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with New York Heart Association Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

Important Safety Information for Adcirca

CONTRAINDICATIONS

- **Nitrates and Guanylate Cyclase (GC) Stimulators:** Do not use Adcirca in patients taking medicines that contain nitrates or guanylate cyclase stimulators (such as riociguat), as the combination could cause a sudden, unsafe drop in blood pressure
- **Hypersensitivity Reactions:** Patients with a known serious hypersensitivity to tadalafil should not take Adcirca

WARNINGS AND PRECAUTIONS

- **Cardiovascular:** Patients who experience anginal chest pain after taking Adcirca should seek immediate medical attention
- **Cardiovascular:** PDE-5is, including tadalafil, have mild systemic vasodilatory properties that may result in transient decreases in blood pressure. Before prescribing Adcirca, physicians should carefully consider whether their patients with underlying cardiovascular disease could be adversely affected by such actions. Pulmonary vasodilators may significantly worsen the cardiovascular status of patients with pulmonary veno-occlusive disease (PVOD) and administration of Adcirca to these patients is not recommended
- **Cardiovascular:** The use of Adcirca with alpha blockers, blood pressure medications, or alcohol may lower blood pressure significantly and may lead to symptomatic hypotension (light-headedness or fainting)
- **Potential Drug Interactions:** Tadalafil is metabolized predominately by CYP3A in the liver. Use of Adcirca with potent CYP3A inhibitors, such as ketoconazole and itraconazole, should be avoided. For patients on Adcirca therapy that require treatment with ritonavir, Adcirca should be discontinued at least 24 hours prior to starting ritonavir. For patients on ritonavir therapy that require treatment with Adcirca, start Adcirca at 20 mg once a day. Use of Adcirca with potent inducers of CYP3A, such as rifampin, should be avoided
- **Special Populations:** The use of Adcirca is not recommended for patients with severe renal or hepatic impairment. Please see Full Prescribing Information for dosing recommendations for patients with mild to moderate renal or hepatic impairment
- **Potential Drug Interactions:** Adcirca contains the same ingredient (tadalafil) as Cialis®, which is used to treat erectile dysfunction (ED) and the signs and symptoms of benign prostatic hyperplasia (BPH). The safety and efficacy of combinations of Adcirca with Cialis or other PDE-5is have not been studied. Therefore, the use of such combinations is not recommended
- **Vision/Hearing:** Patients who experience a sudden loss of vision in one or both eyes, which could be a sign of non-arteritic anterior ischemic optic neuropathy (NAION), or sudden decrease or loss of hearing after taking Adcirca should seek immediate medical attention.
- **Prolonged Erection:** In rare instances, men taking PDE-5is (including tadalafil) for ED reported an erection lasting more than four hours. Male patients who experience a prolonged erection should seek immediate medical attention

ADVERSE REACTIONS

- **Adverse Reactions:** The most common adverse event with Adcirca is headache (42% Adcirca vs 15% placebo). Other common adverse events (reported by ?9% of patients on Adcirca and more frequent than placebo by 2%) include myalgia (14% vs 4%), nasopharyngitis (13% vs 7%), flushing (13% vs 2%), respiratory tract infection (13% vs 6%), extremity pain (11% vs 2%), nausea (11% vs 6%), back pain (10% vs 6%), dyspepsia (10% vs 2%), and nasal congestion (9% vs 1%)

For more information about Adcirca, please see the full prescribing information available at www.adcirca.com, or call 1-800-545-5979.

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 generic competition for Adcirca. 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 November 20, 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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