Study Results Present Efficacy and Safety Findings from the PHIRST-1 Study of Patients with Pulmonary Arterial Hypertension Taking Tadalafil Tablets Once Daily

--Data Findings Published in June Issue of Circulation

SILVER SPRING, Md. and INDIANAPOLIS, June 9, 2009 /PRNewswire-FirstCall via COMTEX News Network/ -- United Therapeutics Corporation (Nasdaq: UTHR) and Eli Lilly and Company (NYSE: LLY) today announced the results of a pivotal 16-week study showing that a once-daily dose of tadalafil was generally well tolerated, improved exercise capacity and improved time to clinical worsening in patients with pulmonary arterial hypertension (PAH)(1). The randomized, double-blind, 16-week, placebo-controlled Phase 3 study followed 405 patients with PAH, either treatment-naive or taking bosentan, randomized to placebo or tadalafil 2.5 mg, 10 mg, 20 mg or 40 mg orally. Results from the study entitled, "Tadalafil Therapy for Pulmonary Arterial Hypertension," were published in today's issue of Circulation.

The study formed the basis of the United States Food and Drug Administration (FDA) approval to market tadalafil tablets for the treatment of PAH under the brand name ADCIRCA(TM).

"PAH is a rare, life-threatening disease," said lead investigator Dr. Nazzareno Galie, Associate Professor of Cardiology at the University of Bologna and head of the Pulmonary Hypertension Centre at the Institute of Cardiology. "The results of this study are encouraging for PAH clinicians and the patients they treat."

About the Study

The randomized, double-blind, 16-week, placebo-controlled Phase 3 study monitored 405 patients with idiopathic PAH or PAH associated with anorexigen use, connective tissue disease, human immunodeficiency virus (HIV) infection, or congenital systemic-to-pulmonary shunts.

Patients were randomized in groups and received one of five treatments, tadalafil 2.5 mg, 10 mg, 20 mg, 40 mg or placebo, orally once a day as monotherapy or as add-on therapy to bosentan. The primary endpoint was change from baseline to Week 16 in six-minute walk distance (6MWD)(2). Demographics, clinical data and health-related quality of life data were collected at baseline. Clinical and health-related quality of life data were collected again at weeks eight and sixteen(3).

Tadalafil increased 6MWD in a dose-dependent manner, only the 40 mg dose met the pre-specified level of statistical significance of less than 0.01 ($p<0.01$). Overall, the placebo-corrected treatment effect was 33m (95 percent confidence-interval, 15m to 50m). In the bosentan-naive group, the treatment effect was 44m (95 percent confidence-interval, 20m to 69m), as compared to 23m (95 percent confidence-interval, -2m to 48m) in patients on background bosentan therapy.

Among secondary objectives, patients administered tadalafil 40 mg showed improvement in time to clinical worsening, as compared to placebo (5 percent for tadalafil 40 mg, versus 16 percent with placebo)(4,5). Additionally, the incidence of clinical worsening was reduced in the 40 mg tadalafil group ($p=0.038$; relative risk reduction 68 percent less than placebo).

Improvements in the tadalafil 40 mg dose group, compared to placebo, from baseline to Week 16 were observed in six of the eight domains of the SF-36 health survey and for all sections of the EQ-5D questionnaire(6).

The most commonly reported adverse events for tadalafil 40 mg were headache (42 percent for tadalafil 40 mg, versus 15 percent with placebo), myalgia (14 percent for tadalafil 40 mg, versus 4 percent with placebo) and flushing (13 percent for tadalafil 40 mg, versus 2 percent with placebo)(7,8,9). Most adverse events were reported as mild or moderate and discontinuation rates were similar across all treatment groups(10).

About ADCIRCA

ADCIRCA is a prescription medicine used to treat PAH, a life-threatening disease that constricts the flow of blood through the pulmonary vasculature.

United Therapeutics Corporation licensed the rights to develop, market, promote and commercialize ADCIRCA for pulmonary hypertension in the United States and Puerto Rico from Eli Lilly & Company in November 2008. ADCIRCA contains the same

active ingredient as CIALIS(R) (tadalafil), which is marketed by Eli Lilly & Company to treat erectile dysfunction (impotence) in more than 100 countries.

Important Safety Information for ADCIRCA

ADCIRCA should not be used in patients taking medicines that contain nitrates (often used for chest pain) as the combination could cause a sudden, unsafe drop in blood pressure. If a patient experiences anginal chest pain after taking ADCIRCA they should seek immediate medical attention. Patients with a known serious hypersensitivity to tadalafil (ADCIRCA or CIALIS) should not take ADCIRCA.

PDE5 inhibitors, 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 effects. 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. Patients should discuss their medical condition and all medications with their physician before starting ADCIRCA.

The use of ADCIRCA with alpha blockers, blood pressure medications, and alcohol may cause a lowering of blood pressure. 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, dosage adjustments are required. Certain populations of PAH patients such as those with mild-to-moderate renal or hepatic impairment or those taking the drug ritonavir should use a dose of 20 mg daily when beginning therapy with ADCIRCA. Use of ADCIRCA with potent inducers of CYP3A, such as rifampin, should be avoided. The safety and efficacy of combinations of ADCIRCA with CIALIS or other PDE5 inhibitors have not been studied. Therefore, the use of such combinations is not recommended.

The most common side effects with ADCIRCA seen in the PHIRST-1 clinical trial were headache, myalgia, nasopharyngitis, flushing, respiratory tract infection, extremity pain, nausea, back pain, dyspepsia and nasal congestion.

In rare instances, patients taking PDE5 inhibitors (including tadalafil) reported a sudden decrease or loss of vision or hearing, or in men, an erection lasting more than four hours. A patient who experiences a decrease or loss in vision or hearing or prolonged erection should seek immediate medical attention.

For full patient information and/or full prescribing information, visit http://www.ADCIRCA.com or call 1-800-545-5979 (1-800-LILLY-RX).

Important Safety Information for CIALIS (tadalafil)

CIALIS is available by prescription only and is not for everyone. Men should discuss their medical conditions and all medications with their doctors to ensure CIALIS is right for them and that they are healthy enough for sexual activity.

Men taking nitrates, often used for chest pain, should not take CIALIS. Such a combination could cause a sudden, unsafe drop in blood pressure.

CIALIS for once daily use provides continuous plasma tadalafil levels which should be considered when evaluating the potential for interactions with certain medications (e.g., nitrates, alpha-blockers, anti-hypertensives and potent inhibitors of CYP3A4) and with substantial amounts of alcohol.

CIALIS does not protect a man or his partner from sexually transmitted diseases, including HIV. Men should not drink alcohol in excess with CIALIS. The most common side effects with CIALIS were headache, upset stomach, backache or muscle ache.

As with any ED tablet, in the rare event of priapism (an erection lasting more than four hours), men should seek immediate medical attention to avoid long-term injury.

In rare instances, men taking prescription ED tablets (including CIALIS) reported a sudden decrease or loss of vision, or a sudden decrease or loss of hearing (sometimes with ringing in the ears and dizziness). It's not possible to determine if these events are related directly to the ED tablets or to other factors. If a man has a sudden decrease or loss of vision or hearing, he should stop taking any ED tablet including CIALIS and seek medical attention right away.

For full patient information and/or full prescribing information, visit http://www.cialis.com or call 1-800-545-5979 (1-800-LILLY-RX).

About United Therapeutics Corporation

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

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

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(1)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 3.

(2)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 6. (3)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 6. (4)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 10. (5)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 31, Table 2.

(6)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 10. (7)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 11. (8)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 31, Table 2.

(9)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 32, Table 2.

(10)Galie, N., et al. "Tadalafil therapy for pulmonary arterial hypertension" manuscript. Registration Trial Number: NCT00125918. Page 11.

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