# Freedom-C Trial of Oral Treprostinil in Pulmonary Arterial Hypertension Fails to Meet Primary Endpoint

**Preliminary Analysis Demonstrates an 11-Meter Improvement in Six-Minute Walk Distance at Week 16 (p=0.072)**

***Conference Call to be Held at 9:00 a.m. Eastern Time on November 17, 2008***

Silver Spring, MD, November 17, 2008: United Therapeutics Corporation (NASDAQ: UTHR) announced today the results of the FREEDOM-C trial of oral treprostinil, a sustained-release formulation of treprostinil, in pulmonary arterial hypertension (PAH). Preliminary analysis demonstrates that the trial did not achieve statistical significance for the primary endpoint, six minute walk (6MW) distance at Week 16.

The FREEDOM-C trial was a randomized, double-blind, placebo-controlled trial of patients with severe PAH, a chronic, life-threatening illness. The study population consisted of 354 patients who were optimized on an endothelin receptor antagonist, a phosphodiesterase-5 inhibitor, or both. In addition to one of these oral therapy regimens, patients were administered oral treprostinil or placebo twice daily with the dose titrated (increased to tolerability) over the 16-week trial. The majority (~75%) of patients were World Health Organization (WHO) Class III of varied etiologies, including idiopathic or familial PAH (~65%), collagen vascular disease associated PAH (~25%), and PAH associated with HIV or other associated conditions (~10%). Mean baseline walk distance was approximately 345 meters.

The primary efficacy endpoint of the trial was the median change in 6MW distance at 16 weeks relative to baseline. With regard to the primary efficacy results, the placebo-corrected median change in 6MW distance at Week 16 was 11 meters (p=0.072). A statistically significant treatment effect was observed at Week 12, with a placebo-corrected median change of 13 meters (p=0.015).

Exploratory analyses suggest that the inability to dose titrate was a limiting issue that muted the overall treatment effect. Of the 174 patients who received active drug, 135 completed the study, 25 patients discontinued due to an adverse event and 33 patients were unable to titrate their dose above 1 mg twice daily. Accordingly, 58 (33%) patients in the active treatment group did not maintain a dose of oral treprostinil above 1 mg twice daily, and in this study a dose of 1 mg twice daily or less appeared to be a suboptimal dose. **These patients had a markedly lower exercise benefit at Week 16 compared to the other patients who received active drug, with an observed median improvement of only 4 meters. Patients achieving a dose of 1.25 mg to 3.25 mg twice daily had a median improvement of 18 meters, and patients achieving a dose of 3.25 mg to 16 mg twice daily had a median improvement of 34 meters.**

Adverse events that led to discontinuation or inability to dose-escalate included headache, nausea and vomiting. Dropouts due to adverse events were most common in patients who only had access to 1 mg tablets during the study, which was the lowest strength tablet available at the start of the study. There were no dropouts due to adverse events by patients who had access to the 0.25 mg strength tablet, which was added later in the study.

Preliminary analysis of other secondary efficacy measures, including change in combined 6MW distance and Borg Dyspnea Score rating (shortness of breath test) and Dyspnea-Fatigue index, demonstrated statistically significant improvements ($p<0.05$) compared to placebo. Other secondary efficacy measures including change in WHO functional class, time to clinical worsening, and PAH signs and symptoms did not differ significantly between oral treprostinil and placebo ($p>0.05$).

Further review and analysis of the preliminary results and safety data, including adverse events, is ongoing. A summary of the analysis conducted thus far can be accessed via United Therapeutics' website at http://ir.unither.com/events.cfm.

"While we are disappointed we did not achieve a statistically significant result for the primary endpoint, we believe the results fully support the continued development of oral treprostinil, especially when the treatment effect is evaluated based on the dose achieved in the FREEDOM-C study," said Roger Jeffs, Ph.D., United Therapeutics' President and

Chief Operating Officer. "We remain excited for the prospects of our Phase 3 study of oral treprostinil, FREEDOM-M, which evaluates the utility of oral treprostinil without the presence of background therapy. This study is fully enrolled, and results are expected to be available at the end of March 2009. Further, we expect enrollment of our Phase 3 study of oral treprostinil, FREEDOM-DR, to commence shortly, which will employ the 0.25 mg tablet for patient dosing. Finally, our inhaled treprostinil study produced highly statistically significant results and is under review by the FDA with an anticipated action date in April of 2009. Submission in Europe via the centralized procedure is expected in January 2009." Dr. Jeffs concluded, "Today's result has not altered the fact that we believe that we have in place today all of the pieces that we need to continue growing our business."

**Conference Call**

A one hour teleconference will be held on Monday, November 17, 2008, at 9:00 a.m. Eastern Time. The teleconference is accessible by dialing (800) 603-1777, with international callers dialing (706) 679-8129. A rebroadcast of the teleconference will be available for one week following the teleconference by dialing (800) 642-1687, with international callers dialing (706) 645-9291, and using access code 74119757.

This teleconference is also being webcast and can be accessed via United Therapeutics' website at http://ir.unither.com/events.cfm.

**About United Therapeutics**

United Therapeutics is a biotechnology company focused on the development and commercialization of unique products for patients with chronic and life-threatening cardiovascular, cancer and infectious diseases.

**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 Reform Act of 1995. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic reports filed with the Securities and Exchange Commission, which could cause actual results to differ materially from anticipated results. These risks and uncertainties include, among others: (i) with respect to the FREEDOM-C trial, the conclusions we reached from our exploratory and preliminary analyses, our belief that the inability to dose titrate was a limiting issue that muted the overall treatment effect in the trial, our belief that the results of the trial fully support the continued development of oral treprostinil and the final results of our ongoing review and analysis of the results of the trial, which may differ from our preliminary findings; (ii) with respect to inhaled treprostinil, when the FDA will act and when our submission in Europe will be made; (iii) when results will be available from the FREEDOM-M trial; (iv) when the FREEDOM-DR trial will commence; and (v) our belief that we have in place all of the pieces that we need to continue growing our business. Consequently, 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 Reform Act of 1995 for forward-looking statements. We are providing this information as of November 17, 2008, 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. [uthr-g]

For Immediate Release
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