

## **Pivotal Phase III Findings With Investigational Drug Cleviprex(TM) (Clevidipine) Demonstrate Perioperative Blood Pressure Control In Cardiac Surgery**

### **First Presentation of Comparative Data from ECLIPSE, Largest Safety Program of Intravenous Antihypertensive Agents**

NEW ORLEANS, March 27, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- Favorable findings of the investigational drug Cleviprex(TM) (clevidipine) (The Medicines Company [Nasdaq: MDCO]) compared to current intravenous antihypertensive agents in controlling perioperative hypertension -- a potentially harmful elevation in blood pressure just before, during and/or after surgery -- were presented for the first time at a late-breaking session here at the 56th Annual Scientific Session of the American College of Cardiology. The findings were from ECLIPSE\*, the largest safety program to date comparing intravenous antihypertensive therapies.

"This analysis from ECLIPSE showed tight perioperative blood pressure control with Cleviprex," said lead author of the presentation, Solomon Aronson, MD, Duke University Medical Center\*\*. "If approved, Cleviprex may provide a potentially important new treatment option for acute hypertension, a condition which affects nearly 3 million people in the U.S. each year."

"We are extremely pleased with the favorable findings of Cleviprex in the ECLIPSE program," said John Kelley, President and Chief Operating Officer of The Medicines Company. "Given the trial successfully met all of its primary endpoints, this marks the completion of our Phase III efforts for Cleviprex. The Medicines Company remains committed and on track to expeditiously move forward with an NDA submission before the end of June."

#### **Study and Findings**

The ECLIPSE program included a total of 1,964 cardiac surgery patients each enrolled in one of three randomized, open-label trials comparing Cleviprex to current intravenous antihypertensive agents: nitroglycerin, sodium nitroprusside or nicardipine (ECLIPSE-NTG, ECLIPSE-SNP and ECLIPSE-NIC trials, respectively). Beginning just before surgery, investigators monitored patients' blood pressure (BP) and administered the assigned antihypertensive agent, at their discretion, if BP became too high. Based on each patient's BP response for 24 hours after initiating the therapy, investigators determined "BP excursions" -- how much and how long systolic BP went above or below predefined, acceptable perioperative BP ranges.

The ECLIPSE analysis evaluated BP excursions from data pooled from all three studies and from the individual studies. In the pooled analysis, for the widest predefined acceptable perioperative BP range of 75-145 mm Hg pre- and post-operatively and 65-135 mm Hg during surgery, Cleviprex resulted in approximately half the BP excursion compared to the other agents (3.8 vs. 7.8 mm Hg x min/h,  $p = 0.0004$ ). Results for the narrowest BP range of 105-145 mm Hg pre- and post-operatively and 95-135 mm Hg during surgery also favored Cleviprex (87.7 vs. 111.5 mm Hg x min/h,  $p = 0.0002$ ).

In the individual ECLIPSE-NTG and ECLIPSE-SNP studies, for the widest BP range, Cleviprex resulted in approximately half the BP excursion compared to nitroglycerin (4.14 vs. 8.87 mm Hg x min/h,  $p = 0.0006$ ) and sodium nitroprusside (4.37 vs. 10.50 mm Hg x min/h,  $p = 0.0027$ ), respectively. At this BP range, there was no significant difference in BP excursions for Cleviprex vs. nicardipine (1.76 vs. 1.79 mm Hg x min/h,  $p = 0.8508$ ), however that comparison was restricted to the post-operative period only, since nicardipine is not generally used before or during surgery due to its relatively slow onset and offset of action. Other standard intravenous BP control agents were administered, as deemed appropriate, just before or during surgery in the ECLIPSE-NIC trial.

For the narrowest BP range, Cleviprex also resulted in less BP excursion compared to sodium nitroprusside (100.17 vs. 127.87 mm Hg x min/h,  $p = 0.0068$ ), nicardipine (76.5 vs. 101.59 mm Hg x min/h,  $p = 0.0231$ ), and nitroglycerin (83.74 vs. 108.57 mm Hg x min/h,  $p = 0.0556$ ).

The ECLIPSE-SNP trial also showed that the rate of death was significantly lower with Cleviprex than with sodium nitroprusside (1.7% vs. 4.7%,  $p = 0.045$ ). Other than this difference, the primary endpoints -- rates of death, stroke, heart attack and kidney dysfunction -- were similar for Cleviprex compared to the other three agents.

#### **About Perioperative Hypertension**

Perioperative hypertension affects patients in the operating room, post- anesthesia care unit and intensive care unit. It is thought to be caused by the rapid shifts in blood volume and increased activity of the sympathetic nervous system that

accompany surgery, which in turn increase vasoconstriction, vascular resistance, and both systolic and diastolic BP. The increased pressure can damage blood vessels, resulting in inflammation and leaking of fluid or blood into tissues, and complications such as hemorrhagic stroke, ischemic stroke, encephalopathy, myocardial ischemia or infarction, heart arrhythmia, congestive heart failure, and bleeding at the surgical site.

Perioperative hypertension is treated using intravenous antihypertensive agents, but current therapies have various shortcomings. For example, nitroglycerin and sodium nitroprusside dilate both arteries and veins, which can result in less predictable BP control. Nicardipine is selective for arteries, but because it has a slower onset and longer duration of action, and accumulates over time in the body, it is rarely used to control BP during surgery, and is only used occasionally after surgery.

#### About Cleviprex

Cleviprex is a novel, investigational drug rationally designed to meet the needs of the acute care practitioner for an intravenous hypertensive agent. It is the first third-generation dihydropyridine calcium channel blocker that acts rapidly and reliably, is vascular- and arterial-selective, and has an ultrashort half-life. Cleviprex recently completed Phase III clinical trials.

#### MDCO-G

#### About The Medicines Company

The Medicines Company is committed to delivering innovative, cost-effective acute care products in the worldwide hospital marketplace. The Company markets AngiomaxR (bivalirudin) in the U.S. and other countries for use in patients undergoing coronary angioplasty, a procedure to clear restricted blood flow in arteries around the heart. The Company also has two products in late-stage development, Cleviprex(TM) (clevidipine) and cangrelor. The Company's website is <http://www.themedicinescompany.com>.

Statements contained in this press release about The Medicines Company and Cleviprex that are not purely historical, and all other statements that are not purely historical, may be deemed to be forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words "believes," "anticipates" and "expects" and similar expressions are intended to identify forward-looking statements. These forward-looking statements involve known and unknown risks and uncertainties that may cause the Company's actual results, levels of activity, performance or achievements to be materially different from those expressed or implied by these forward-looking statements. Important factors that may cause or contribute to such differences include whether the Company's products will advance in the clinical trials process on a timely basis or at all, whether clinical trial results will warrant submission of applications for regulatory approval, whether the Company will be able to obtain regulatory approvals, whether physicians, patients and other key decision makers will accept clinical trial results, and such other factors as are set forth in the risk factors detailed from time to time in the Company's periodic reports and registration statements filed with the Securities and Exchange Commission including, without limitation, the risk factors detailed in the Company's Annual Report on Form 10-K filed on March 1, 2007, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements.

\* Evaluation of Clevidipine In the Postoperative Treatment of Hypertension  
Assessing Safety Events

\*\* Dr. Solomon Aronson is a paid consultant for The Medicines Company

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