



### FOR IMMEDIATE RELEASE

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### **In Phase III Study Merck's Investigational CETP Inhibitor Anacetrapib Met Safety and Efficacy Endpoints in Patients with coronary heart disease (CHD)**

MONTREAL, QUEBEC, Nov.18, 2010 – On November 17, 2010, researchers presented results from the Phase III DEFINE (Determining the Efficacy and Tolerability of CETP INhibition with AnacEtrapib) study with Merck's investigational CETP inhibitor, anacetrapib. In the trial of 1,623 patients with coronary heart disease (CHD) or CHD risk equivalents, anacetrapib showed no significant differences from placebo in the primary safety measures studied. There were no significant differences in mean changes in blood pressure between the anacetrapib and placebo treatment groups, nor were there any significant differences in serum electrolytes or aldosterone levels. During the 76-week treatment phase, the pre-specified adjudicated cardiovascular endpoint (defined as cardiovascular death, myocardial infarction, unstable angina or stroke) occurred in 16 anacetrapib-treated patients (2.0 percent) compared with 21 placebo-treated patients (2.6 percent) ( $p=0.40$ ). At 24 weeks, anacetrapib decreased LDL-C by 40 percent (from 2.1 to 1.2 mmol/L vs. 2.1 to 2.0 mmol/L for placebo,  $p<0.001$ ) and increased HDL-C by 138 percent (from 1.0 to 2.6 mmol/L vs. 1.0 to 1.2 mmol/L for placebo,  $p<0.001$ ) in patients already treated with a statin and at guideline-recommended LDL-C goal. The DEFINE data were presented at the American Heart Association Scientific Sessions and published concurrently online in the *New England Journal of Medicine*.

"These results are promising and serve as the basis for our decision to further develop anacetrapib," said Michael Mendelsohn, M.D., senior vice president and franchise head, Cardiovascular, Merck Research Laboratories. "We look forward to continuing to study anacetrapib in a large cardiovascular clinical outcomes trial."

#### **Safety and Efficacy of Anacetrapib**

The DEFINE trial was an 18-month study in more than 1,600 patients with or at high risk for CHD who were already receiving statins and were at guideline-established LDL-C goal. The

study was designed to assess the lipid-modifying efficacy, safety and tolerability of anacetrapib 100 mg daily added to ongoing statin therapy with or without other lipid-modifying agents.

There were no significant differences between the anacetrapib and placebo-treated patients in mean change from baseline in systolic (0.2 mmHg,  $p=0.83$ ) or diastolic blood pressure (0.0 mmHg,  $p=0.96$ ), nor in the percentage of patients reported to have increased blood pressure. The number of patients with clinically important changes in serum electrolytes (sodium, potassium, chloride and bicarbonate) was not significantly different between those who received anacetrapib and those given placebo during the 76-week treatment period ( $p$  value range 0.25 to 0.99), nor was there any difference in mean change from baseline in aldosterone levels between the two groups over 76 weeks (0.54 pmol/L vs. 0.49 pmol/L, respectively). In addition, there were no cases of rhabdomyolysis (severe muscle injury infrequently associated with lipid-lowering drugs) in either the anacetrapib or the placebo treatment groups. There was one case of elevated liver enzymes (two consecutive values greater than or equal to three times the upper limit of normal) in the anacetrapib-treated patients compared to eight cases in patients given placebo.

An early member of the CETP inhibitor class, torcetrapib, was found to cause an excess of deaths and cardiovascular events. In the DEFINE study, all cardiovascular serious adverse events and deaths from any cause were adjudicated by a blinded, external, independent adjudication committee. Reports of revascularization and heart failure were collected and adjudicated, but were not part of the pre-specified cardiovascular composite endpoint. In DEFINE, pre-specified adjudicated cardiovascular events occurred in 16 patients given anacetrapib (2.0 percent) compared with 21 patients who received placebo (2.6 percent) ( $p=0.40$ ), coronary revascularization was carried out in significantly fewer people given anacetrapib compared with those taking placebo (8 vs. 28, respectively,  $p<0.001$ ), and death from any cause occurred in 11 patients taking anacetrapib and in eight patients given placebo ( $p=0.5$ ). Based on these results, there is confidence in moving forward to study anacetrapib in a large cardiovascular clinical outcomes trial.

Rates of drug-related adverse experiences (AEs), serious AEs, and drug-related serious AEs were similar between the anacetrapib and placebo groups (11.4 percent vs. 10.7 percent, 15.2 percent vs. 14.8 percent, and 0.2 percent vs. 0.5 percent, respectively). Clinical and drug-related AEs leading to discontinuation were also similar in patients taking anacetrapib and those given placebo (5.4 percent vs. 5.7 percent and 2.7 percent vs. 2.2 percent, respectively).

At 24 weeks, treatment with anacetrapib resulted in a placebo-subtracted 40 percent reduction in mean LDL-C (from 2.1 to 1.2 mmol/L vs. 2.1 to 2.0 mmol/L for placebo,  $p<0.001$ )

and a 138 percent increase in mean HDL-C (from 1.0 to 2.6 mmol/L vs. 1.0 to 1.2 mmol/L for placebo,  $p < 0.001$ ). Compared to placebo, anacetrapib also raised mean apolipoprotein (apo) A-1 (a major protein component of HDL particles) by 45 percent, lowered mean apo B (a major protein component of atherogenic lipoprotein particles, including LDL) by 21 percent and reduced mean non-HDL-C by 32 percent ( $p < 0.001$  for all measures). Anacetrapib reduced median Lp(a) (an LDL-like particle) by 36 percent compared to placebo. All changes in lipids were sustained throughout the 76-week treatment period. There were no significant differences between the treatment groups in C-reactive protein (CRP). There was a pre-specified discontinuation rule for patients whose LDL-C fell below 0.64 mmol/L, which occurred in 18 percent of patients treated with anacetrapib and in one patient in the placebo group.

"These additional data add to our enthusiasm for continued study of anacetrapib in a large clinical outcomes trial, an important next step," said Yale Mitchel, M.D., vice president, Cardiovascular Disease, Global Clinical Development and Regulatory Affairs, Merck Research Laboratories.

#### **More than 1,600 patients participated in 18-month study in 20 different countries**

DEFINE was a randomized, double-blind, placebo-controlled trial designed to assess the lipid-modifying efficacy, safety and tolerability of anacetrapib 100 mg daily added to ongoing statin therapy (with or without other lipid-modifying medications) in patients with CHD or CHD risk equivalents. A total of 2,757 participants were screened at 153 centers in 20 different countries, and 1,623 patients were randomized to either anacetrapib or placebo. Patients had baseline LDL-C levels of 1.28 to 2.56 mmol/L while on statin and possibly other LDL-C-lowering therapy, HDL-C levels less than 1.54 mmol/L, and triglycerides levels of 4.56 mmol/L or lower.

The primary efficacy endpoint was the percent change from baseline in LDL-C after 24 weeks of treatment along with the safety and tolerability assessments (i.e., adverse experiences, safety laboratory tests including electrolytes and aldosterone and vital signs including BP, ECG, and physical exam) assessed over the 76-week treatment period. Secondary efficacy endpoints included change from baseline in LDL-C at week 76, as well as HDL-C, non-HDL-C, apo B and apo A-1 after 24 and 76 weeks of treatment.

The pre-specified cardiovascular composite endpoint used for evaluation of safety was comprised of cardiovascular death, nonfatal myocardial infarction, stroke and hospitalization for unstable angina. All cardiovascular serious adverse events and death from any cause were adjudicated by a blinded, external, independent adjudication committee. Reports of revascularization and heart failure were collected and adjudicated, but were not part of the pre-specified cardiovascular composite endpoint. An external, independent safety monitoring

committee reviewed unblinded safety data on a regular basis throughout the study to assure patient safety. All statistical analyses were conducted by the independent statistical data analysis center. Anacetrapib is an investigational medicine and is not approved for use in Canada

### **About Merck**

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### **Merck Forward Looking Statement**

This news release includes “forward-looking statements” within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. The forward-looking statements may include statements regarding product development, product potential, the company’s plans, objectives, expectations and intentions and other statements that are not historical facts. Such statements are based upon the current beliefs and expectations of Merck’s management and are subject to significant risks and uncertainties. Actual results may differ from those set forth in the forward-looking statements.

The following factors, among others, could cause actual results to differ from those set forth in the forward-looking statements: the impact of pharmaceutical industry regulation and health care legislation; Merck’s ability to accurately predict future market conditions; dependence on the effectiveness of Merck’s patents and other protections for innovative products; the risk of new and changing regulation and health policies in the United States and internationally and the exposure to litigation and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck’s 2009 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site ([www.sec.gov](http://www.sec.gov)).

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