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COMBINATION HDL/LDL THERAPY HAS NO EFFECT ON PLAQUE BUILD-UP IN HEART ARTERIES

NEW ORLEANS, La. (March 26, 2007) — For some patients with high cholesterol, even the most aggressive treatment with statin drugs fails to prevent coronary artery disease. Patients with hyperlipidemia – high LDL or “bad” cholesterol and triglycerides, and low HDL or “good” cholesterol – and those with a family history of high cholesterol are at a high risk for atherosclerosis, or plaque build up in the coronary arteries, which can lead to a heart attack or stroke. While lowering LDL levels with statin drugs is effective in reducing risk, adding an agent that raises HDL levels may offer additional benefit.

Two studies presented today at the American College of Cardiology's 56th Annual Scientific Session assessed the effects of adding torcetrapib to atorvastatin among patients to improve their cholesterol levels. Although the ILLUMINATE study and other trials involving torcetrapib were recently stopped because of safety concerns, the effect of the drug on carotid intima-media thickness (CIMT) may provide useful information on whether it slows the progression of atherosclerosis. The studies will be simultaneously published in the *New England Journal of Medicine*. ACC.07 is the premier cardiovascular medical meeting, bringing together cardiologists and cardiovascular specialists to further breakthroughs in cardiovascular medicine.

The “Rating Atherosclerotic Disease Change by Imaging with A New CETp Inhibitor” trials, also known as the RADIANCE studies, tested a combination therapy with torcetrapib and atorvastatin in two groups of patients. RADIANCE 1 involved 907 patients with heterozygous familial hypercholesterolemia

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2 – 2 – 2 LDL/HDL Therapy and CIMT

(HeFH), the type of high cholesterol that runs in families, while RADIANCE 2 enrolled 758 patients with mixed hyperlipidemia.

Both groups of patients started an atorvastatin-only period during which the patients' doses were titrated up until LDL levels reached national guidelines. Subjects were then randomized to either a combination of torcetrapib and atorvastatin or atorvastatin alone. Atherosclerotic progression was assessed by ultrasound twice within the first week and at six-month intervals. The effects of the combination therapy were determined by examining the change in CIMT of 12 predefined carotid segments. Ultrasound is used to measure the thickness of the arterial walls of the common carotid artery, carotid bifurcation and the internal carotid artery to arrive at CIMT, which is generally accepted to be a predictor of coronary atherosclerosis.

Study results showed that the CETP inhibitor torcetrapib led to unparalleled increases of HDL-C and robust decreases of LDL-C but despite this had no benefit on atherosclerosis progression while one secondary endpoint of the study even suggested progression of disease in torcetrapib-treated patients. Also, torcetrapib significantly raised blood pressure, but the negative findings of the RADIANCE trials could not be explained by this undesirable side effect.

"The addition of torcetrapib to statin therapy has no benefit at all on atherosclerosis progression, but it remains to be investigated whether this is a consequence of the molecule Torcetrapib or whether the concept of CETP inhibition is a flawed hypothesis," said John J.P. Kastelein, M.D., Ph.D., of the Academic Medical Center in Amsterdam, and lead author of the studies. "Additional data from the ILLUMINATE study later this year will hopefully shed more light on this issue."

Dr. Kastelein will present the results of the "The Effect of Torcetrapib/Atorvastatin Compared With Atorvastatin Alone on Carotid Intima-Media Thickness in Subjects With Mixed Hyperlipidemia" and "Carotid B-Mode Ultrasound Evaluation of the Anti-Atherosclerotic Efficacy of Torcetrapib/Atorvastatin Compared with Atorvastatin Alone in Subjects With Heterozygous Familial Hypercholesterolemia" studies on Monday, March 26 beginning at 8:58 a.m. in Hall A.

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The American College of Cardiology (www.acc.org) represents the majority of board certified cardiovascular physicians in the United States. Its mission is to advocate for quality cardiovascular care through education, research, promotion, development

and application of standards and guidelines- and to influence health care policy. ACC.07 and the i2 Summit is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in the treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.