

New Analyses Demonstrate that INEGY™ (ezetimibe/simvastatin) was more effective than Atorvastatin (LIPITOR™ or SORTIS™) at Reducing Atherogenic Particles and Raising Protective Particles in Cardiovascular Disease (CVD)

Submitted by: Hill & Knowlton (UK)

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Treating Two Sources of Cholesterol Provides Greater LDL Cholesterol (LDL-C) Reduction and Greater Goal Attainment than Statin Therapy Alone

Prague, Czech Republic, 24 April 2005 – Results from clinical studies presented at the 2005 European Atherosclerosis Society (EAS) annual meeting show that INEGY™ (ezetimibe/simvastatin) provided greater reductions in LDL-C than atorvastatin, and INEGY also has a positive effect on key atherogenic particles - apolipoprotein B (Apo B), apolipoprotein A-1 (Apo A-1) and C-reactive protein, a risk marker for atherosclerosis.^{1,2} INEGY is the first single tablet to provide powerful LDL cholesterol reduction by treating two sources of cholesterol – inhibiting the production of cholesterol mainly in the liver and inhibiting the absorption of cholesterol in the intestine. Atherogenic particles are found in the blood stream and are associated with atherosclerosis, the process by which arteries become narrow over time due to the formation of cholesterol plaques. In addition, INEGY demonstrated a greater reduction in Apo B/Apo A-1, an interesting finding as evaluating plasma levels of

Apo B, Apo A-1 and CRP are emerging as possible additional ways to assess cardiovascular disease (CVD) risk.

Christie Ballantyne, M.D., director of the Center for Cardiovascular Disease Prevention, Methodist DeBakey Heart Center, Houston, Texas, U.S.A., and lead investigator of the clinical studies noted, “Recent data shows that INEGY, which treats the two sources of cholesterol, was more effective than atorvastatin in reducing LDL-C and achieving greater goal attainment. In addition, INEGY demonstrated a greater reduction in Apo B and Apo A-1, an interesting finding given ongoing research in identifying additional risk markers for heart disease.”

Dr. Ballantyne presented similar data at the 2005 American College of Cardiology Annual Scientific Sessions. In that clinical study, INEGY demonstrated superior LDL-C lowering and greater goal attainment in comparison to atorvastatin, as well as comparable reductions in CRP.

INEGY was more effective than atorvastatin at reducing the ratio Apo B and Apo A-

The study, involving 1,902 patients with hypercholesterolemia, aimed to investigate the ratios between atherogenic particles (that increase atherosclerosis) and cardioprotective particles (that reduce atherosclerosis) after six weeks of treatment with either atorvastatin or INEGY, thus providing an indication of a potential cholesterol-depositing capacity of the blood during treatment with either therapy. The efficacy of INEGY and atorvastatin was monitored in terms of percent change improvement of Apo B/Apo A-I and non-HDL-C/HDL-C ratios at four milligram-equivalent statin dose comparisons (10, 20,

40, 80 mg) and averaged across dose ranges after six weeks of treatment, by total population and by baseline triglyceride level (<200, ≤200mg/dL). When averaged across dose ranges, in this study INEGY demonstrated significantly greater improvements, compared with atorvastatin, in reducing Apo B/Apo A-I ratios (INEGY -45 percent vs. atorvastatin -38.7 percent; p≤0.00

1) at all milligram-equivalent statin doses. These results also significantly correlated with more practical and easily calculated non-HDL-C/HDL-C ratios (INEGY -52 percent vs. atorvastatin -43.8 percent; p≤0.001).

Commenting further on the data, Dr. Ballantyne said, "There is mounting evidence that aggressive lipid-lowering efficacy shows cardiovascular benefits for the patients studied. This leads many practitioners to conclude that lower LDL cholesterol is better, particularly when treating patients with multiple risk factors."

INEGY lowered hs-CRP similarly to atorvastatin

Further results of the study show that INEGY provides the same reduction in highly sensitive C-reactive protein (hs-CRP), an independent marker of CVD risk, as atorvastatin. Geometric mean reductions from baseline hs-CRP levels were similar averaged across dose ranges (INEGY 24.8 percent vs. atorvastatin 25.1 percent), and similar by milligram-equivalent statin doses suggesting INEGY lowers hs-CRP similarly to atorvastatin across the dose ranges and by milligram-equivalent statin doses.

The lipid lowering effects of INEGY are consistent across gender, race, age and baseline LDL-C levels

Results of another trial presented at the meeting confirm the enhanced and consistently greater lipid-lowering effects of INEGY versus simvastatin across gender, race, age and baseline LDL-C levels, highlighting INEGY as an effective and reliable therapeutic option for the treatment of primary hypercholesterolemia.³ In the study, pooled data from three similarly designed studies was analyzed. After a six to eight week washout of lipid lowering drugs and four week diet / placebo run-in, 3,083 patients with LDL-C 3.8 – 6.5 mmol/L and triglycerides (TG) ≤4.0mmol/L were randomized to receive either INEGY (10/10, 10/20, 10/40, 10/80 mg), simvastatin (10, 20, 30, 80 mg), EZETROL (10 mg), or placebo, for 12 weeks. The primary endpoint in each study was the percent change from baseline in LDL-C. Patient subgroups were defined according to gender, race, baseline age, and baseline LDL-C.

Treatment with INEGY led to significantly greater improvements in LDL-C, non HDL-C, Apo B, TG and CRP compared to simvastatin alone. Additionally, more patients attained LDL-C goal levels (<2.60 mmol/L) with INEGY than with simvastatin. These results were consistent across all subgroups and confirm that greater cholesterol goal-attainment was achieved by treating two sources of cholesterol through Dual Inhibition INEGY, than with the single inhibition of statin therapy. The potential clinical outcomes importance of reducing LDL-C to new lower levels must be confirmed by prospective clinical trials such as IMPROVE-IT, a trial that has been initiated by Merck and Schering-Plough.

Baseline results for new outcomes study investigating the efficacy of INEGY on CV events in aortic stenosis (SEAS study)

Additionally, baseline results for the SEAS study were also announced at the meeting,⁴

The study, involving 1,873 patients from 173 study sites in seven countries, will

investigate whether treatment with INEGY compared to placebo reduces the risk of a

composite endpoint of major CV events including aortic valve replacement in patients with in aortic stenosis. Secondary endpoints include aortic valve events, echocardiographic progression of aortic stenosis (AS) and safety and tolerability of around four years exposure to daily INEGY. AS patients have a high frequency of traditional CV risk factors, and the SEAS study will provide valuable data on the effect of aggressive lipid lowering therapy through Dual Inhibition with INEGY on AS. Final results of the outcomes study are expected in 2008. The SEAS study is just one of several outcomes studies currently underway to demonstrate the additional benefits of INEGY on CVD.

Defining two sources of cholesterol

Cholesterol in the body originates from two main sources: production by hepatic and extra hepatic tissues and absorption in the intestine. Cholesterol-lowering agents (statins) reduce cholesterol levels through inhibition of one pathway; that is, by inhibiting the synthesis (production) of cholesterol in the liver. EZETROL™ (ezetimibe), the first cholesterol absorption inhibitor, works by inhibiting intestinal absorption of cholesterol. Cholesterol present in the intestines comes from both dietary sources (food) and, predominantly, from internal cholesterol production that is recirculated in the bile. INEGY (ezetimibe/simvastatin) is the first single product to powerfully target both of the main sources of cholesterol in the body, production and absorption. The human body's natural control mechanism responds to the reduced cholesterol plasma level by an increased expression of LDL receptor, which is the main mechanism for LDL reduction. Thus, targeting production and absorption with use of INEGY provides a significantly greater reduction of LDL-C plasma levels.

About INEGY

INEGY (ezetimibe/simvastatin) has been developed and is being marketed by Merck & Co., Inc. (NYSE: MRK) and Schering-Plough Corporation (NYSE: SGP) in connection with a partnership formed by both companies to develop and market worldwide (excluding Japan) new prescription medicines in cholesterol management. Branded as INEGY in Europe, Middle East and Africa, the product is indicated (in the EU) as adjunctive therapy to diet for use in patients with primary (heterozygous familial and non-familial) hypercholesterolemia or mixed hyperlipidemia where use of a combination product is appropriate: 1)

patients not appropriately controlled with a statin alone; and 2) patients already treated with a statin and ezetimibe. It has been approved in more than 30 nations around the world including the United States, where the Food and Drug Administration approved it on July 23, 2004 – under the brand name VYTORIN – for the treatment of high LDL cholesterol as adjuvant therapy to diet. The tolerability profile of INEGY is similar to simvastatin or atorvastatin and is maintained over long-term therapy.

About Merck

Merck & Co., Inc. is a global research-driven pharmaceutical company dedicated to putting patients first. Established in 1891, Merck discovers, develops, manufactures and markets vaccines and medicines in over 20 therapeutic categories. The company also devotes extensive efforts to increase access to medicines through far-reaching programs that not only donate Merck medicines but help deliver them to the people who need them. Merck also publishes unbiased health information as a not-for-profit service. For more information, visit www.merck.com

About Schering-Plough

Schering-Plough Corporation is a global science-based health care company with leading prescription, consumer and animal health products. Through internal research and collaborations with partners, Schering-Plough discovers, develops, manufactures and markets advanced drug therapies to meet important medical needs. Schering-Plough's vision is to earn the trust of the physicians, patients and customers served by its more than 30,000 people around the world. The company is based in Kenilworth, N.J., and its Web site is www.schering-plough.com.

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3. A Rossebo: Increased cardiovascular risk factors in aortic stenosis – baseline characteristics of the simvastatin+ezetimibe in aortic stenosis study; 2005 Annual Meeting of the European Atherosclerosis Society (EAS) – 24 April 2005 – Poster presentation

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