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VYTORIN[®] (ezetimibe/simvastatin) Significantly Reduced Major Vascular Events in Patients With Chronic Kidney Disease in a New 9,000-Patient Investigational Study

SHARP is the First and Only Prospective Clinical Study in Patients With Chronic Kidney Disease to Show That an LDL Cholesterol-Lowering Medicine Reduced Major Vascular and Atherosclerotic Events

DENVER, CO, Nov. 20, 2010 – In a new investigational study of VYTORIN[®] (ezetimibe/simvastatin), the cholesterol-lowering medicine from Merck (known as MSD outside the US and Canada), VYTORIN 10/20 mg reduced the incidence of first major vascular events -- defined as non-fatal heart attacks or cardiac death, stroke or any revascularization procedure -- by a highly statistically significant 16.1 percent compared to placebo (p=0.0010). This was the pre-specified primary endpoint of the study. The SHARP (**S**tudy of **H**eart and **R**enal **P**rotection) study involved more than 9,000 patients who, on average, had advanced or end-stage chronic kidney disease (CKD), and is the first prospective clinical study in patients with CKD to demonstrate the benefit of lowering LDL (bad) cholesterol on major vascular events. The results were presented today during Renal Week, the American Society of Nephrology's annual meeting, by Professor Colin Baigent, F.F.P.H., F.R.C.P., and Dr. Martin Landray, Ph.D., F.R.C.P., the principal investigators of SHARP, from the Oxford University Clinical Trial Service Unit (CTSU), Oxford, England.

"This is an important study," said Dr. Peter S. Kim, Ph.D., president, Merck Research Laboratories. "Patients with CKD have a high risk of ischemic vascular disease and increased rates of heart attack, stroke, other cardiovascular events and revascularization procedures. In SHARP, the investigational use of VYTORIN significantly reduced the risk of these events in a spectrum of patients with chronic kidney disease -- and this was the first demonstration that an LDL-cholesterol lowering medicine could do so."

Merck plans to seek regulatory approvals for the use of VYTORIN in patients with CKD based on the results from the SHARP study. VYTORIN is currently indicated as adjunctive therapy to diet for the reduction of LDL cholesterol in patients with primary hypercholesterolemia or mixed hyperlipidemia.

VYTORIN[®] is a registered trademark of MSP Singapore Company, LLC.

VYTORIN is a prescription medicine and should not be taken by people who are hypersensitive to any of its components. VYTORIN should not be taken by anyone with active liver disease or unexplained persistent elevations of serum transaminases. Women who are of childbearing age (unless highly unlikely to conceive), are nursing or who are pregnant should not take VYTORIN.

SHARP is the largest prospective study of LDL-lowering in patients with CKD

SHARP is the largest clinical trial of VYTORIN conducted to date, and enrolled a total of 9,438 patients under the care of a nephrologist for chronic kidney disease. One-third of patients were undergoing dialysis therapy for end-stage kidney disease at the time of entry, and the remaining patients were pre-dialysis patients with advanced CKD with an average estimated glomerular filtration rate (a measure of kidney function) of 26.5 ml/min/1.73m². Patients with a prior history of myocardial infarction or a revascularization procedure were excluded from the study. At randomization, the average LDL cholesterol of all patients enrolled in SHARP was 108 mg/dL.

Patients were initially randomized in a ratio of 4:4:1 to receive VYTORIN 10/20 mg daily versus placebo versus simvastatin 20 mg alone (for purposes of assessing drug safety). After one year, patients initially allocated to simvastatin alone were re-randomized to either VYTORIN 10/20 mg daily or placebo for the remainder of the study period. Patients were followed for a median of 4.9 years.

The protocol-specified primary endpoint for the study was the incidence of first major vascular events, defined as the composite of non-fatal heart attack or cardiac death, stroke or revascularization procedure in the two groups randomized to VYTORIN or placebo at study initiation. (This analysis did not include patients initially randomized to simvastatin alone for the first year.) In the intention-to-treat analysis, VYTORIN reduced first major vascular events by 16.1 percent compared to placebo (p=0.0010). In the group that received VYTORIN (n=4,193) 15.2 percent of patients had a major vascular event, compared to 17.9 percent of patients taking placebo (n=4,191).

In addition, in the full study population of patients, including patients who took simvastatin alone for the first year and were then re-randomized to either VYTORIN or placebo, VYTORIN reduced first major vascular events by 15.3 percent compared to placebo (p=0.0012). The rate of major vascular events in patients taking VYTORIN (n=4,650) was 15.1 percent, compared to 17.6 percent of patients taking placebo (n=4,620).

Results on Major Atherosclerotic Events Also Presented

Based on information from clinical studies of other LDL-lowering medicines that became available after the original SHARP study protocol was implemented in 2003 and before the study ended, the independent SHARP Steering Committee determined that the most relevant "key outcome" for the study should be the incidence of first "major atherosclerotic events." Major atherosclerotic events were defined as the combination of non-fatal heart attack, coronary death, ischemic stroke or any revascularization procedure; this analysis excluded non-coronary cardiac

death and hemorrhagic stroke from the protocol-specified primary endpoint of major vascular events. (The Steering Committee's rationale and statistical analysis plan are discussed in a paper published on-line in the *American Heart Journal*). In the intention-to-treat analysis, VYTORIN also reduced first major atherosclerotic events by 16.5 percent compared to placebo ($p=0.0022$). The rate of first major atherosclerotic events in patients taking VYTORIN ($n=4,650$) was 11.3 percent, compared to 13.4 percent in patients taking placebo ($n=4,620$).

In the first year of the trial, VYTORIN 10/20 mg lowered LDL cholesterol by 40 percent compared to placebo, while simvastatin 20 mg lowered LDL cholesterol by 28 percent versus placebo; the reduction achieved by VYTORIN was 30 percent greater than that achieved by simvastatin alone. After two and half years of treatment, which was approximately mid-way through the study, VYTORIN lowered LDL cholesterol by 32 mg/dL, or 30 percent from baseline, compared to placebo.

The researchers noted that the reduction in major vascular events and major atherosclerotic events based on the LDL-cholesterol reduction achieved with VYTORIN in SHARP was consistent with reduction of outcomes that would be predicted based on the recently published Cholesterol Treatment Trialists' (CTT) meta-analysis of large-scale statin trials. The CTT analysis, published online in *The Lancet*, examined the relationship between LDL-cholesterol lowering and reduced rates of cardiovascular events.

One of the secondary endpoints for SHARP was the progression to end-stage renal disease (ESRD) among patients who were not yet on dialysis at the start of the study. A patient was considered to have progressed to ESRD if they started long-term dialysis or proceeded to kidney transplantation following randomization. On this endpoint, there was no difference between VYTORIN and placebo; 33.9 percent of patients receiving VYTORIN ($n=3,117$) proceeded to ESRD, compared to 34.6 percent of patients on placebo ($n=3,130$).

VYTORIN 10/20 mg Safety Profile Over the Nearly Five Years of Follow-up

In terms of assessing safety in SHARP, the researchers assessed reports of serious adverse events as well as adverse events that were pre-specified: cancer, myopathy with levels of creatine phosphokinase (CK) >10 x but ≤ 40 x upper limit of normal (ULN), and reports of myopathy with CK >40 x ULN, hepatitis, persistently elevated liver enzymes (ALT/AST >3 x ULN), complications of gallstones, other hospitalizations for gallstones, and pancreatitis without gallstones.

Overall, the safety profile of VYTORIN 10/20 mg in this study was consistent with the profile described in the current approved label.

VYTORIN ($n=4,650$) was comparable to placebo ($n=4,620$) in the incidence of cancer and cancer-related deaths: cancer was reported in 9.4 percent of patients taking VYTORIN versus 9.5 percent of patients taking placebo ($p=0.89$); mortality due to cancer was reported in 3.2 percent of patients taking VYTORIN versus 2.8 percent of patients taking placebo ($p=0.20$).

For other safety analyses that were pre-specified, VYTORIN was also comparable to placebo in the incidence of CK $> 10 \times$ but $\leq 40 \times$ ULN (0.4 percent for VYTORIN versus 0.3 percent for placebo), CK $>40 \times$ ULN (0.1 percent in each group), hepatitis (0.5 percent for VYTORIN versus 0.4 percent for placebo), persistently elevated ALT/AST $>3 \times$ ULN (0.6 percent in each group), complications of gallstones (1.8 percent for VYTORIN versus 1.6 percent for placebo), other hospitalizations for gallstones (0.5 percent for VYTORIN versus 0.6 percent for placebo) and pancreatitis without gallstones (0.3 percent for VYTORIN versus 0.4 percent for placebo).

"Merck is proud to support clinical trials such as SHARP and we thank the Oxford University and the thousands of patients and health care professionals who participated in SHARP for their contributions to this study to address this important medical question for patients with CKD," Kim said.

Important Information about VYTORIN

VYTORIN contains simvastatin and ezetimibe. VYTORIN is indicated as adjunctive therapy to diet for the reduction of elevated total cholesterol, LDL cholesterol, Apo B, triglycerides and non-HDL cholesterol and to increase HDL cholesterol in patients with primary (heterozygous familial and non-familial) hypercholesterolemia or mixed hyperlipidemia.

VYTORIN is not indicated to reduce major vascular events or atherosclerotic events in patients with chronic kidney disease. The prescribing information for VYTORIN states that it has not been shown to reduce heart attacks or strokes more than simvastatin alone.

No dosage adjustment is necessary in patients with mild or moderate renal impairment. Caution should be exercised when VYTORIN is administered to patients with severe renal insufficiency. VYTORIN should not be initiated in such patients unless the patient has already tolerated treatment with simvastatin.

VYTORIN is a prescription medicine and should not be taken by people who are hypersensitive to any of its components. VYTORIN should not be taken by anyone with active liver disease or unexplained persistent elevations of serum transaminases. Women who are of childbearing age (unless highly unlikely to conceive), are nursing or who are pregnant should not take VYTORIN.

Muscle pain, tenderness or weakness in people taking VYTORIN should be reported to a doctor promptly because these could be signs of a serious side effect. VYTORIN should be discontinued if myopathy is diagnosed or suspected. To help avoid serious side effects, patients should talk to their doctor about medicine or food they should avoid while taking VYTORIN.

In three placebo-controlled, 12-week trials, the incidence of consecutive elevations ($\geq 3 \times$ ULN) in serum transaminases were 1.7 percent overall for patients treated with VYTORIN and 2.6 percent for patients treated with VYTORIN 10/80 mg. In controlled long-term (48-week) extensions, which included both newly-treated and previously-treated patients, the incidence of consecutive elevations ($\geq 3 \times$ ULN) in serum transaminases was 1.8 percent overall and 3.6 percent for patients

treated with VYTORIN 10/80 mg. These elevations in transaminases were generally asymptomatic, not associated with cholestasis and returned to baseline after discontinuation of therapy or with continued treatment. Doctors should perform blood tests before, and periodically during treatment with VYTORIN when clinically indicated to check for liver problems. People taking VYTORIN 10/80 mg should receive an additional liver function test prior to and three months after titration and periodically during the first year.

Due to the unknown effects of increased exposure to ezetimibe (an ingredient in VYTORIN) in patients with moderate or severe hepatic insufficiency, VYTORIN is not recommended in these patients. The safety and effectiveness of VYTORIN with fibrates have not been established; therefore, co-administration with fibrates is not recommended. Caution should be exercised when initiating VYTORIN in patients treated with cyclosporine and in patients with severe renal insufficiency.

VYTORIN has been evaluated for safety in more than 10,100 patients in clinical trials. In clinical trials, the most commonly reported side effects, regardless of cause, included headache (5.8 percent), increased ALT (3.7 percent), myalgia (3.6 percent), upper respiratory tract infection (3.6 percent), and diarrhea (2.8 percent).

VYTORIN is available as tablets containing 10 mg of ezetimibe combined with 10, 20, 40 or 80 mg of simvastatin (VYTORIN 10/10, 10/20, 10/40 or 10/80 mg, respectively).

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com.

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. Such statements may include, but are not limited to, statements about the benefits of the merger between Merck and Schering-Plough, including future financial and operating results, the combined 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 possibility that the expected synergies from the merger of

Merck and Schering-Plough will not be realized, or will not be realized within the expected time period; the impact of pharmaceutical industry regulation and health care legislation; the risk that the businesses will not be integrated successfully; disruption from the merger making it more difficult to maintain business and operational relationships; 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 U.S. 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).

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Prescribing Information and Patient Product Information for VYTORIN[®] is available at http://www.msppharma.com/msppharma/documents/vytorin_pi.pdf and http://www.msppharma.com/msppharma/documents/vytorin_ppi.pdf.
