Lilly, Kowa and Kowa Pharmaceuticals America Announce Co-Promotion and Licensing Agreement

Companies to co-promote newly-approved statin LIVALO in the U.S. market
Lilly licenses LIVALO commercialization rights for Latin America

INDIANAPOLIS and MONTGOMERY, Ala., Dec 23, 2009 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY), Kowa Company, Limited, and Kowa's U.S. subsidiary, Kowa Pharmaceuticals America, Inc., today announced that Lilly and Kowa Pharmaceuticals America have entered into a co-promotion agreement in the United States to commercialize LIVALO(R) (pitavastatin). Lilly and Kowa have also entered into a licensing agreement in Latin America. LIVALO is a statin approved by the U.S. Food and Drug Administration (FDA) in August 2009 for the treatment of primary hyperlipidemia and mixed dyslipidemia.

Under the terms of the agreements, Kowa Pharmaceuticals America will receive an undisclosed upfront payment. Lilly and Kowa Pharmaceuticals America will co-promote LIVALO in the U.S. market, with both companies providing sales force resources and sharing development and marketing costs. Kowa Pharmaceuticals America will record all U.S. sales of LIVALO and will pay Lilly an escalating co-promotion fee based on the level of annual net sales. In addition, Lilly has acquired an exclusive license from Kowa to commercialize LIVALO in Latin American markets, including Mexico, Central America and South America. Additional deal terms were not disclosed.

"We are pleased to partner with Kowa to help bring this new statin to market and provide patients a new option to help control their cholesterol," said John Lechleiter, Ph.D., Lilly chairman and chief executive officer. "Our co-promotion arrangement in the U.S. and licensing arrangement in Latin America will allow Lilly to expand our product offerings in the cardiovascular therapeutic area and more efficiently utilize our existing cardiovascular sales force."

"Physicians are challenged by some patients who do not always do well on their current statin therapy, and who also must deal with potential interactions with other medications. LIVALO offers a new statin option, with LDL lowering consistent with the commonly administered doses of Lipitor(R) and Zocor(R), and significantly greater LDL lowering in the elderly compared to Pravachol(R)," stated LeRoy LeNarz, M.D., senior medical director at Lilly.

"It is with great pleasure that we partner with an internationally-renowned company like Lilly," said Yoshihiro Miwa, Kowa president and CEO. "With a joint effort by Lilly, Kowa and Kowa Pharmaceuticals America, we hope to pave the way for the efficient market entry and establish a presence with LIVALO in the statin market in the U.S. and Latin America."

"We are excited to partner with Lilly as we work to establish the LIVALO brand and expand Kowa Pharmaceuticals America's presence in the U.S. market," said Ben Stakely, president and CEO of Kowa Pharmaceuticals America.

About LIVALO

LIVALO is a fully synthetic statin originating from Japan. The efficacy of LIVALO has been evaluated against atorvastatin, simvastatin, and pravastatin in patients with primary hyperlipidemia or mixed dyslipidemia. In these studies, LIVALO effectively reduced LDL-C, including in patients with diabetes, the elderly, and patients with 2 or more risk factors for coronary artery disease. Unlike many statins, LIVALO is only minimally metabolized by the liver Cytochrome P450 enzyme system, suggesting that the potential for clinically significant drug interactions between LIVALO and drugs that inhibit or that are metabolized by CYP450 enzymes, including warfarin, would be reduced.

Since its launch in Japan, South Korea, Thailand and China, LIVALO has been successfully used in these countries to treat hypercholesterolemia and familial hypercholesterolemia, and has accumulated millions of patient-years of exposure. In Japan, sales of LIVALO for fiscal year 2008 reached 34 billion yen (approximately $380 million) and its market share was about 12%.

About Dyslipidemia and Hypercholesterolemia

Dyslipidemia refers to abnormal levels of fatty substances in the blood, or a disorder of the production or breakdown process of lipoprotein. Dyslipidemia may be marked by an elevation of total cholesterol, LDL-C, and triglyceride (TG) concentrations and a decrease in HDL-C in the blood. An elevated level of cholesterol in the blood is called hypercholesterolemia, commonly

referred to as high cholesterol.

LDL-C lowering is well established as one of the strongest independent predictors of cardiovascular morbidity and mortality. Despite the availability of treatments in the U.S., there is still a need for better control of and treatment for dyslipidemia. According to the American Heart Association, approximately one out of every three American adults has an LDL cholesterol level of 130mg/dL or higher, which is a major risk factor for coronary heart disease (CHD) and stroke. In addition, less than half of patients who qualify for any kind of lipid-modifying treatment for CHD risk reduction are receiving it, and only about one-third of patients who are on treatment are achieving their LDL goals.

IMPORTANT SAFETY INFORMATION ABOUT LIVALO(R) (PITAVASTATIN) TABLETS

INDICATIONS AND USAGE

Drug therapy should be one component of multiple-risk-factor intervention in individuals who require modifications of their lipid profile. Lipid-altering agents should be used in addition to a diet restricted in saturated fat and cholesterol only when the response to diet and other nonpharmacological measures has been inadequate.

LIVALO is a HMG-CoA reductase inhibitor indicated as an adjunctive therapy to diet to reduce elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and to increase HDL-C in adult patients with primary hyperlipidemia or mixed dyslipidemia.

Limitations of Use: Doses of LIVALO greater than 4 mg once daily were associated with an increased risk for severe myopathy in premarketing clinical studies. Do not exceed 4 mg once daily dosing of LIVALO. The effect of LIVALO on cardiovascular morbidity and mortality has not been determined. LIVALO has not been studied in patients with severe renal impairment (glomerular filtration rate < 30 mL/min/1.73 m2) not on hemodialysis. LIVALO should not be used in this patient population. LIVALO has not been studied with the protease inhibitor combination lopinavir/ritonavir. LIVALO should not be used with this combination of protease inhibitors. LIVALO has not been studied in Fredrickson Type I, III, and V dyslipidemias.

General Dosing Information: The dose range for LIVALO is 1 to 4 mg orally once daily at any time of the day with or without food. The recommended starting dose is 2 mg and the maximum dose is 4 mg. The starting dose and maintenance doses of LIVALO should be individualized according to patient characteristics, such as goal of therapy and response.After initiation or upon titration of LIVALO, lipid levels should be analyzed after 4 weeks and the dosage adjusted accordingly.

*Dosage in Patients with Renal Impairment:P*atients with moderate renal impairment (glomerular filtration rate 30 to < 60 mL/min/1.73 m2) and end -stage renal disease receiving hemodialysis should receive a starting dose of LIVALO 1 mg once daily and a maximum dose of LIVALO 2 mg once daily. LIVALO should not be used in patients with severe renal impairment (glomerular filtration rate < 30 mL/min/1.73 m2) In patients taking erythromycin, a dose of LIVALO 1 mg once daily should not be exceeded. In patients taking rifampin, a dose of LIVALO 2 mg once daily should not be exceeded.

CONTRAINDICATIONS

The use of LIVALO is contraindicated in the following conditions:

- Patients with a known hypersensitivity to any component of this product. Hypersensitivity reactions including rash, pruritus, and urticaria have been reported with LIVALO.
- Patients with active liver disease which may include unexplained persistent elevations of hepatic transaminase levels
- Women who are pregnant or may become pregnant. Because HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, LIVALO may cause fetal harm when administered to pregnant women. Additionally, there is no apparent benefit to therapy during pregnancy, and safety in pregnant women has not been established. If the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus and the lack of known clinical benefit with continued use during pregnancy.
- Nursing mothers. Animal studies have shown that LIVALO passes into breast milk. Since HMG-CoA reductase inhibitors have the potential to cause serious adverse reactions in nursing infants, LIVALO, like other HMG-CoA reductase inhibitors, is contraindicated in pregnant or nursing mothers.

-- Co-administration with cyclosporine.

WARNINGS AND PRECAUTIONS

Skeletal Muscle Effects: Cases of myopathy and rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with HMG-CoA reductase inhibitors, including LIVALO. These risks can occur at any dose level, but increase in a dose-dependent manner.LIVALO should be prescribed with caution in patients with predisposing factors for myopathy. These factors include advanced age (>65 years), renal impairment, and inadequately treated hypothyroidism. The risk of myopathy may also be increased with concurrent administration of fibrates or lipid-modifying doses of niacin. LIVALO should be administered with caution in patients with impaired renal function, in elderly patients, or when used concomitantly with fibrates or lipid-modifying doses of niacin. LIVALO therapy should be discontinued if markedly elevated creatine kinase (CK) levels occur or myopathy is diagnosed or suspected. LIVALO therapy should also be temporarily withheld in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g., sepsis, hypotension, dehydration, major surgery, trauma, severe metabolic, endocrine, and electrolyte disorders, or uncontrolled seizures). All patients should be advised to promptly report unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.

Liver Enzyme Abnormalities and Monitoring: Increases in serum transaminases (aspartate aminotransferase [AST]/serum glutamic-oxaloacetic transaminase, or alanine aminotransferase [ALT]/serum glutamic-pyruvic transaminase) have been reported with HMG-CoA reductase inhibitors, including LIVALO. In most cases, the elevations were transient and resolved or improved on continued therapy or after a brief interruption in therapy.

In placebo-controlled Phase 2 studies, ALT >3 times the upper limit of normal was not observed in the placebo, LIVALO 1 mg, or LIVALO 2 mg groups. One out of 202 patients (0.5%) administered LIVALO 4 mg had ALT >3 times the upper limit of normal.

It is recommended that liver enzyme tests be performed before and at 12 weeks following both the initiation of therapy and any elevation of dose and periodically (e.g., semiannually) thereafter. Patients who develop increased transaminase levels should be monitored until the abnormalities have resolved. Should an increase in ALT or AST of >3 times upper limit of normal persist, reduction of dose or withdrawal of LIVALO is recommended.

As with other HMG-CoA reductase inhibitors, LIVALO should be used with caution in patients who consume substantial quantities of alcohol. Active liver disease, which may include unexplained persistent transaminase elevations, is a contraindication to the use of LIVALO.

ADVERSE REACTIONS:

The following serious adverse reactions are discussed in greater detail in the full prescribing information:

-- rhabdomyolysis (a serious muscle disorder) with myoglobinuria (a laboratory test result), and acute renal (kidney) failure and myopathy including myositis (muscular pains), and
-- liver enzyme abnormalities (a laboratory test result).

In controlled clinical trials of up to 12 weeks duration adverse reactions were infrequent, the common adverse reactions, including their MedDRA and common names, reported by 2% or more of treated patients are: back pain, constipation or diarrhea, myalgia (muscular pain), and pain in the extremities (pain in arms or legs). Other adverse reactions reported from clinical studies were arthralgia (joint pain), headache, influenza (the flu), and nasopharyngitis (common cold). The following laboratory abnormalities have also been reported: elevated creatine phosphokinase, transaminases, alkaline phosphatase, bilirubin, and glucose.

In controlled clinical studies and their open-label extensions, 3.9% (1 mg), 3.3% (2 mg), and 3.7% (4 mg) of pitavastatin-treated patients were discontinued due to adverse reactions. The most common adverse reactions that led to treatment discontinuation were: elevated creatine phosphokinase (0.6% on 4 mg) and myalgia (0.5% on 4 mg).

DRUG INTERACTIONS:

As with other statin medications there is a chance of certain drug interactions while taking LIVALO. Caution is advised. The physician should consult the full prescribing information regarding suggested dose reductions or avoidance of LIVALO therapy when coadminstration of any of the following is being considered:

-- the AIDS drugs, lopinavir and ritonavir. LIVALO should not be used with

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    this drug combination,
--  the antibiotics, erythromycin and rifampin. A LIVALO dose reduction may
    be indicated.
--  the cholesterol drugs, fibrates and niacin.  A LIVALO dose reduction may
    be indicated.
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While taking LIVALO, the patient should be advised not to start taking any of these medicines without speaking to their doctor or pharmacist first. Additional drug-drug pharmacokinetic interaction studies were conducted; the results of these studies are tabulated in the full prescribing information.

PATIENT COUNSELING INFORMATION

The patient should be informed of the following:

Dosing Time: LIVALO can be taken at any time of day with or without food.

Muscle Pain: Patients should be advised to promptly notify their physician of any unexplained muscle pain, tenderness, or weakness. They should discuss all medication, both prescription and over the counter, with their physician.

Pregnancy: Women of childbearing age should use an effective method of birth control to prevent pregnancy while using LIVALO. Discuss future pregnancy plans with your healthcare professional, and discuss when to stop LIVALO if you are trying to conceive. If you are pregnant, stop taking LIVALO and call your healthcare professional.

Breastfeeding: Women who are breastfeeding should not use LIVALO. If you have a lipid disorder and are breastfeeding, stop taking LIVALO and consult with your healthcare professional.

Liver Enzymes: It is recommended that liver enzymes be checked before and at 12 weeks following both the initiation of therapy and any elevation of dose, and periodically (e.g., semiannually) thereafter.

For complete product prescribing information you should consult the current LIVALO (pitavastatin) package insert which may be found on the Kowa Pharmaceuticals America, Inc. web page at http://www.kowapharma.com/companyLivalo.htm

About Kowa Company, Ltd. and Kowa Pharmaceuticals America, Inc.

Kowa Company, Ltd. is a privately held multinational company headquartered in Nagoya, Japan. Established in 1894, Kowa is actively engaged in various manufacturing and trading activities in the fields of pharmaceutical, life science, information technology, textiles, machinery and various consumer products. Kowa's pharmaceutical division is focused on cardiovascular therapeutics. In the US, Kowa has two subsidiaries in the pharmaceutical business, Kowa Pharmaceuticals America, Inc. and Kowa Research Institute, Inc., located in the Research Triangle Park area of North Carolina and responsible for the clinical development of Kowa's drug candidates.

Kowa Pharmaceuticals America, Inc. is a specialty pharmaceutical company focused primarily in the area of cardiometabolic disease. The company started in 2001 as ProEthic Pharmaceuticals, Inc., and a majority stake in the company was acquired by Kowa Company, Ltd. in September, 2008. A privately held company, Kowa Pharmaceuticals America focuses its efforts on the acquisition, development, licensing and marketing of pharmaceutical products. Its lead product, LIPOFEN(R) (fenofibrate capsules), is indicated as adjunctive therapy to diet to reduce elevated triglycerides and to increase HDL-C in adult patients with primary hypercholesterolemia or mixed dyslipidemia.

For more information about KPA, please visit www.kowapharma.com.

About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers - through medicines and information - for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com. C: LLY

This news release contains forward-looking statements. These statements are subject to known and unknown risks and uncertainties that may cause actual future experience and results to differ materially from the statements made. Factors that might cause such a difference include, among others, Lilly and Kowa' abilities to successfully commercialize and market Livalo, competition from other pharmaceutical companies (including generic versions of other statin products), potential regulatory

developments affecting the product, and other factors described in Lilly's most recent filings with the Securities and Exchange Commission. For additional information about the factors that affect the company's business, please see Lilly's latest Form 10-K, filed February 2009, and Form 10-Q filed October 2009. Lilly undertakes no duty to update forward-looking statements.

LIVALO(R) (pitavastatin, Kowa Pharmaceuticals America Inc.)

Lipitor(R) (atorvastatin, Pfizer Inc.)

Zocor(R) (simvastatin, Merck and Co., Inc)

Pravachol(R) (pravastatin, Bristol-Myers Squibb Company)

SOURCE Eli Lilly and Company

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