Lilly Announces Review of Data on Long-Term Raloxifene Treatment for Postmenopausal Osteoporosis Published in Current Medical Research & Opinion

INDIANAPOLIS, Aug. 9, 2011 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that data on EVISTA® (raloxifene HCl tablets) therapy for more than three years was published online in *Current Medical Research & Opinion*. The review includes summaries of previously published information; new, previously unpublished observations; and new data on EVISTA use. EVISTA is indicated for the treatment of osteoporosis in postmenopausal women and reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis.

The majority of available data came from the Multiple Outcomes of Raloxifene Evaluation (MORE) trial and the Continued Outcomes of Raloxifene Evaluation (CORE) trial. In these trials, patients were evaluated for up to eight years. While available information is supportive of EVISTA use for more than three years, the optimum duration of EVISTA therapy is not known.

"Because of the chronic nature of postmenopausal osteoporosis and the risk of invasive breast cancer associated with the disease in postmenopausal women with osteoporosis, it is critical to evaluate medications that treat these conditions that require therapy over a prolonged period of time," said lead author Robert Recker, M.D., professor of medicine, chief, division of endocrinology, director, Osteoporosis Research Center, Creighton University School of Medicine.

Use of EVISTA was evaluated by changes in vertebral fracture risk reduction, bone mineral density (BMD), markers of bone turnover, iliac crest bone biopsies, and invasive breast cancer risk reduction:

- *Vertebral fracture risk reduction:* In the MORE trial, the relative risk reduction during the fourth year of the study was similar to the relative risk reduction during years zero to three.
- *BMD:* Patients who stopped EVISTA therapy in the one-year period between the end of the MORE trial and the beginning of the CORE trial experienced a significant decrease in BMD. Once treatment resumed in the CORE trial, lumbar spine and femoral neck BMD increased in the EVISTA group.
- *Bone turnover:* In a previously unpublished analysis of data from the MORE study, patients who received EVISTA for three continuous years had lower bone resorption as measured by c-terminal telopeptide (CTX) values, with the average being similar to that found in premenopausal women. EVISTA is not for use in premenopausal women.
- *Iliac crest bone biopsies:* Newly reported data from a subset of patients in the CORE trial included results of iliac crest biopsies in three patients treated with EVISTA for eight years. These iliac crest biopsies showed normal bone and bone cells and double label in all specimens.
- *Invasive breast cancer risk reduction:* In a subset of postmenopausal women followed for up to eight years from randomization of the MORE trial to the end CORE, a reduction in the incidence of invasive breast cancer was observed in the EVISTA versus placebo group. The long term effects and the recommended length of therapy are not known.

Study safety findings included:

- In clinical trials, patients in the EVISTA versus placebo group had higher incidence of venous thromboembolic events (blood clots in the legs, lungs or eyes), including deep vein thrombosis and pulmonary embolism, compared with patients who received placebo. EVISTA is contraindicated in women with active or past history of venous thromboembolism (VTE), including deep vein thrombosis, pulmonary embolism and retinal vein thrombosis.
- The safety profile of EVISTA after four years of treatment was similar to that of EVISTA following three years of therapy.
- Additional adverse events (>2% and more common with EVISTA than with placebo) included hot flashes, leg cramps, swelling, flu-like symptoms, joint pain and sweating.

"Lilly is committed to providing information regarding our therapies to help healthcare professionals and their patients engage in more informed discussions about available treatment options for postmenopausal osteoporosis," said co-author John Krege, M.D., medical fellow, Eli Lilly and Company.

About the Review

"Long-term Raloxifene for Postmenopausal Osteoporosis" is a literature review of available information concerning EVISTA use for greater than three years for the treatment of postmenopausal osteoporosis and invasive breast cancer risk reduction in

postmenopausal women with osteoporosis. Two reviewed studies were the Multiple Outcomes of Raloxifene Evaluation (MORE) trial and the Continued Outcomes of Raloxifene Evaluation (CORE) trial. The review includes summaries of previously published information, as well as a number of previously unpublished observations from analyses of the clinical study databases. In addition, new data from three patients who underwent iliac crest bone biopsies after eight years of EVISTA therapy were reported.

About EVISTA® (raloxifene HCl tablets)

EVISTA is an estrogen agonist/antagonist, commonly referred to as a selective estrogen receptor modulator (SERM), which appears to act like estrogen in bone and to block the effects of estrogen in some tissues. It is an osteoporosis therapy for postmenopausal women that also reduces the risk of invasive breast cancer in postmenopausal women with osteoporosis.

EVISTA is approved by the U.S. Food and Drug Administration (FDA) for the treatment and prevention of osteoporosis in postmenopausal women. EVISTA is also indicated for the reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis. There are Important Limitations of Use for breast cancer risk reduction:

- There are no data available regarding the effect of EVISTA on invasive breast cancer incidence in women with inherited mutations (BRCA1, BRCA2) to be able to make specific recommendations on the effectiveness of EVISTA.
- EVISTA is not indicated for the treatment of invasive breast cancer or reduction of the risk of recurrence.
- EVISTA is not indicated for the reduction in the risk of noninvasive breast cancer.

EVISTA 60 mg tablets are taken once daily and can be taken with calcium and vitamin D supplements, with or without food.

Important Safety Information about EVISTA® (raloxifene HCl tablets)

What is the most important information patients should know about EVISTA?

Patients should not take EVISTA if they have had or are at risk for getting blood clots in the legs, lungs or eyes, as it may increase the risk of blood clots. Patients should stop taking EVISTA and call their doctor if they have leg pain or warmth, swelling of the legs, hands or feet, chest pain, shortness of breath or a sudden vision change, as these may be signs of a blood clot. Being unable to move around for long periods may increase this risk. If patients will need to be still for a long time, they should talk to their doctor about ways to reduce the risk of blood clots.

EVISTA does not increase the risk of a heart attack or stroke in women who have had or are at risk for a heart attack; however, EVISTA increases the likelihood of dying from stroke in these women, should one occur. Before taking EVISTA patients should tell their doctor if they have had a stroke, a mini-stroke, irregular heartbeat, high blood pressure, heart attack, history of smoking, or believe they have other risk factors for stroke or a heart attack.

EVISTA is not right for everyone. Patients should not take EVISTA if they:

- have had blood clots in their legs, lungs or eyes.
- are pregnant, nursing or may become pregnant, as EVISTA may cause fetal harm.

What should patients tell their doctor before taking EVISTA?

Patients should talk to their doctor about all their medical conditions including:

- If they have had blood clots in their legs, lungs or eyes.
- If they have had a stroke, mini-stroke, irregular heartbeat, high blood pressure, heart attack, history of smoking, or think they have other risk factors for stroke or heart attack.
- EVISTA should not be used for prevention of heart disease.
- If they are premenopausal. Patients should only take prescription EVISTA if they are past menopause.
- If they have liver or kidney disease. Women with liver or kidney disease should use EVISTA with caution.
- EVISTA should not be taken with estrogens in the form of pills, patches or injections.
- If they have taken estrogen in the past and had a high increase of triglycerides (a kind of fat in the blood).

What are the possible side effects of EVISTA?

- Side effects may include hot flashes, leg cramps, swelling, flu-like symptoms, joint pain, and sweating. Patients are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-

FDA-1088.

What are the possible drug interactions with EVISTA?

- If patients take warfarin (Coumadin®, Jantoven®) or other coumarin blood thinners, they may need to do a blood test (prothrombin time, pro-time or INR) when they first start or if they need to stop taking EVISTA. Their doctor may need to adjust the dose of their warfarin or other coumarin blood thinners.
- EVISTA should not be taken with cholestyramine or estrogens.

For more information about EVISTA, please see the Full Prescribing Information (http://pi.lilly.com/us/evista-pi.pdf) including Boxed Warning, and Medication Guide (http://pi.lilly.com/us/evista-ppi.pdf).

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About Eli Lilly and Company

Eli Lilly and Company, a leading innovation-driven company, 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. Information about Lilly is available at www.lilly.com. P-LLY

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