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Lilly Announces Study Results Regarding Postmenopausal Women with Back Pain Caused by Vertebral Fractures

INDIANAPOLIS, Aug. 7, 2012 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced data from a Phase III trial comparing the effects of FORTEO® (teriparatide [rDNA origin] injection) and risedronate on back pain in postmenopausal women with osteoporotic vertebral fractures. The study showed no difference between FORTEO and risedronate on the primary endpoint of at least a 30 percent reduction in worst back pain from baseline to six months of therapy, as assessed by a numeric rating scale in each treatment group.[1] However, there were statistically significant differences in favor of FORTEO in some exploratory measures, including greater increases in bone mineral density (BMD) and fewer patients with new vertebral fractures. The results of the study are published in the August issue of *Osteoporosis International*.

"With many available options to treat osteoporosis, this study is important because it compares two established osteoporosis medicines in a direct head-to-head design," said lead investigator Peyman Hadji, M.D., department head, endocrinology, osteoporosis and reproductive medicine at Philipps-University of Marburg.

At six months, more than half of patients in both treatment groups reported a 30 percent or greater reduction in worst back pain (FORTEO — 59.2 percent, risedronate — 57.4 percent; p=0.64).[1] (A 30 percent or greater reduction is considered a clinically meaningful change.)[1] There were no statistically significant differences between treatments in the secondary and exploratory endpoints of at least a 30 percent reduction in worst or average back pain at six, 12 or 18 months;[1] quality of life; disability; days of bed rest; days of disability; and amount of concomitant analgesics used. Significantly fewer patients treated with FORTEO experienced a worsening of average back pain between six and 18 months (23.6 percent vs. 30.6 percent of risedronate-treated patients; p=0.04).[1] Significantly fewer patients treated with FORTEO had one or more new vertebral fractures at 18 months (4.4 percent vs. 9.4 percent of risedronate-treated patients; p=0.01).[1] Among patients with new vertebral fractures, those treated with FORTEO had overall less severe new fractures compared to those who received risedronate, as measured by spine radiograph (p=0.04).[1] There was no significant difference between treatment groups in the number of patients with new nonvertebral fractures.

Additional findings included:

- patients treated with FORTEO had a greater average increase in BMD at the lumbar spine (+7.80 +/- 0.5 percent vs. +2.63 +/- 0.5 percent in risedronate-treated patients; $p < 0.001$) and at the femoral neck (+2.11 +/- 0.4 percent vs. +0.77 +/- 0.4 percent, respectively; p=0.02) at 18 months;[1]
- patients in the FORTEO group had significantly less height loss compared to the risedronate group at 18 months (0.44 centimeters vs. 0.70 centimeters; $p < 0.05$).[1]

"The study provides additional information regarding the use of FORTEO in patients who are considered at high risk for osteoporotic fractures," said Bruce Mitlak, M.D., Distinguished Medical Fellow, Bone Muscle and Joint Platform, Eli Lilly and Company. "The results may help guide healthcare professionals in treating severe osteoporosis."

In the study, the overall safety profile was consistent with the known FORTEO safety profile seen in this patient population.[1] The overall incidence of serious adverse events, treatment-emergent adverse events and adverse events leading to discontinuation were similar between the FORTEO and risedronate treatment groups.[1] There were nine deaths in the study (four in the FORTEO group and five in the risedronate group), but none of the deaths were considered related to treatment.[1]

FORTEO is used in both men and postmenopausal women with osteoporosis who are at high risk for having broken bones (fractures). FORTEO is used in both men and women with osteoporosis due to use of glucocorticoid medicines, such as prednisone, for several months, who are at high risk for having broken bones (fractures). FORTEO can be used by people who have had a fracture related to osteoporosis, or who have several risk factors for fracture, or who cannot use other osteoporosis treatments.[2]

During the drug testing process, the medicine in FORTEO caused some rats to develop osteosarcoma, which, in humans, is a serious but rare bone cancer. Osteosarcoma has been reported rarely in people who took FORTEO, and it is unknown if people who take FORTEO have a higher chance of getting the disease. Before patients take FORTEO, patients should tell their healthcare provider if they have Paget's disease of bone, are a child or young adult whose bones are still growing or have had radiation therapy.[2] For more information about FORTEO, please see the important safety information, including Boxed

Warning regarding osteosarcoma, below.

About the Study[1]

"The Effect of Teriparatide Compared with Risedronate on Reduction of Back Pain in Postmenopausal Women with Osteoporotic Vertebral Fractures" was a Phase III, prospective, randomized, double-blind, double-dummy, active-controlled, 18-month trial involving 710 postmenopausal women with at least one moderate or severe vertebral fracture thought to be the cause of back pain. The primary objective was to compare the efficacy of FORTEO (20 micrograms/day) and risedronate (35 milligrams/week) based on the proportion of women who reported a 30 percent or greater reduction in worst back pain severity, as assessed by an 11-point numeric rating scale (0=no pain; 10=severe pain), from baseline to six months of therapy. Pre-specified secondary and exploratory outcomes included assessments of average and worst back pain at additional time points, the mean change in disability as assessed by the Roland Disability Questionnaire, the mean change in quality of life as assessed by Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO), change in BMD, incidence of fractures, and safety.

Important Safety Information about FORTEO

What is the most important information I should know about FORTEO?

WARNING: POTENTIAL RISK OF OSTEOSARCOMA

During the drug testing process, the medicine in FORTEO caused some rats to develop a bone cancer called osteosarcoma. In people, osteosarcoma is a serious but rare cancer. Osteosarcoma has been reported rarely in people who took FORTEO. It is not known if people who take FORTEO have a higher chance of getting osteosarcoma. Before you take FORTEO, you should tell your healthcare provider if you have Paget's disease of bone, are a child or young adult whose bones are still growing, or have had radiation therapy.

Who should not take FORTEO?

- You should not take FORTEO for more than 2 years over your lifetime.
- Do not use FORTEO if you are allergic to any of the ingredients in FORTEO. Serious allergic reactions have been reported.

What should I tell my healthcare provider before taking FORTEO?

- Before you take FORTEO, you should tell your healthcare provider if you have a bone disease other than osteoporosis, have cancer in your bones, have trouble injecting yourself and do not have someone who can help you, have or have had kidney stones, have or have had too much calcium in your blood, take medications that contain digoxin (Digoxin, Lanoxicaps, Lanoxin), or have any other medical conditions.
- You should also tell your healthcare provider, before you take FORTEO, if you are pregnant or thinking about becoming pregnant. It is not known if FORTEO will harm your unborn baby. If you are breastfeeding or plan to breastfeed, it is not known if FORTEO passes into your breast milk. You and your healthcare provider should decide if you will take FORTEO or breastfeed. You should not do both.

What are the possible side effects of FORTEO?

- FORTEO can cause serious side effects including a decrease in blood pressure when you change positions. Some people feel dizzy, get a fast heartbeat, or feel faint right after the first few doses. This usually happens within 4 hours of taking FORTEO and goes away within a few hours. For the first few doses, take your injections of FORTEO in a place where you can sit or lie down right away if you get these symptoms. If your symptoms get worse or do not go away, stop taking FORTEO and call your healthcare provider. FORTEO may also cause increased calcium in your blood. Tell your healthcare provider if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs there is too much calcium in your blood.
- Common side effects of FORTEO include nausea, joint aches, pain, leg cramps, and injection site reactions including injection site pain, swelling and bruising. These are not all the possible side effects of FORTEO. You are encouraged to report negative side effects of Prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Additional safety information about FORTEO

- There is a voluntary patient registry for people who take FORTEO. The purpose of the registry is to collect information about the possible risk of osteosarcoma in people who take FORTEO. For information about how to sign up for this patient registry, call 1-866-382-6813 or go to www.forteoregistry.org.
- The FORTEO Delivery Device has enough medicine for 28 days. It is set to give a 20-microgram dose of medicine each day. Before you try to inject FORTEO yourself, a healthcare provider should teach you how to use the FORTEO Delivery

Device to give your injection the right way. Inject FORTEO one time each day in your thigh or abdomen (lower stomach area). Do not inject all the medicine in the FORTEO Delivery Device at any one time. Do not transfer the medicine from the FORTEO Delivery Device to a syringe. This can result in taking the wrong dose of FORTEO. If you take more FORTEO than prescribed, call your healthcare provider. If you take too much FORTEO, you may have nausea, vomiting, weakness, or dizziness.

How should I store FORTEO?

- Keep your FORTEO Delivery Device in the refrigerator between 36 degrees F to 46 degrees F (2 degrees C to 8 degrees C). Do not freeze the FORTEO Delivery Device. Do not use FORTEO if it has been frozen. Do not use FORTEO after the expiration date printed on the delivery device and packaging. Throw away the FORTEO Delivery Device after 28 days even if it has medicine in it (see the User Manual).

For more safety information, please see Medication Guide (http://pi.lilly.com/us/forteo-medguide.pdf) and Prescribing Information, including Boxed Warning (http://pi.lilly.com/us/forteo-pi.pdf). Please see full user manual that accompanies the delivery device.

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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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This press release contains forward-looking statements about Forteo for the treatment of osteoporosis. It reflects Lilly's current beliefs; however, as with any such undertaking, there are substantial risks and uncertainties in the process of drug development and commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that Forteo will continue to be commercially successful. For further discussion of these and other risks and uncertainties, please see Lilly's latest Forms 10-Q and 10-K filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

[1] P. Hadji , J. R. Zanchetta , L. Russo, C. P. Recknor, K. G. Saag, F. E. McKiernan, S. L. Silverman, J. Alam, R. T. Burge, J. H. Krege, M. C. Lakshmanan, D. N. Masica, B. H. Mitlak & J. L. Stock. The effect of teriparatide compared with risedronate on reduction of back pain in postmenopausal women with osteoporotic vertebral fractures. Osteoporos Int (2012) 23:2141—2150. DOI 10.1007/s00198-011-1856-y

[2] FORTEO PI. Available at http://pi.lilly.com/us/forteo-pi.pdf

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