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New Data on FORTEO® (teriparatide [rDNA origin] injection) Show Increased Bone Mineral Density in Men with Glucocorticoid-Induced Osteoporosis

INDIANAPOLIS, May 29, 2013 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced new data showing that FORTEO significantly increased lumbar spine volumetric bone mineral density (vBMD) compared to risedronate in men with glucocorticoid-induced osteoporosis. Glucocorticoid-induced osteoporosis is caused by excess intake of glucocorticoids, a class of steroid hormones used to treat inflammatory, autoimmune and allergic disorders.[1] Study results are published in the June issue of the *Journal of Bone and Mineral Research*.

Results from the study's primary endpoint showed that at 18 months, both FORTEO and risedronate significantly increased lumbar spine vBMD, and greater increases were observed in patients taking FORTEO (mean change from baseline: 16.3% vs. 3.8%; p=0.004).[2]

Measurement was completed using conventional and high-resolution quantitative computed tomography (QCT), a newer technology that uses modern clinical scanners to provide tri-dimensional BMD and bone structural evaluations. QCT is better able to discriminate between subjects with and without prevalent vertebral fractures compared to conventional areal dual X-ray absorptiometry (DXA) and is better suited to identify patients with glucocorticoid-induced osteoporosis at highest risk for fracture.[3]

"Though we often think of osteoporosis as a women's disease, men can get it too. In fact, approximately two million American men have osteoporosis," said Claus-C. Gluer, Ph.D., professor of medical physics, Department of Diagnostic Radiology, University Medical Center Schleswig-Holstein. "These study results can help healthcare professionals better determine which treatment may be best suited for individual male patients with glucocorticoid-induced osteoporosis."

Secondary outcomes observed in the study include:[2]

- a significant increase in estimated vertebral strength in both treatment groups, with statistically higher increases in patients taking FORTEO (26.0% to 34.0%) compared to risedronate (4.2% to 6.7%) ($0.005 < p < 0.015$) after 18 months of therapy;
- a trend toward higher bone volume fraction in patients taking FORTEO (mean change from baseline: +23.1% vs. +7.3%; p=0.098);
- a significant increase in microstructural bone tissue variables derived from high-resolution QCT, such as cortical thickness and trabecular numbers in patients taking FORTEO and risedronate, with no significant differences between the two groups;
- differences between treatments in the change from baseline in biochemical markers of bone turnover, with significant increases in bone formation marker (PINP) in patients taking FORTEO (up to 175%), and suppression (-30%) in patients taking risedronate;
- a significant increase in areal BMD at the lumbar spine and the total hip after 18 months of treatment for both groups, with statistically significantly higher increases for FORTEO at the lumbar spine (mean: +6.94% vs. +3.33%; p=0.045), and at the femoral neck (mean: +1.52% vs -1.10%; p=0.026);
- a trend toward fewer clinical fractures in patients taking FORTEO (0/45, 0%) compared to patients taking risedronate (5/47, 10.6%) (p=0.056);
- and no statistically significant safety differences between the groups.

"Data evaluating osteoporosis medications in men are relatively scarce," said Fernando Marin, M.D., Ph.D., medical fellow, Eli Lilly and Company. "Lilly is committed to furthering scientific knowledge in this underserved patient population to help reduce barriers to men with osteoporosis getting the treatment they need."

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.[4]

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.[4] For more information about FORTEO, please see the important safety information, including Boxed Warning regarding osteosarcoma, below.

About the Study[2]

"Comparative Effects of Teriparatide and Risedronate in Glucocorticoid-Induced Osteoporosis in Men: 18-Month Results of the EuroGIOPS Trial" was an 18-month randomized, open-label, controlled trial conducted in four European countries in men who had taken glucocorticoids (steroids) for more than three months (prednisone equivalent > 5 mg/d) and had an areal bone mineral density (BMD) T-score < -1.5 SD. Participants received either 20 mg/d teriparatide (TPTD, n=45) or 35 mg/wk risedronate (RIS, n=47) and 1 g calcium and 1200 IU vitamin D daily.

The primary objective was to compare the increase in lumbar spine (L1-L3) vBMD between groups, as measured by QCT. Secondary outcomes included changes in 3-D microstructure variables measured by high-resolution QCT (HRQCT) at T12, biomechanical effects evaluated by finite element (FE) analysis, areal BMD determined by DXA, biochemical markers and safety.

Radiological evaluations were performed at baseline, six and 18 months. The calibrated HRQCT images of T12 were converted into digital FE models and subjected to axial compression, anterior bending and axial torsion. Stiffness and strength were computed for each model and loading mode. A predefined mixed model repeated measures was used to analyze the changes from baseline and the between-group differences.

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°F to 46°F (2°C to 8°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 (http://pi.lilly.com/us/forteo-pi.pdf), including Boxed Warning regarding osteosarcoma. 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.

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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] The National Osteoporosis Foundation, "Medicines That May Cause Bone Loss." Accessed on May 9, 2013 from http://www.nof.org/articles/6 .

[2] Gluer, C-C et al. "Comparative Effects of Teriparatide and Risedronate in Glucocorticoid-Induced Osteoporosis in Men: 18-Month Results of the EuroGIOPs Trial." *Journal of Bone and Mineral Research* (2013), DOI [10.1002/jbmr.1870].

[3] Graeff C, et al. High Resolution Quantitative Computed Tomography-based Assessment of Trabecular Microstructure and Strength Estimates by Finite-element Analysis of the Spine, but not DXA, Reflects Vertebral Fracture Status in Men with Glucocorticoid-induced Osteoporosis. *Bone*. (2013); 52:568-577.

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

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