



Phase III Trial Showed Investigational Compound Arzoxifene Was Superior to Evista® (raloxifene HCl) in Increasing BMD in Postmenopausal Women with Osteoporosis

Results from the "NEXT" Study Also Showed Arzoxifene Significantly Suppressed Bone Turnover Markers versus Raloxifene in Postmenopausal Women with Osteoporosis

Athens, Greece - Eli Lilly and Company (NYSE: LLY) presented new data showing arzoxifene, an investigational selective estrogen receptor modulator (SERM), was superior to raloxifene at increasing bone mineral density (BMD) in the lumbar spine, total hip and femoral neck, and at suppressing bone turnover as assessed by serum markers of bone metabolism. In this study of 320 patients, more women reported bronchitis and nasopharyngitis in the arzoxifene group versus the raloxifene group, whereas significantly fewer women reported new or worsening hot flashes in the arzoxifene group. The data were presented at the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ECCEO) annual meeting.

Arzoxifene is being studied for the prevention and treatment of osteoporosis in postmenopausal women and the reduction of risk of invasive breast cancer in postmenopausal women with osteoporosis or low bone mass.

About the "NEXT" Study

Arzoxifene versus Raloxifene: 12-month Effects on Bone Mineral Density, Bone Turnover Markers, and Safety Parameters in Postmenopausal Women with Osteoporosis

This Phase III trial, powered to show superiority, was a double-blind, active comparator, controlled, 12-month study. In the study, 320 postmenopausal women with osteoporosis were randomized to receive arzoxifene 20 mg/day (N= 158) or raloxifene hydrochloride 60 mg/day (N= 162). In addition, supplements containing 500 mg/day calcium and 400-600 IU/day vitamin D were provided. The study's primary endpoint was lumbar spine BMD. Secondary objectives included assessment of femoral neck and total hip BMD, serum bone turnover markers, mammographic breast density and safety.¹ The study included postmenopausal women with osteoporosis with a mean age of 63 years and a mean lumbar spine BMD T-score of -2.9.

12-month results included:¹

- Arzoxifene significantly increased BMD at all sites to a greater extent than raloxifene, respectively ($p < 0.05$ for all comparisons):
 - Lumbar spine BMD (2.8 percent vs. 1.7 percent)
 - Femoral neck BMD (1.5 percent vs. 0.5 percent)
 - Total hip BMD (1.5 percent vs. 0.8 percent)
 - For lumbar spine and femoral neck, this effect was statistically significant as early as six months.
- Arzoxifene significantly suppressed bone turnover to a greater extent than raloxifene, respectively ($p < 0.05$ for all comparisons):
 - CTX (biochemical marker of bone resorption); -40.6 percent vs. -29.8 percent
 - PINP (biochemical marker of bone formation) : -41.5 percent vs. -30.8 percent
 - Arzoxifene suppressed bone turnover to a greater extent than raloxifene as early as three months.
- New or worsening hot flashes were reported less frequently with arzoxifene versus raloxifene (7.0 percent vs. 16.7 percent; $p = 0.009$).
- There were not any between-group or within-group differences in change of percentage of breast density.
- The proportion of women reporting one or more adverse events, including vaginal bleeding, did not differ between treatment groups.
- No cases of endometrial polyps, hyperplasia or cancer were reported.
- Nasopharyngitis and bronchitis were reported more frequently with arzoxifene versus raloxifene (10.1 percent vs. 2.5 percent, and 5.1 percent vs. 0 percent, respectively; $p \leq 0.005$).

"The significant increases in BMD and suppression of markers of bone turnover seen in these data show the potential benefits of arzoxifene for the treatment of osteoporosis in postmenopausal women," said investigator Jose Zanchetta, M.D., specialist in osteology and mineral metabolism, Metabolic Research Institute, Buenos Aires, Argentina. "I'm encouraged by these results and interested in seeing the next Phase III data for arzoxifene."

These data are from the "NEXT" Study, the second of three Phase III trials for arzoxifene. In September 2008, results from the "FOUNDATIONS" Phase III prevention study were first presented at the American Society for Bone and Mineral Research (ASBMR) Annual Meeting in Montréal. The third Phase III trial, the "GENERATIONS" Study, is a 5-year, randomized, double-

blind, placebo-controlled study assessing the effects of arzoxifene on vertebral fracture incidence and on invasive breast cancer incidence in postmenopausal women with osteoporosis or with low bone density. Results from that trial are anticipated in late 2009.

"We are pleased with the results of the 'NEXT' Study and its implications for arzoxifene as a potential treatment option for postmenopausal women with osteoporosis," said Adrien Sipos, M.D., Ph.D., medical director for Eli Lilly and Company. "We are committed to research that will help bring innovative prevention and treatment options to patients suffering from this devastating disease, which affects one in three women over 50." 2

Osteoporosis is a disease in which bones become fragile and more likely to break. Primary osteoporosis, which is deterioration of bone mass that is unassociated with other chronic illness, is related to aging and decreased gonadal function, including menopause. If not prevented, or if left untreated, osteoporosis can progress painlessly until a bone breaks. These broken bones, or fractures, typically occur in the hip, spine and wrist. According to the International Osteoporosis Foundation, 30 percent to 50 percent of women will suffer a fracture related to osteoporosis in their lifetime.²

About Lilly

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class 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.

This press release contains forward-looking statements about the safety and efficacy of arzoxifene and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is no guarantee that arzoxifene will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

¹ Zanchetta, J., et al. "Arzoxifene versus Raloxifene: 12-month Effects on Bone Mineral Density, Bone Turnover Markers, and Safety Parameters in Postmenopausal Women with Osteoporosis." *Osteoporosis International* 2009;20:166.

² International Osteoporosis Foundation. Facts and Statistics About Osteoporosis and its Impact. Available at: <http://www.iofbonehealth.org/facts-and-statistics.html#factsheet-category-17>. Accessed October 29, 2008.

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