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**EMBARGOED UNTIL MARCH 17, 2004 5:00 P.M. E.S.T.**

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**FOSAMAX<sup>®</sup> Continues to Help Build Bone Through 10 Years  
of Treatment, Study in *New England Journal of Medicine* Finds**

**Longest Prospective Clinical Trial in the Treatment of Postmenopausal  
Osteoporosis Shows FOSAMAX Maintained Bone Mineral Density at all Skeletal  
Sites Measured**

UPPER GWYNEDD, Pa., March 17, 2004 -- In the longest prospective clinical trial ever conducted in the treatment of postmenopausal osteoporosis -- a chronic condition that can lead to bone loss and susceptibility to fractures -- researchers found that postmenopausal women taking FOSAMAX<sup>®</sup> (alendronate sodium) maintained or continued to experience increases in bone mineral density (BMD) at the hip and spine through 10 years of treatment. Results from the trial were published today in the *New England Journal of Medicine*. FOSAMAX is the only medicine approved by the Food and Drug Administration in the treatment of osteoporosis to increase BMD and reduce the incidence of both spine and hip fractures in postmenopausal women.

“Assessing the effect of treatment on BMD over time is important because osteoporosis is a chronic disease,” said lead study author Dr. Henry G. Bone, Chief of Endocrinology and Metabolism at St. John Hospital and Medical Center and Director of the Michigan Bone and Mineral Clinic. “Other studies have shown that alendronate increased BMD and reduced fracture risk in postmenopausal women with osteoporosis. This study shows that alendronate maintained or continued to increase bone density throughout 10 years of treatment, demonstrating a sustained therapeutic effect.”

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Over 10 million people in the U.S. are estimated to have osteoporosis and another 34 million are estimated to have low bone mass.<sup>i</sup> The majority are women.<sup>ii</sup> These women can experience one-third of their lifetime bone loss within the first five years after menopause.<sup>iii</sup> The loss of bone mass that can occur after menopause increases the risk that a woman will develop osteoporosis and related fractures.<sup>iv</sup> A separate study found that postmenopausal women who discontinued hormone replacement therapy, a treatment prescribed for symptoms associated with menopause, lost 4.5 percent of their bone mass at the lumbar spine within one year of discontinuation.<sup>v</sup>

### **Study evaluated FOSAMAX through 10 years of treatment**

The multi-center, international, double-blind, randomized, placebo-controlled study began in 1991 as a three-year trial with 994 osteoporotic, postmenopausal women between the ages of 44 and 84 and was extended three times to allow longer study of the treatment effects of FOSAMAX. At the start of the study, patients were randomized into four groups: patients taking FOSAMAX 5 mg once daily, FOSAMAX 10 mg once daily, FOSAMAX 20 mg once daily, or placebo. The analysis published today reports on patients who participated in years eight through 10 of the decade-long study. Of the 247 women participating in these last years of the study, 78 women received FOSAMAX 5 mg once daily for the entire study and 86 women received FOSAMAX 10 mg once daily for the entire study. Eighty-three women received FOSAMAX 20 mg once daily for years one and two, FOSAMAX 5 mg once daily for years three through five, and placebo for the remaining five years; these women represent the discontinuation arm of the study. All treatment groups received 500 mg of calcium daily.

The study's primary endpoint was change in BMD at the lumbar spine, measured yearly by dual-energy x-ray absorptiometry and interpreted centrally by a quality-assurance center in a blinded fashion. Secondary endpoints were changes in BMD at the femoral neck, hip trochanter, total proximal femur, total body and forearm regions as well as changes in biochemical markers of bone formation and resorption.

After 10 years of study, FOSAMAX 10 mg once daily increased mean cumulative BMD at all measured sites. FOSAMAX significantly increased mean BMD by

13.7 percent at the lumbar spine, by 10.3 percent at the hip trochanter and by 5.4 percent at the femoral neck, compared to baseline (all  $p \leq 0.001$ ).

During years eight through 10 of the 10-year study, safety profiles were similar among all treatment groups. The incidence of all upper gastrointestinal events was also similar across groups.

### **FOSAMAX returned markers of bone turnover to premenopausal levels**

In addition to the increases in BMD, treatment with FOSAMAX also reduced biochemical markers of bone remodeling in the study. These markers reflect the process through which old bone is replaced with new tissue. At the end of year 10, mean urinary N-telopeptides of type 1 collagen, a marker of bone resorption, declined from 66.6 to 22.0 nmol bone collagen equivalents/nmol in women receiving FOSAMAX 10 mg, a level similar to published levels for premenopausal women. In this same group of patients, mean serum bone-specific alkaline phosphatase, a marker of bone formation, was reduced from 17.8 ng/mL at baseline to 9.1 ng/mL at the end of year 10, a level also similar to the published mean value for premenopausal women. In patients who discontinued treatment with FOSAMAX, remodeling markers increased within a year after discontinuation of treatment, but remained below baseline. Analyses of biochemical markers were performed in women who were in compliance with the study protocol (per-protocol analysis).

“The work that went into this study by the many researchers and patients around the world should be a source of pride,” Dr. Bone said. “This study, in which the effects of an osteoporosis therapy were tracked for a full decade in a prospective clinical trial, represents an exceptional accomplishment.”

### **Important information about FOSAMAX**

FOSAMAX, like other bisphosphonates, should be used with caution in people with certain stomach or digestive problems. FOSAMAX should not be used if the patient has certain disorders of the esophagus that delay emptying or if the patient is unable to stand or sit upright for at least 30 minutes. In addition, FOSAMAX should not be used in patients with severe kidney disease or low levels of calcium in their blood, in

patients who are allergic to FOSAMAX or in patients who are pregnant or nursing. Patients who have difficulty swallowing liquids should not take FOSAMAX oral solution.

Some patients may develop severe digestive reactions including irritation, inflammation or ulceration of the esophagus. The risk of severe esophageal experiences appears to be greater in patients who fail to follow dosing instructions (see prescribing information for more details). Patients who experience new or worsening heartburn, difficulty or pain when swallowing or chest pain should stop taking the drug and consult their doctor. The most commonly reported side effects with FOSAMAX have been abdominal pain, musculoskeletal pain, indigestion, regurgitation and nausea.

**FOSAMAX is a medicine from Merck & Co., Inc.**

Introduced in 1995 for the treatment of postmenopausal osteoporosis, FOSAMAX is approved for: the treatment of Paget's disease of bone (40 mg once daily); the prevention of osteoporosis in postmenopausal women at risk of osteoporosis (5 mg once daily, 35 mg once weekly); the treatment of postmenopausal osteoporosis and the reduction in the incidence of hip and spine fractures in postmenopausal women who have osteoporosis (10 mg once daily, 70 mg once weekly).

In addition, FOSAMAX is approved for the treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and who have low bone mineral density (5 mg once daily, except for postmenopausal women not receiving estrogen, for whom the recommended dosage is 10 mg once daily); and for the treatment to increase bone mass in men with osteoporosis (10 mg once daily; alternatively, 70 mg once weekly may be considered).

**About Merck**

Merck & Co., Inc. is a global research-driven pharmaceutical products company. Merck discovers, develops, manufactures and markets a broad range of innovative products to improve human and animal health, directly and through its joint ventures.

**Forward-looking statement**

This document contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements involve risks and

uncertainties, which may cause results to differ materially from those set forth in the statements. The forward-looking statements include statements regarding product development. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Forward-looking statements in this document should be evaluated together with the many uncertainties that affect our businesses, particularly those mentioned in the cautionary statements in Item 1 of our Form 10-K for the year ended Dec. 31, 2003, and in our periodic reports on Form 10-Q and Form 8-K (if any) which we incorporate by reference.

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**Full prescribing information for FOSAMAX is attached.**

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<sup>i</sup> National Osteoporosis Foundation. Disease Statistics. Available at <http://www.nof.org/osteoporosis/stats.htm>. Accessed February 2004.

<sup>ii</sup> National Osteoporosis Foundation. Disease Statistics. Available at <http://www.nof.org/osteoporosis/stats.htm>. Accessed February 2004.

<sup>iii</sup> Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. *Am J Med.* 1993; 94:646-650.

<sup>iv</sup> National Osteoporosis Foundation . Disease Statistics. Available at <http://www.nof.org/osteoporosis/stats.htm>. Accessed February 2004.

<sup>v</sup> Data available on request from Professional Services, WP1-27, Merck & Co., Inc., West Point, PA 19486. Information package 20350429(1)-FOS.