Two-Year Trial Results of Amgen Investigational Therapy for Bone Loss, Denosumab, Show Increased Bone Mineral Density with Twice-Yearly Dosing

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Phase 2 Trial Results of a Pre-Planned Exploratory Analysis in Postmenopausal Women Released at American College of Rheumatology Annual Scientific Meeting

SAN DIEGO, Nov 13, 2005 (BUSINESS WIRE) -- Amgen (NASDAQ:AMGN), the world's largest biotechnology company, today announced that twice-yearly subcutaneous injections of denosumab (60 mg) (previously referred to as AMG 162) increased bone mineral density (BMD) in the lumbar spine, total hip, distal 1/3 radius and total body compared to placebo at 24 months. The study also included an open label FOSAMAX(R)(1) (alendronate) arm. Investigators reported on a pre-planned exploratory analysis at the American College of Rheumatology Annual Scientific Meeting in San Diego, California.

The ongoing, multi-center, Phase 2 dose-ranging trial includes results from 337 healthy postmenopausal women with low BMD who completed two years of study. Researchers reported denosumab 60mg increased BMD of the lumbar spine by 7.4 percent in women administered the therapy twice yearly and 6.2 percent for FOSAMAX(R) 70mg weekly. Across all doses and dosing intervals, denosumab increased the BMD of the lumbar spine by 4.3 to 9.0 percent over baseline.

"The two-year results showed the continued effect of denosumab in increasing bone mineral density in postmenopausal patients with low bone mass," said Michael Lewiecki, M.D., clinical assistant professor of medicine, University of New Mexico School of Medicine, Albuquerque, NM. "These data suggest denosumab, when administered twice a year, may offer a promising alternative for the prevention and treatment of osteoporosis."

Denosumab is designed to target RANK Ligand, a protein that acts as the primary signal to promote bone removal. In many bone loss conditions, RANK Ligand overwhelms the body's natural defense against bone destruction.

Preclinical models have demonstrated that inhibiting RANK Ligand leads to significant improvements in cortical and trabecular bone density, volume and strength.

Denosumab is currently being studied for its potential in a broad range of bone loss conditions including osteoporosis, treatment-induced bone loss, bone metastases, multiple myeloma and rheumatoid arthritis.

"Because denosumab targets RANK Ligand, it functions in a way that is entirely different than other bone loss treatments," said Willard Dere, M.D., senior vice president of global development and chief medical officer, Amgen. "We believe its unique, targeted approach to regulating bone loss may have the ability to transform how we treat these conditions."

Researchers also reported twice-yearly injections of denosumab (60 mg) increased total hip BMD by 5.1 percent after 24 months. FOSAMAX(R) 70 mg weekly produced a 3.4 percent increase during the same time period. Denosumab, at all doses and dosing intervals studied, increased total hip BMD from 2.8 to 5.1 percent. Across all doses and dosing intervals, distal 1/3 radius BMD increased from 0.6 to 2.5 percent, and total body BMD increased from 0.9 to 4.5 percent.

Occurrence of adverse events was similar among the denosumab, placebo, and FOSAMAX(R) groups and showed no new pattern of events in the second year of treatment. No neutralizing antibodies to denosumab were observed throughout the two years.

Denosumab (AMG 162) Study Design

Investigators randomized 412 postmenopausal women, average age 63, with low BMD to receive denosumab, placebo or FOSAMAX(R). The purpose of the study was to determine the safety and efficacy of denosumab on lumbar spine BMD compared with placebo at 12 months. The doses of denosumab evaluated included 6, 14 or 30 mg every three months or 14, 60, 100 or 210 mg every six months. The researchers administered all doses of denosumab via subcutaneous injection. Patients receiving FOSAMAX(R) followed the approved indication and oral dosing instructions of 70 mg once weekly.

At entry, the women averaged -2.1 on their T-scores, a densitometric rating of BMD in which scores between -1.0 and -2.5 indicate osteopenia (thinning bone) and below -2.5 indicate osteoporosis, according to the World Health Organization (WHO).

The Need for Bone Loss Treatments

Osteoporosis

Bone loss represents a significant clinical and economic burden. Osteoporosis is a major public health threat for an estimated 44 million Americans, or 55 percent of the people 50 years of age and older. In the U.S. today, 10 million individuals are estimated to already have the disease and almost 34 million more are estimated to have low bone mass, placing them at increased risk for osteoporosis.

Of the 10 million Americans estimated to have osteoporosis, eight million are women and two million are men. In addition, one in two women and one in four men over age 50 will have an osteoporosis-related fracture in their remaining lifetime.

In Europe, recent estimates have stated that approximately 3.8 million people have experienced bone fractures related to osteoporosis.

About Amgen

Amgen discovers, develops and delivers innovative human therapeutics. A biotechnology pioneer since 1980, Amgen was one of the first companies to realize the new science's promise by bringing safe and effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have

changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, and other serious illnesses. With a broad and deep pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. To learn more about our pioneering science and our vital medicines, visit www.amgen.com.

Forward-Looking Statement

This news release contains forward-looking statements that involve significant risks and uncertainties, including those discussed below and others that can be found in Amgen's Form 10-K for the year ended December 31, 2004, and in Amgen's periodic reports on Form 10-Q and Form 8-K. Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly or sometimes even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify side effects or manufacturing problems with our products after they are on the market. In addition, sales of our products are affected by the availability of reimbursement and the reimbursement policies imposed by third party payors, including governments, private insurance plans and managed care providers, and may be affected by domestic and international trends toward managed care and healthcare cost containment as well as possible U.S. legislation affecting pharmaceutical pricing and reimbursement. Government regulations and reimbursement policies may affect the development, usage and pricing of our products.

In addition, we compete with other companies with respect to some of our marketed products as well as for the discovery and development of new products. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. In addition, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, the discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration (FDA), and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Only the FDA can determine whether the product candidates are safe and effective for the use(s) being investigated. Further, the scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the FDA for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses. Only the FDA can determine whether the products are safe and effective for these uses. Healthcare professionals should refer to and rely upon the FDA-approved labeling for the products, and not the information discussed in this news release.

(1) FOSAMAX(R) is a registered trademark of Merck & Co., Inc.

SOURCE: Amgen

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