Investigational Therapy Denosumab Increased Bone Mineral Density with Twice-Yearly Dosing; One Year Data Published in New England Journal of Medicine

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THOUSAND OAKS, Calif., Feb 22, 2006 (BUSINESS WIRE) -- Amgen (NASDAQ: AMGN), the world's largest biotechnology company, announced today the publication of Phase 2 data demonstrating twice-yearly injections of denosumab (previously referred to as AMG 162), a RANK Ligand inhibitor, significantly increased bone mineral density (BMD) in the total hip, lumbar spine, distal 1/3 radius and total body compared to placebo. The results of this one-year study appeared in the Feb. 23, 2006 issue of the New England Journal of Medicine. Data results also included an open-label FOSAMAX(R) (alendronate)(a) arm of the same clinical trial.

Researchers reported that subcutaneous injections of denosumab significantly increased BMD at the total hip from 1.9 to 3.6 percent in women who were administered the therapy twice yearly as compared with a decrease of 0.6 percent in the placebo group (p less than 0.001) at one year. The open label FOSAMAX(R) group receiving 70 mg weekly had an increase of 2.1 percent during the same time frame. Results also indicated that denosumab had a rapid onset of action. A significant decrease in serum levels of C-telopeptide, a biomarker of bone resorption, was achieved within 72 hours after dosing.

"These exciting data suggest that denosumab, when administered in twice-yearly injections, may show promise in the treatment of osteoporosis," said Michael McClung, MD, FACP, principal investigator of the denosumab study, Providence Portland Medical Center, and director of the Oregon Osteoporosis Center, Portland, Ore. "Continued research will further our understanding of the potential of denosumab in bone loss management."

Denosumab targets RANK Ligand, a protein that acts as the primary mediator of osteoclast (cells that break down bone) activity. This investigational therapy is the first RANK Ligand inhibitor in late stage development.

Amgen is studying denosumab for its potential in a broad range of conditions associated with bone destruction including osteoporosis, treatment-induced bone loss, bone metastases, multiple myeloma and rheumatoid arthritis. Data recently presented at the American College of Rheumatology 2005 Annual Scientific Meeting show further increase in bone mineral density in postmenopausal women with osteoporosis after two years of treatment.

"These data reinforce the essential role that RANK Ligand inhibition plays in decreasing bone loss," said Willard Dere, MD, senior vice president of global development and chief medical officer, Amgen. "We are committed to expanding our data on denosumab with an extensive Phase 3 clinical program to evaluate the effect of denosumab on preventing fractures in men and women."

In the one-year trial results, researchers also reported twice-yearly subcutaneous injections of denosumab significantly increased lumbar spine BMD from 3.0 to 6.7 percent after 12 months as compared with a decrease of 0.8 percent in the placebo-treated patients (p less than 0.001). Across all doses and dosing intervals, distal 1/3 radius BMD increased from 0.4 to 1.3 percent as compared with a decrease of 2.0 percent in those taking placebo (p less than 0.001), and total body BMD increased from 0.6 to 2.8 percent as compared with a decrease of 0.2 percent in the placebo group (p less than 0.01).

The incidence of adverse events was similar among the denosumab, placebo, and FOSAMAX(R) groups, with the exception of dyspepsia. Dyspepsia occurred in 7 percent of placebo patients, 6-15 percent of denosumab patients and 26 percent of open-label FOSAMAX(R) patients. The most common adverse events among all groups included upper respiratory infection (common cold), arthralgia (joint pain), nasopharyngitis (sore throat), back pain and headache. No neutralizing antibodies to denosumab were observed.

Denosumab Study Design

This is an ongoing, multi-center dose-ranging trial. Investigators randomized 412 healthy 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 average lumbar spine T score ranged from -2.0 to -2.2 across dose groups, consistent with a diagnosis of osteopenia (thinning bone). Approximately a quarter of the patients had osteoporosis as defined by a T score equal to or below -2.5 at the lumbar spine.

About RANK Ligand

Bone is constantly formed and removed through a natural process of remodeling. Bone resorption is dependent on RANK Ligand, the protein that acts as the primary mediator of osteoclast formation, function and survival. Osteoclasts are cells responsible for bone removal.

Preclinical models have demonstrated that inhibiting RANK Ligand significantly improves cortical and trabecular bone density, volume and strength. Cortical bone is the protective outer shell around every bone in the body. Trabecular bone is known as spongy bone and is surrounded by the harder cortical layer.

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 population 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.

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

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SOURCE: Amgen

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