Phase 2 Interim Data Show Denosumab Decreased Bone Turnover in Advanced Cancer Patients with Bone Metastases

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Denosumab, a Fully Human Monoclonal Antibody that Inhibits RANK Ligand, Showed Activity in Patients Naive to and on Established IV Bisphosphonate Therapy

ATLANTA--(BUSINESS WIRE)--June 4, 2006-- Amgen (NASDAQ:AMGN), the world's largest biotechnology company, announced interim data from two Phase 2 clinical studies of denosumab, an investigational fully human monoclonal antibody that inhibits RANK Ligand. As reported at the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO), denosumab treatment resulted in a rapid suppression of bone turnover among advanced cancer patients with bone metastases; these results were also sustained at all time points measured in the study.

Bone metastases are one of the most frequent causes of pain in people with cancer and may lead to skeletal-related events (SREs) such as fractures, the need for bone surgery or radiation, and other complications. When tumor cells invade bone, they secrete growth factors that stimulate RANK Ligand production, promoting increased bone resorption. RANK Ligand is an essential mediator of the formation, function and survival of osteoclasts, the cells responsible for resorbing or breaking down bone.

"By targeting RANK Ligand, denosumab works differently from bisphosphonates because it inhibits osteoclasts at all stages of development and activity. As the only investigational RANK Ligand inhibitor in late-stage development, denosumab represents a potential new way to treat bone disease," said Allan Lipton, M.D., professor of Medicine/Oncology at Penn State University, Milton S. Hershey College of Medicine in Hershey, Pa., and an investigator in both studies. "Our data show denosumab was clinically active as it reduced levels of a bone turnover biomarker in both IV bisphosphonate-naive and -treated patients."

Interim results from the ongoing Phase 2 study of 255 IV bisphosphonate-naive breast cancer patients with established bone metastases, evaluating different doses of denosumab administered monthly or every three months, were presented in an oral session this morning. Urinary N-telopeptide levels, a biomarker for bone turnover, are increased by metastatic bone disease. Researchers reported that at study week 13, there was a median decrease in urinary N-telopeptide for each denosumab treatment cohort ranging from 63 percent to 82 percent. Based on the dose responses, the Phase 3 trial will evaluate 120 mg dosed monthly. (Abstract #512)

In this study, the most frequent adverse events reported for denosumab-treated patients were nausea, vomiting, asthenia (weakness), and diarrhea. No binding or neutralizing antibodies were detected. The most frequent adverse events reported for the IV bisphosphonate-treated patients were pyrexia (infection-induced fever), arthralgia (joint pain), asthenia, and bone pain.

In an interim analysis of a separate Phase 2 study of 49 prostate, breast, and multiple myeloma patients on established IV bisphosphonate therapy, twice as many patients achieved normalization of bone turnover when they were switched from IV bisphosphonate therapy to denosumab. Specifically, at week 13, 76 percent of denosumab patients, and 38 percent of patients who remained on the IV bisphosphonate, achieved normal levels of bone turnover. This reduction in bone turnover was also achieved more rapidly (ten days versus 112 days) among the denosumab arm than in the IV bisphosphonate arm. The median time to uNTx less than 50 nM BCE / nM Cr was ten days (95 percent CI: 9, 11) for the combined denosumab-treated group and 112 days (95 percent CI: 16, -) for the IV bisphosphonate-treated group. (Abstract #8562)

In this study, the most frequent adverse events reported for denosumab-treated patients were nausea, peripheral edema, anemia, and bone pain. For patients receiving IV bisphosphonates the most frequently reported adverse events were bone pain, constipation, anemia, back pain, chills, and fatigue. In both trials, both sets of patients were also on standard cancer treatments such as chemotherapy and hormone therapy.

About the Phase 2 Study of Bisphosphonate-Naive Patients

The Phase 2 randomized, active-controlled study of denosumab was designed to evaluate dosing options and its effect in decreasing bone turnover in breast cancer patients with bone metastases who had not previously received intravenous bisphosphonate therapy. The study enrolled 255 patients with bone metastases who were receiving concurrent chemotherapy or hormonal therapy. Patients were randomized to one of five double-blind denosumab-treated groups (30 mg, 120 mg, or 180 mg monthly; 60 mg or 180 mg every three months) or an open-label bisphosphonate arm. The primary endpoint was the percentage change from baseline to week 13 in the level of urinary N-telopeptide. Also evaluated were the percentage of patients with greater than or equal to a 65 percent decrease in urinary N-telopeptide from baseline, time to a 65 percent reduction in urinary N-telopeptide, incidence of SREs, and safety.

About the Phase 2 Study of Patients on Established IV Bisphosphonate Therapy

The Phase 2 randomized, open-label study of denosumab was designed to evaluate its effect in decreasing bone turnover in advanced cancer patients with bone metastases who had previously received intravenous bisphosphonate therapy. Patients were randomized to one of two denosumab-treated groups (180 mg monthly or 180 mg every three months) or a bisphosphonate arm. An interim analysis was performed on 49 patients completing week 13. The primary endpoint was the percentage of patients with a urinary N-telopeptide less than 50 nM BCE/mM creatinine at week 13. Also evaluated was the time to a urinary N-telopeptide level less than 50 nM BCE/mM creatinine, and safety. At the time of the analysis, 49 patients were enrolled in the study at a mean age range of 62.5 years and the median duration of prior IV bisphosphonate therapy was 5.1 months. Tumors included prostate (n=24), breast (n=20), and other/multiple myeloma (n=5).

About Bone Metastases

Bone metastases are deposits of cancer cells that separate from tumors, enter the bloodstream or the lymph system, and migrate to bone tissue where they settle and grow. These bone metastases often occur in bones near the center of the body including the spine, ribs, pelvis, hips and shoulders.

More than 10 million people worldwide suffer from bone metastases. Approximately 452,000 people in the United States have cancer with metastases to the bone.

About Denosumab

Denosumab is an investigational RANK Ligand inhibitor being studied for its potential to prevent and treat bone destruction. Denosumab is currently being studied to determine its potential to delay bone metastases as well as inhibit and treat bone destruction across many stages of cancer. It is also being studied in a range of other bone loss conditions including treatment-induced bone loss, multiple myeloma, osteoporosis, and rheumatoid arthritis.

Denosumab: Clinical Studies in Cancer

A comprehensive clinical program evaluating denosumab is ongoing including: a Phase 3 trial investigating the frequency of SREs in advanced breast cancer patients; a Phase 3 study in the prevention of bone metastases in prostate cancer; two Phase 3 studies in treatment-induced bone loss (one in breast cancer patients and another in prostate cancer patients); two Phase 2 studies in advanced cancer patients (one in patients naive to bisphosphonates and one in patients on established IV bisphosphonate therapy); and a Phase 2 study for the treatment of patients with multiple myeloma.

Denosumab: Additional Clinical Studies

Denosumab is also being studied in a range of bone loss conditions outside the oncology setting including osteoporosis and bone erosions in rheumatoid arthritis. Other ongoing studies include two Phase 3 studies (one in prevention and one in treatment) in postmenopausal osteoporosis and a Phase 2 study in the treatment of bone erosions in rheumatoid arthritis.

For more information about ongoing denosumab clinical trials, please visit www.amgentrials.com or www.clinicaltrials.gov.

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, 2005, 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 Amgen projects. 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 Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future. Amgen develops 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 Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify side effects or manufacturing problems with Amgen's products after they are on the market. In addition, sales of Amgen's 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 Amgen's products. In addition, Amgen competes with other companies with respect to some of Amgen's marketed products as well as for the discovery and development of new products. Amgen believes that some of the newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Amgen 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 Amgen routinely obtains patents for Amgen's products and technology, the protection offered by Amgen's patents and patent applications may be challenged, invalidated or circumvented by Amgen's competitors and there can be no guarantee of Amgen's ability to obtain or maintain patent protection for Amgen's products or product candidates. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of Amgen's existing products. Amgen's stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of Amgen's products or product candidates.

Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's 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.

EDITOR'S NOTE: An electronic version of this news release may be accessed via our Web site at www.amgen.com. Journalists and media representatives may sign up to receive all news releases electronically at time of announcement by filling out a short form in the Media section of the Web site.

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