The Journal of Clinical Oncology Publishes Phase 3 XGEVA(TM) (Denosumab) Results in Advanced Cancer Patients With Solid Tumors or Multiple Myeloma

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THOUSAND OAKS, Calif., Feb. 22, 2011 /PRNewswire via COMTEX/ --

Amgen (Nasdaq: AMGN) today announced the publication of results from a pivotal Phase 3 study of 1,776 advanced cancer patients with different types of solid tumors (not including breast and prostate cancer) or multiple myeloma, which compared XGEVA**(TM)** (denosumab) to Zometa(R) (zoledronic acid) in preventing skeletal-related events (SREs). The study, which appeared today in the *Journal of Clinical Oncology*, found that XGEVA was non-inferior to Zometa in delaying or preventing SREs.

"Almost every type of cancer has the potential to spread to the bone, putting patients at risk for devastating bone complications, like fracture or compression of the spinal cord," said David H. Henry, M.D., clinical professor of medicine, Pennsylvania Hospital, Philadelphia, PA. "Once a patient has bone metastases one of our major goals is to prevent events like fracture or spinal cord compression. XGEVA is an important new option to help prevent these debilitating complications."

XGEVA, the first and only RANK Ligand inhibitor indicated for the prevention of SREs in patients with bone metastases from solid tumors was approved by the U.S. Food and Drug Administration (FDA) on Nov. 18, 2010. The approval was based in part on results described in this publication. XGEVA is not indicated for the prevention of SREs in patients with multiple myeloma.

Key Study Results

For the primary endpoint of this study, the median time to first on-study SRE (defined as fracture, radiation to bone, surgery to bone, or spinal cord compression) was 20.6 months for patients receiving XGEVA and 16.3 months for patients receiving Zometa (hazard ratio 0.84, 95 percent CI: 0.71-0.98), which is statistically significant for non-inferiority (p=0.0007). Although numerically greater, the delay in the time to first SRE associated with XGEVA was not statistically superior compared to Zometa based upon the statistical testing strategy (adjusted p=0.06) (secondary endpoint). The time to first- and subsequent SRE was also numerically greater but not statistically superior compared to Zometa (hazard ratio 0.90, 95 percent CI: 0.77-1.04, p=0.14) (secondary endpoint).

In a subgroup analysis of patients with multiple myeloma, mortality appeared to be higher for denosumab-treated patients compared to those in the control arm (hazard ratio [95 percent CI] of 2.26 [1.13, 4.50]; n = 180). The limited number of patients in this subgroup, however, precludes definitive conclusions regarding the effects of XGEVA in multiple myeloma patients.

In the study, hypocalcemia occurred more frequently with XGEVA, while osteonecrosis of the jaw (ONJ) occurred at similar rates in both groups. Acute phase reactions after the first dose occurred more frequently in the Zometa arm, as did renal adverse events and elevation in serum creatinine. No dose adjustments or dose withholding for renal function are required for XGEVA.

Study Design

This study was an international, randomized, double-blind, double-dummy, active-controlled study, in which advanced cancer patients with solid tumors or multiple myeloma were randomized to receive either subcutaneous denosumab 120 mg and intravenous placebo (N=886), or Zometa administered intravenously as at least a 15 minute infusion at a dose of 4 mg (or equivalent creatinine clearance-adjusted dose in patients with baseline creatinine clearance less than or equal to 60 mL/min) every four weeks as per the labeled instructions (N=890). All patients were strongly recommended to take daily calcium and vitamin D supplements. The primary endpoint was time to first on-study SRE.

XGEVA Important Safety Information

XGEVA can cause severe hypocalcemia. Correct pre-existing hypocalcemia prior to XGEVA treatment. Monitor calcium levels and administer calcium, magnesium, and vitamin D as necessary. Advise patients to contact a healthcare professional for symptoms of hypocalcemia.

ONJ can occur in patients receiving XGEVA. Patients who are suspected of having or who develop ONJ while on XGEVA should receive care by a dentist or an oral surgeon. In these patients, extensive dental surgery to treat ONJ may exacerbate the condition.

The most common adverse reactions in patients receiving XGEVA were fatigue/asthenia, hypophosphatemia, and nausea. The most common serious adverse reaction in patients receiving XGEVA was dyspnea. The most common adverse reactions resulting in discontinuation of XGEVA were osteonecrosis and hypocalcemia. Please visit www.xgeva.com for full prescribing information.

Denosumab is also marketed as Prolia(R) in other indications.

XGEVA Skeletal-Related Events Regulatory Status

XGEVA was approved by the FDA for the prevention of SREs in patients with bone metastases from solid tumors on Nov. 18, 2010. XGEVA is not indicated to prevent SREs in patients with multiple myeloma.

Administered as a single 120 mg subcutaneous injection every four weeks, XGEVA provides a new option for urologists and oncologists to prevent serious bone complications in men with prostate cancer.

Amgen has also submitted marketing applications for XGEVA in the European Union, Australia, Canada and Switzerland. In Japan, Amgen is working with its licensing partner, Daiichi-Sankyo Company, Limited and a marketing application was submitted.

Bone Metastases and Skeletal Related Events: Prevalence and Impact

Bone metastases occur in more than 1.5 million patients with cancer worldwide and are most commonly associated with cancers of the prostate, lung, and breast, with incidence rates as high as 75 percent of patients with metastatic disease.(i)

Approximately 50-70 percent of cancer patients with bone metastases will experience debilitating SREs.(ii iii iv) Events considered to be SREs include fractures, spinal cord compression, and severe bone pain that may require surgery or radiation.(v) Such events can profoundly disrupt a patient's life and can cause disability and pain.(vi vii viii)

Denosumab and Amgen's Research in Bone Biology

The denosumab development program demonstrates Amgen's commitment to researching and delivering pioneering medicines to patients with unmet medical needs. Amgen is studying denosumab in numerous tumor types across the spectrum of cancer-related bone diseases. Over 11,000 patients have been enrolled in the denosumab oncology clinical trials. In addition to this newly approved indication, XGEVA is also being investigated for its potential to delay bone metastases in prostate and breast cancer.

About Amgen

Amgen discovers, develops, manufactures, 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, 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, bone disease, and other serious illnesses. With a deep and broad 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 vital medicines, visit www.amgen.com.

Forward-Looking Statements

This news release contains forward-looking statements that are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen, including Amgen's most recent annual report on Form 10-K and most recent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to our business. Unless otherwise noted, Amgen is providing this information as of Feb. 22, 2011 and expressly disclaims any duty to update information contained in this news release.

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 safety, side effects or manufacturing problems with our products after they are on the market. Our business may be impacted by government investigations, litigation and products liability claims. We depend on third parties for a significant portion of our manufacturing capacity for the supply of certain of our current and future products and limits on supply may constrain sales of certain of our current products and product candidate development.

In addition, sales of our products are affected by the reimbursement policies imposed by third-party payors, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' 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 relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration (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.

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