Denosumab Demonstrates Superiority Over Zometa(R) in Delay of Complications Due to Bone Metastases in Advanced Breast Cancer Patients

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THOUSAND OAKS, Calif., Sept. 22 /PRNewswire-FirstCall/ -- Amgen (Nasdaq: AMGN) today announced detailed results from a Phase 3, head-to-head trial evaluating denosumab versus Zometa(R) (zoledronic acid) in the treatment of bone metastases in 2,046 patients with advanced breast cancer that met its primary and secondary endpoints and demonstrated superior efficacy compared to Zometa. These results were presented today during the Presidential Session at the 2009 ECCO 15 - ESMO 34 European Multidisciplinary Congress in Berlin, Germany (Abstract Number 2LBA).

Denosumab administered subcutaneously demonstrated superiority for both delaying the time to the first on-study skeletal related events (SREs) (fracture, radiation to bone, surgery to bone, or spinal cord compression) (hazard ratio 0.82, 95 percent CI: 0.71, 0.95), and delaying the time to first-and-subsequent SREs (hazard ratio 0.77, 95 percent CI:0.66, 0.89). Both results were statistically significant in this 34 month study. The median time to first on-study SRE was not reached for denosumab and therefore could not be estimated. The median time to first on-study SRE was 26.5 months for Zometa, the current standard of care.

"Up to 80 percent of patients with advanced breast cancer will develop bone metastases that are often associated with severe and painful bone complications, which are a serious concern for both patients and physicians," said Alison Stopeck, M.D., associate professor of Medicine, Arizona Cancer Center, University of Arizona Health Sciences Center, Tucson, AZ, United States of America. "Denosumab was superior to Zometa in preventing skeletal related events and delayed worsening of bone pain. In addition, denosumab also presented some potential tolerability advantages for many patients, including a lower incidence of renal toxicity and acute phase reactions, combined with the convenience of a monthly subcutaneous injection. Denosumab would be a welcome new treatment option for advanced breast cancer patients."

Denosumab also delayed the median time to first on-study SRE or hypercalcemia of malignancy (HCM) compared to Zometa (hazard ratio 0.82, 95 percent CI: 0.70, 0.95; p=0.007). The median time to first on-study SRE or HCM was not reached for denosumab and therefore could not be estimated. The median time to first on-study SRE or HCM was 25.2 months for Zometa.

Bone pain can dominate the daily lives of patients with metastatic disease involving bone and is often characterized as severe or intolerable.(1) In a pre-specified exploratory analysis, patients on the denosumab arm reported worsening of pain later than those on the Zometa arm (88 days versus 64 days, respectively; hazard ratio 0.87, 95 percent CI: 0.79, 0.97; p=0.009).

Overall, the incidence of adverse events (96 percent denosumab, 97 percent Zometa) and serious adverse events (44 percent denosumab, 46 percent Zometa) was consistent with what has previously been reported for these two agents. Adverse events potentially associated with renal toxicity occurred in 4.9 percent of patients treated with denosumab compared to 8.5 percent in patients treated with Zometa. Osteonecrosis of the jaw (ONJ) was seen infrequently in both treatment groups (20 patients receiving denosumab (2.0 percent) as compared with 14 patients (1.4 percent) receiving Zometa). There was no statistically significant difference in the rate of ONJ between the two treatment arms. Overall survival (hazard ratio 0.95, 95 percent CI: 0.81, 1.11; p=0.50) and time to cancer progression (hazard ratio 0.99, 95 percent CI: 0.89, 1.11; p=0.90) was balanced between treatment arms.

Detailed data from another Phase 3, head-to-head trial evaluating denosumab versus Zometa was presented yesterday (Abstract #20LBA). In this study of 1,776 advanced cancer patients with solid tumors (not including breast and prostate cancer) or multiple myeloma, denosumab met its primary endpoint and demonstrated non-inferiority compared to Zometa in the treatment of bone metastases.

Webcast Information

An analyst/investor event will also be held from the Congress on September 24th, at 6:30 a.m. Eastern Time to discuss data presented at ECCO-ESMO. A webcast of the event can be found on Amgen's Web site at *www.amgen.com*, under Investors. The audio webcast will be archived and available for replay for at least 72 hours.

Study Design

This was an international, Phase 3, randomized, double-blind study comparing denosumab with Zometa in the treatment of bone metastases in patients with advanced breast cancer. Patients enrolled in the study were randomized in a one-to-one ratio to receive either 120 mg of denosumab subcutaneously every four weeks (Q4W) or Zometa administered intravenously at a dose of 4 mg in a 15 minute infusion every four weeks as per the label instructions.

In clinical trials testing new medications for bone metastases, treatment success has been measured by whether the bone complications, or SREs, caused by the tumor are reduced or delayed. The primary and secondary endpoints of the denosumab bone metastases studies use a composite endpoint of four SREs - fracture, the need for radiation to bone, the need for bone surgery, and spinal cord compression - to measure the effectiveness of denosumab versus Zometa.

The primary endpoint was to evaluate if denosumab is non-inferior to Zometa with respect to the first, on-study SRE in patients with advanced breast cancer and bone metastases. Secondary endpoints were to evaluate if denosumab was superior to Zometa with respect to the first, on-study SRE, as well as the first-and-subsequent on-study SREs, and to assess the safety and tolerability of denosumab compared with Zometa.

About Denosumab and Amgen's Research in Bone Biology

Denosumab is the first fully human monoclonal antibody in late stage clinical development that specifically targets RANK Ligand, the essential regulator of osteoclasts (the cells that break down bone). With more than 19,000 patients in trials across indications worldwide, the denosumab development program is the largest ever initiated by Amgen. This broad and deep 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-induced bone disease. Over 11,000 patients have been enrolled in the denosumab oncology clinical trials, testing the drug for the reduction of SREs in breast cancer patients, for the amelioration of treatment-induced bone loss in patients with breast or prostate cancers, for the prevention of SREs due to the spread of cancer to the bone in patients with multiple myeloma or those suffering from a variety of solid tumors, and for its potential to delay bone metastases in prostate cancer.

Bone Metastases: Impact and Prevalence

Bone metastases, cancer cells that separate from tumors and migrate to bone tissue where they settle and grow, occur in more than 1.5 million people worldwide.(2) With improvements in cancer care, including earlier diagnosis and new treatment options, leading to increases in survival rates(3), the number of patients developing metastatic disease secondary to a primary cancer is increasing. Bone metastases are a significant problem for patients with certain types of advanced cancer, with incidence rates of nearly 100 percent in myeloma patients and as high as 75 percent in breast and prostate cancer patients.

With bone metastases the growing cancer cells weaken and destroy the bone around the tumor. The damage the tumor has caused to the bone can result in a number of serious complications, collectively called SREs. These include fracture of a bone, the need for radiation to bone, the need for bone surgery, or spinal cord compression. All are serious complications for advanced cancer patients.

The economic burden of United States (U.S.) patients with bone metastases is significant and was estimated to be $12.6 billion last year.(4) Patients with bone metastases who experience an SRE incur significantly higher medical costs compared with those who do not experience an SRE.(5)

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 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 our 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 Sept. 22, 2009 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 health care 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.

ZOMETA is a registered trademark of Novartis Oncology.

*Editors Note: The FDA has provisionally approved the trade name Prolia(TM) for the proposed indications of treatment and prevention of osteoporosis in postmenopausal women, and treatment and prevention of bone loss in patients undergoing hormone ablation for non-metastatic prostate or breast cancer, for which denosumab is administered twice yearly subcutaneously at a 60 mg dose. The Prolia(TM) trade name is only for these indications and may not apply for other indications of denosumab.

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(6) GVD/Barber ISPOR 2008 Poster; Schulman 2007; Delea et al. 2006

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