FDA Approves Amgen's XGEVA® (Denosumab) For The Treatment Of Hypercalcemia Of Malignancy Refractory To Bisphosphonate Therapy

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This Approval Provides a New Treatment Option for a Patient Population With High Unmet Medical Need

THOUSAND OAKS, Calif., Dec. 8, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved a new indication for XGEVA® (denosumab) for the treatment of hypercalcemia of malignancy (HCM) refractory to bisphosphonate therapy. XGEVA was approved and granted Orphan Drug Designation by the FDA, which is reserved for drugs that are intended for the treatment of rare diseases affecting fewer than 200,000 people in the U.S.

HCM is a serious complication in patients with advanced cancer, including those with hematologic malignancies, and indicates poor prognosis.[1,2] The condition results from cancer-driven increases in bone resorption, and if untreated, can lead to renal failure, progressive mental impairment, coma and death.[1-3]

"Our continued study of XGEVA reinforces Amgen's ongoing commitment to address the unmet needs of cancer patients," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "This latest FDA approval for XGEVA provides an important new therapeutic option for patients with a rare condition that cannot be resolved with bisphosphonate therapy."

The approval of XGEVA is based on positive results from an open-label, single-arm study, which enrolled patients with advanced cancer and persistent hypercalcemia after recent bisphosphonate treatment. The primary endpoint was the proportion of patients with a response, defined as albumin-corrected serum calcium (CSC) ≤11.5 mg/dL (2.9 mmol/L; Common Terminology for Adverse Events [CTCAE] grade ≤1) within 10 days after the first dose of XGEVA. Secondary endpoints included the proportion of patients who experienced a complete response (defined as CSC ≤10.8 mg/dL [2.7 mmol/L]) by day 10, time to response and response duration (defined as the number of days from the first occurrence of CSC ≤11.5 mg/dL). The study achieved its primary endpoint with a response rate at day 10 of 63.6 percent in the 33 patients evaluated. The overall complete response rate was 63.6 percent. The estimated median time to response (CSC ≤11.5 mg/dL) was nine days, and the median duration of response was 104 days.[4,5]

The most common adverse reactions in patients receiving XGEVA for hypercalcemia of malignancy were nausea, dyspnea, decreased appetite, headache, peripheral edema, vomiting, anemia, constipation and diarrhea.[5]

For patients with HCM, XGEVA is administered as a subcutaneous injection (120 mg) every four weeks with additional doses of 120 mg on days eight and 15 of the first month of therapy.[5]

XGEVA binds to RANK Ligand (RANKL), a protein essential for the formation, function and survival of osteoclasts, the cells responsible for bone resorption, thereby modulating calcium release from bone. XGEVA prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts, thereby decreasing bone destruction and calcium release.[5]

About Hypercalcemia of Malignancy

Hypercalcemia of malignancy (HCM) is a serious complication in patients with advanced cancer, including those with hematological malignancies.[1] In 2012, the estimated prevalence of HCM in cancer patients in the U.S. was 2.7 percent.[6] HCM is indicative of poor prognosis and occurs most often in patients with squamous cell cancer (e.g., lung cancer, head and neck cancer), breast cancer, kidney cancer, myeloma and lymphoma.[1,2,7] HCM results from cancer-driven increases in bone resorption, and, if untreated, can lead to renal failure, progressive mental impairment, coma and death.[1-3]

About XGEVA

XGEVA was approved by the FDA for the prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors in 2010. XGEVA is not indicated for the prevention of SREs in patients with multiple myeloma. In clinical trials, XGEVA demonstrated a clinically meaningful improvement compared to the previous standard of care in preventing SREs. In 2013, XGEVA was approved by the FDA as the first-and-only treatment for adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

XGEVA Important Safety Information

Hypocalcemia

Pre-existing hypocalcemia must be corrected prior to initiating therapy with XGEVA. XGEVA can cause severe symptomatic hypocalcemia, and fatal cases have been reported. Monitor calcium levels and administer calcium, magnesium, and vitamin D as necessary. Monitor levels more frequently when XGEVA is administered with other drugs that can also lower calcium levels. Advise patients to contact a healthcare professional for symptoms of hypocalcemia.

Hypersensitivity

XGEVA is contraindicated in patients with known clinically significant hypersensitivity to XGEVA, including anaphylaxis that has been reported with use of XGEVA. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue XGEVA therapy permanently.

Drug Products with Same Active Ingredient

Patients receiving XGEVA should not take Prolia® (denosumab).

Osteonecrosis of the Jaw

Osteonecrosis of the jaw (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. In clinical trials in patients with osseous metastasis, the incidence of ONJ was higher with longer duration of exposure.

Atypical Subtrochanteric and Diaphyseal Femoral Fracture

Atypical femoral fracture has been reported with XGEVA. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution.

Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. During XGEVA treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Patient presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of XGEVA therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Embryo-Fetal Toxicity

XGEVA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use highly effective contraception during therapy, and for at least five months after the last dose of XGEVA.

Adverse Reactions

The most common adverse reactions in patients receiving XGEVA with bone metastasis from solid tumors were fatigue/asthenia, hypophosphatemia, and nausea. The most common serious adverse reaction was dyspnea.

The most common adverse reactions in patients receiving XGEVA for giant cell tumor of bone were arthralgia, headache, nausea, back pain, fatigue, and pain in extremity. The most common serious adverse reactions were osteonecrosis of the jaw and osteomyelitis. The most common adverse reactions resulting in discontinuation of XGEVA were osteonecrosis of the jaw and tooth abscess or tooth infection.

The most common adverse reactions in patients receiving XGEVA for hypercalcemia of malignancy were nausea, dyspnea, decreased appetite, headache, peripheral edema, vomiting, anemia, constipation, and diarrhea.

Denosumab is also marketed as Prolia® in other indications.

Please visit www.amgen.com for Full Prescribing Information.

About Amgen

Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its biologics manufacturing expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be the world's largest independent biotechnology company, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

Forward-Looking Statements

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen Inc. and its subsidiaries (Amgen, we or us) 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 Inc., including Amgen Inc.'s most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen Inc.'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 Dec. 8, 2014, 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 and our partners 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 product liability claims. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. 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 (including products of our wholly-owned subsidiaries) are affected by the reimbursement policies imposed by third-party payers, 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 and our partners routinely obtain patents for our and their products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by our or our partners' competitors and there can be no guarantee of our or our partners' 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. Our efforts to integrate the operations of companies we have acquired may not be successful. Cost savings initiatives may result in us incurring impairment or other related charges on our assets. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our recently announced restructuring plans. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase common stock.

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 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.

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