FDA Approves Amgen's XGEVA® (denosumab) For The Treatment Of Giant Cell Tumor Of Bone

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XGEVA Becomes First FDA-Approved Treatment for This Rare Disease

THOUSAND OAKS, Calif., June 13, 2013 /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 adults and skeletally mature adolescents with giant cell tumor of bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity. XGEVA was approved following a priority review by the FDA, a designation reserved for drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists.

GCTB typically affects individuals between the ages of 20 to 40. The disease is characterized by a bone destructive tumor that often results in fractures. When untreated, it often results in complete destruction of the affected bone, leading to bone fracture, joint dysfunction, deformity or amputation.

The approval of XGEVA is based on positive results from two open-label trials that enrolled patients with GCTB that was either recurrent, unresectable, or for which planned surgery was likely to result in severe morbidity. The overall objective response rate of the 187 patients evaluated was 25 percent. The estimated median time to response was three months. In the 47 patients with an objective response, 51 percent (24/47) had a duration of response lasting at least eight months. Three patients experienced disease progression following an objective response.

The safety profile of XGEVA in patients with GCTB was similar to that reported in studies of patients with bone metastases, and also appeared to be similar in skeletally mature adolescents and adults. Safety data was evaluated in 304 patients with GCTB who received at least one dose of XGEVA. Of these patients, 145 were treated for at least one year. The most common adverse reactions were arthralgia, headache, nausea, back pain, fatigue, and pain in the extremity. The most common serious adverse reactions were osteonecrosis of the jaw and osteomyelitis.

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

"With today's XGEVA FDA approval, Amgen can offer a much needed treatment option to patients who suffer from giant cell tumor of bone that cannot be adequately treated with surgery," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Advances in our understanding of the underlying biology of this rare disorder have allowed Amgen to generate compelling clinical evidence to address the medical needs of patients and their healthcare providers."

XGEVA binds to RANK Ligand (RANKL), a protein essential for the formation, function and survival of osteoclasts - the cells responsible for bone resorption. Giant cell tumors of bone consist of stromal cells expressing RANKL and osteoclast-like giant cells expressing RANK receptor. Signaling through the RANK receptor contributes to osteolysis and tumor growth. XGEVA prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts, their precursors and osteoclast-like giant cells.

About Giant Cell Tumor of Bone
GCTB is a locally aggressive, benign tumor afflicting younger adults between the ages 20 to 40. It is estimated that there are approximately 300-800 new cases of GCTB annually in the U.S. GCTB is unresectable in approximately 18-20 percent of cases.

Most tumors occur in the long bones of the body, often around joints, but can also spread to the lungs in rare cases. Although giant cell tumors are slow growing, patients can experience severe bone pain, swelling, loss of mobility and pathologic fracture. Historically, there have been no approved therapies for GCTB. Surgery is the main treatment option for patients with resectable GCTB; however, surgery, such as amputation, may be associated with significant morbidity. These tumors also have a higher recurrence rate within the first three years of surgical intervention. When tumors recur, they become more difficult to treat and more likely to spread to other parts of the body.

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 these bone complications.

In 2013, XGEVA was approved by the FDA as the first and only treatment for adults and skeletally mature adolescents with GCTB that is unresectable or where surgical resection is likely to result in severe morbidity.

XGEVA Important Safety Information
Hypersensitivity
XGEVA is contraindicated in patients with clinically significant hypersensitivity to any component of the product.

Hypocalcemia
XGEVA can cause severe symptomatic hypocalcemia, and fatal cases have been reported. 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.

Osteonecrosis of the Jaw (ONJ)
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.

Atypical Subtrochanteric and Diaphyseal Femoral Fracture
Atypical femoral fracture has been reported with XGEVA. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with anti-resorptive agents. A number of reports note that patients were also receiving treatment with glucocorticoids at the

time of fracture. Any patient who presents with thigh or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. 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 5 months after with 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.

Please visit www.amgen.com for full prescribing information.

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 people around the world in the fight against serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. 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 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 any subsequent 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 June 13, 2013, 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 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 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 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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