FDA Approves New Indication For Prolia® (Denosumab) For The Treatment Of Bone Loss In Men With Osteoporosis At High Risk For Fracture

September 20, 2012

THOUSAND OAKS, Calif., Sept. 20, 2012 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the U.S. Food and Drug Administration (FDA) approved a new indication for Prolia® (denosumab) as a treatment to increase bone mass in men with osteoporosis at high risk for fracture. Prolia, the first FDA-approved RANK Ligand inhibitor, is a subcutaneous injection administered by a health care professional every six months.

"While osteoporosis and osteoporosis-related fractures are more commonly associated with postmenopausal women, osteoporosis in men is a significant issue that is increasing in prevalence as life expectancies rise," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Fractures can be a life-changing event, so we are pleased that we can offer a new treatment option for the growing number of men with osteoporosis at high risk for fracture."

According to the National Osteoporosis Foundation, two million men in the U.S. have osteoporosis and another 12 million are at risk.[1] Osteoporosis and osteoporotic fractures in men remain under diagnosed and under treated.[2]

The new indication for Prolia is based on results from the ADAMO trial[3] (**A** multicenter, randomized, double-blind, placebo-controlled study to compare the efficacy and safety of **D**enosum**A**b 60 mg every six months versus placebo in **M**ales with **O**steoporosis), the pivotal Phase 3 study involving 242 men with low bone mineral density (BMD). In the study, treatment with Prolia resulted in significantly greater gains at the lumbar spine when compared to placebo (5.7 percent vs. 0.9 percent). Effects of Prolia on BMD were independent of age, baseline testosterone levels, BMD status and estimated fracture risk.

Additional results showed that patients in the study who received treatment with Prolia experienced BMD increases at all other skeletal sites assessed compared to placebo, including at the total hip (2.4 percent vs. 0.3 percent) and at the femoral neck (2.1 percent vs. 0.0 percent). Safety findings were consistent with what have been observed in other studies of Prolia in postmenopausal women with osteoporosis. The most common adverse reactions reported (per patient incidence ≥ 5 percent) were back pain, arthralgia and nasopharyngitis.

Prolia Clinical Data
Approval was based on the ADAMO trial 12-month data. Men between the ages of 30 and 85 years with low BMD (T-score ≤–2.0 and ≥–3.5 at the lumbar spine or femoral neck) or who have experienced a prior major osteoporotic fracture and had a T-score ≤–1.0 and ≥–3.5 were enrolled in the study. Patients were randomized (1:1) to receive either 60 mg of Prolia every six months or placebo. All patients received daily calcium and vitamin D supplementation throughout the study. **3**

The primary study endpoint was the percent change from baseline in the lumbar spine BMD at month 12. Secondary efficacy endpoints included percent change in total hip and femoral neck BMD from baseline to one year.

About Male Osteoporosis
Osteoporosis in men has recently been recognized as an important public health issue, as male life expectancies rise and the number of men over the age of 70 grows. [4] Between 2010 and 2020, the number of men with osteoporosis is expected to increase by 17 percent.[1] Approximately one in four men in the U.S. over the age of 50 will have an osteoporosis-related fracture in his remaining lifetime. [5]

About Prolia
Prolia is the first approved therapy that specifically targets RANK Ligand, an essential regulator of osteoclasts (the cells that break down bone).

Prolia is approved in the U.S. for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. Prolia is also approved for treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

Prolia is administered as a single subcutaneous injection of 60 mg once every six months. For further information about Prolia, including prescribing information and medication guide, please visit http://www.prolia.com.

Important U.S. Safety Information
Prolia is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia. Prolia is contraindicated in women who are pregnant and may cause fetal harm. Patients receiving Prolia should not receive XGEVA® (denosumab), as both Prolia and XGEVA contain the same active ingredient, denosumab.

Hypocalcemia may worsen with the use of Prolia, especially in patients with severe renal impairment. All patients should be adequately supplemented with calcium and vitamin D. In the Phase 3 pivotal study of women with postmenopausal osteoporosis (n=7,808), serious infections leading to hospitalizations were reported more frequently in the Prolia-treated patient group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia. Patients should be advised to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis. Endocarditis was reported more frequently in the Prolia-treated patient group. Epidermal and dermal adverse events such as dermatitis, rashes and eczema have been reported. Discontinuation of Prolia should be considered if severe symptoms develop.

In clinical trials in women with postmenopausal osteoporosis, Prolia resulted in significant suppression of bone remodeling. The significance of these findings is unknown. The long-term consequences of the degree of suppression of bone remodeling observed with Prolia may contribute to adverse outcomes such as osteonecrosis of the jaw (ONJ), atypical fractures and delayed fracture healing. ONJ and atypical fractures have been reported in

patients with Prolia. Patients should be monitored for these adverse outcomes. The most common adverse reactions (≥ 5 percent and more common than placebo) in patients with postmenopausal osteoporosis were back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia and cystitis. The most common adverse reactions in men with osteoporosis were back pain, arthralgia and nasopharyngitis. Pancreatitis has also been reported with Prolia.

The extent to which Prolia is present in seminal fluid is unknown. For men treated with Prolia, there is a potential for fetal exposure if the sexual partner is pregnant. While the risk is likely to be low, patients should be advised of this potential risk.

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. 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 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. 20, 2012 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 use(s). 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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(Logo: http://photos.prnewswire.com/prnh/20081015/AMGENLOGO)

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