Amgen Announces Positive Top-Line Results From Phase 3 Study Of Prolia® (Denosumab) In Patients Receiving Glucocorticoid Therapy

August 29, 2016

Study Indicates That Prolia Led to Greater Gains in Bone Mineral Density at 12 Months Compared With Risedronate in Patients Receiving Glucocorticoid Therapy

THOUSAND OAKS, Calif., Aug. 29, 2016 /PRNewswire/ -- Amgen (NASDAQ: AMGN) today announced positive top-line results from the primary analysis conducted in a Phase 3 randomized, double-blind, double-dummy, active-controlled study evaluating the safety and efficacy of Prolia® (denosumab) compared with risedronate in patients receiving glucocorticoid treatment. The study met all primary and secondary endpoints at 12 months. The data showed that treatment with Prolia for 12 months, compared to risedronate, led to significantly greater gains in bone mineral density (BMD) at the lumbar spine and total hip, both in patients receiving continuing glucocorticoid therapy and in patients newly initiating glucocorticoid therapy.

"The impact of glucocorticoid therapy on bone strength is frequently underestimated, and often leads to increased bone loss and ultimately, a fracture," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We are excited that these data support the potential for Prolia use in patients with glucocorticoid-induced osteoporosis, the most common drug-induced form of the disease."

Results from the glucocorticoid-induced osteoporosis (GIOP) study showed that, in patients receiving continuing glucocorticoid therapy, Prolia treatment led to greater gains in BMD, compared with risedronate, both at the lumbar spine (4.4 percent vs. 2.3 percent, respectively) and total hip (2.1 percent vs. 0.6 percent, respectively). Similarly, in patients newly initiating glucocorticoid therapy, Prolia treatment led to greater increases in BMD, compared with risedronate, both at the lumbar spine (3.8 percent vs. 0.8 percent, respectively) and total hip (1.7 percent vs. 0.2 percent, respectively).

Adverse events (AEs) and serious adverse events (SAEs) were similar across treatment groups and consistent with the known safety profile of Prolia. No SAEs were reported with a subject incidence of two percent or greater in either treatment group.

This is a Phase 3 international, multi-center, randomized, double-blind, double-dummy, active-controlled, parallel-group study in men and women receiving oral glucocorticoid therapy. A total of 795 patients were enrolled in the 24-month study to evaluate the safety and efficacy of treatment with Prolia 60 mg subcutaneously every six months compared with oral risedronate 5 mg daily in two patient subpopulations: 505 patients receiving continuing glucocorticoid therapy (defined as patients receiving greater than or equal to 7.5 mg daily prednisone or its equivalent for three months or longer and planning to continue treatment for a total of at least six months) and 290 patients newly initiating glucocorticoid therapy (defined as patients receiving greater than or equal to 7.5 mg daily prednisone or its equivalent for less than three months and who are planning to continue treatment for a total of at least six months).

Evaluation of the primary endpoint (the percent change from baseline in lumbar spine BMD at 12 months, assessing non-inferiority) and two secondary endpoints assessed at 12 months (the percent change from baseline in lumbar spine and total hip BMD, assessing superiority) was conducted; further analysis of these results is ongoing and will be submitted to a future medical conference and for publication. The study remains double-blinded and ongoing for an additional 12 months.

About Glucocorticoid-induced Osteoporosis

Glucocorticoid-induced osteoporosis (GIOP), the most common form of secondary osteoporosis, is caused by taking glucocorticoid medicines which are commonly used to treat inflammatory diseases.[i] Within the first three months of glucocorticoid treatment, patient fracture risk increases up to 75 percent, although BMD will continue to decline significantly in the months to follow.[ii]

About Prolia® (denosumab)

Prolia is the first approved therapy that specifically targets RANK Ligand, an essential regulator of bone-removing cells (osteoclasts). Prolia is approved and marketed in over 80 countries worldwide.

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. In the U.S., 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 also indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer and in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer in the U.S.

Prolia is approved in the EU for the treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures. Prolia is also approved in the EU for the treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures.

Prolia is administered as a single subcutaneous injection of 60 mg once every six months. Please see the Important Safety Information below.

Important Safety Information (U.S.)

Contraindications

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. Prolia is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

Same Active Ingredient

Prolia contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolia should not receive XGEVA®.

Hypersensitivity

Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus, and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia.

Hypocalcemia

Hypocalcemia may worsen with the use of Prolia, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolia injection. Adequately supplement all patients with calcium and vitamin D.

Osteonecrosis of the Jaw (ONJ)

ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia. An oral exam should be performed by the prescriber prior to initiation of Prolia. A dental examination with appropriate preventive dentistry is recommended prior to treatment in patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g., chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment with Prolia. The risk of ONJ may increase with duration of exposure to Prolia.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia should be considered based on individual benefit-risk assessment.

Atypical Femoral Fractures

Atypical low-energy, or low trauma fractures of the shaft have been reported in patients receiving Prolia. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with anti-resorptive agents.

During Prolia treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of Prolia therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Serious Infections

In a clinical trial (N= 7808) in women with postmenopausal osteoporosis, serious infections leading to hospitalization were reported more frequently in the Prolia group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear were more frequent in patients treated with Prolia.

Endocarditis was also reported more frequently in Prolia-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia, prescribers should assess the need for continued Prolia therapy.

Dermatologic Adverse Reactions

In the same clinical trial in women with postmenopausal osteoporosis, epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolia compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolia if severe symptoms develop.

Musculoskeletal Pain

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking Prolia. Consider discontinuing use if severe symptoms develop.

Suppression of Bone Turnover

In clinical trials in women with postmenopausal osteoporosis, Prolia resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for these consequences, including ONJ, atypical fractures, and delayed fracture healing.

Adverse Reactions

The most common adverse reactions (>5% and more common than placebo) in women with postmenopausal osteoporosis are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. The most common adverse reactions (> 5% and more common than placebo) in men with osteoporosis are back pain, arthralgia, and nasopharyngitis. Pancreatitis has been reported with Prolia.

In women with postmenopausal osteoporosis, the overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolia group. In men with osteoporosis, new malignancies were reported in no patients in the placebo group and 4 (3.3%) patients in the Prolia group. A causal relationship to drug exposure has not been established.

The most common (per patient incidence ≥ 10%) adverse reactions reported with Prolia in patients with bone loss receiving ADT for prostate cancer or

adjuvant AI therapy for breast cancer are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials. Additionally, in Prolia-treated men with nonmetastatic prostate cancer receiving ADT, a greater incidence of cataracts was observed.

Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

Prolia® Postmarketing Active Safety Surveillance Program

The surveillance program is available to collect information from prescribers on specific adverse events. Please see https://www.proliasafety.com/ or call 1-800-772-6436 for more information.

For more information, please see the Prolia Important Safety Information, Prescribing Information, and Medication Guide.

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 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 one of the world's leading independent biotechnology companies, 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. 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 reports filed by Amgen, including our most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. 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 results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and 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. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. 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. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. 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. Further, 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, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. 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 acquire other companies or products and to integrate the operations of companies we have acquired may not be successful. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. Our stock price is volatile and may be affected by a number of events. 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 our common stock.

The scientific information discussed in this news release relating to new indications is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration or European Commission 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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[i] Briot K, Roux C. Glucocorticoid-induced osteoporosis. RMD Open. 2015;1:e000014.

[ii] Weinstein RS. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism. ASBMR 8th Edition. 2013.

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