Amgen Announces Results From Several New Exploratory Analyses Evaluating Long-Term Impact Of Treatment With Prolia® (Denosumab) In Postmenopausal Women With Osteoporosis

September 15, 2014

Data Presented at the American Society of Bone and Mineral Research 2014 Annual Meeting

THOUSAND OAKS, Calif., Sept. 15, 2014 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced results from a new exploratory analysis of the open-label extension study of the pivotal Phase 3 fracture trial, which found that treatment with Prolia® (denosumab) for eight years enabled a substantial proportion of women with osteoporosis to achieve non-osteoporotic T-scores (>-2.5) at the lumbar spine and total hip from baseline. Additional Prolia data of interest are detailed below. Prolia is the first approved therapy that specifically targets RANK Ligand, an essential regulator of bone-removing cells (osteoclasts). Data were presented at the American Society for Bone and Mineral Research (ASBMR) 2014 Annual Meeting in Houston, Sept. 12-15, 2014.

"One of the main effects of untreated postmenopausal osteoporosis is increased risk of fractures, which can have significant impact on a patient's life," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We are pleased to present these new Prolia analyses at this year's meeting, which add to the growing body of evidence supporting proven treatments for osteoporosis."

Postmenopausal osteoporosis (PMO) affects many women after menopause as their ability to form new bone cannot counter balance the rate at which bone is being removed. This bone loss leads to weakened bones over time, increasing the potential for a break.[1,2] Such a break, or fracture, may be a life-changing event.[3,4] About half of all women over age 50 will have an osteoporosis-related fracture in their remaining lifetime, and once that happens, the chances of another are much higher.[5] In order to determine the risk for fracture, T-scores are measured to compare a patient's bone density to that of a healthy, young person of the same sex. A T-score of -2.5 or lower is defined as osteoporosis. The lower the score, the greater the fracture risk can be.[6]

Selected Prolia Abstracts of Interest

"Percentage of Women Achieving Non-Osteoporotic BMD T-Scores at the Spine and Hip over 8 Years of Denosumab Treatment"

Results:

- In this exploratory analysis, results showed that Prolia enabled a substantial proportion of women with osteoporosis to achieve non-osteoporotic T-scores after eight years of treatment. By year eight, approximately 1,500 women remained in the open-label extension portion of the study.
- At study baseline, mean lumbar spine and total hip T-scores were -2.83 and -1.85, respectively, for the Prolia pivotal Phase 3 trial fracture extension (EXT) participants.
    - The percentage of women with non-osteoporotic T-scores (>-2.5, >-2.2, >-2.0, and >-1.8) at both the lumbar spine and total hip progressively increased from baseline over eight years of Prolia treatments as follows: 11 to 82 percent (>−2.5), 4 to 65 percent (>−2.2), 2 to 53 percent (>−2.0), and 1 to 39 percent (>−1.8).
    - At individual sites, the percentage of women with a T-score >–2.5 increased from baseline over eight years of Prolia treatment from 19 to 86 percent (lumbar spine) and from 75 to 94 percent (total hip).

Methods:

- Women received three years of Prolia during the pivotal Phase 3 fracture trial and five years of Prolia during the EXT trial for a total of eight years of continued treatment.
    - The study evaluated the percentage of women with T-scores >-2.5, >-2.2, >-2.0, and >-1.8 at both the lumbar spine and total hip, and T-scores >-2.5 at either the lumbar spine or total hip at baseline and over eight years of Prolia treatment.

"Denosumab Restores Cortical Bone Loss at the Distal Radius Associated with Aging and Reduces Wrist Fracture Risk: Analyses from the FREEDOM Extension Cross-over Group"

Results:

- This exploratory analysis showed that in the placebo group, cortical bone density at the radius declined despite calcium and vitamin D supplementation.
- Prolia treatment for three years reversed this bone loss and an additional two years resulted in further bone mineral density (BMD) gains that reduced wrist fracture rates.
- With five years of Prolia treatment, a significant gain in BMD (1.5 percent at EXT year five) was observed, compared with EXT baseline.
- During the first three years of EXT, while BMD recovered to the original baseline levels in response to Prolia, the wrist fracture rate remained comparable to the pivotal Phase 3 fracture trial placebo rate; and with two additional years, BMD increased further, and the wrist fracture rate declined to levels significantly lower than the pivotal Phase 3 fracture trial

placebo rate.

Methods:

- This pivotal Phase 3 fracture trial extension study analysis examined the clinical importance of cortical bone mass in more than 2,000 untreated women with PMO.
- All women received Prolia, daily calcium and vitamin D.
- Analysis of mean percentage changes in BMD over time from pivotal Phase 3 fracture trial and EXT baselines consisted of a repeated measure model.

"Persistence with Osteoporosis Therapies among Osteoporotic Women at High Risk for Fracture within a Commercially-Insured Population in the United States"

Results:

- In this exploratory analysis, persistence and compliance over 12 months was higher among patients who had newly initiated Prolia compared with other osteoporosis therapies.

Methods:

- From January to March 2012, this study examined 6,187 women at or over age 50 at high risk for fracture in the MarketScan Commercial and Medicare databases who newly initiated treatment with Prolia or other osteoporosis therapies (teriparatide, raloxifene, alendronate, ibandronate and risedronate).
- Osteoporosis at high risk for fracture was indicated by: 70 years of age or older, a pre-index fracture, or pre-index use of osteoporosis therapy which was discontinued at least three months prior to index.
- Persistence, indicated by continuous use of index therapy with no gap of more than 60 days; medication coverage ratio (MCR), indicated by the proportion of days covered by therapy; and compliance, defined by an MCR ≥ 0.80, were assessed during the 12-month follow-up.
- The odds of being persistent and compliant across treatments favored Prolia (odds ratios for persistence from 1.62 to 5.75, $p<0.0001$; for compliance from 2.36 to 7.25, $p<0.0001$).

About the Open-Label Extension Study of the Pivotal Phase 3 Fracture Trial
The pivotal Phase 3 fracture trial, also known as The Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM), was an international, randomized, placebo-controlled trial involving 7,868 women 60 to 90 years of age with a BMD T-score of less than -2.5 but not less than -4.0 at the lumbar spine or total hip who were assigned to denosumab, 60 mg every six months, or placebo for three years. The majority of the original participants continued in the open-label extension study, with those in the placebo group all crossing over to denosumab therapy. The 7-year extension phase of the trial will permit evaluation of denosumab for up to 10 years of treatment.

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 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 approved in the EU plus Switzerland, Norway, Iceland and Liechtenstein 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 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 nonmetastatic prostate cancer.

Prolia is administered as a single subcutaneous injection of 60 mg once every six months. For further information on Prolia, including prescribing information and medication guide, please visit: 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. Prolia is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Patients receiving Prolia should not receive XGEVA® (denosumab), as both Prolia and XGEVA contain the same active ingredient, denosumab.

Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia. 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.

Osteonecrosis of the jaw (ONJ) and atypical femoral fractures have been reported in patients with Prolia. In the pivotal Phase 3 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. Epidermal and dermal adverse events such as dermatitis, rashes and eczema have been reported. Discontinuation of Prolia should be considered if severe symptoms

develop.

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported. 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 ONJ, atypical fractures and delayed fracture healing. 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 in patients with osteoporosis. The most common (per patient incidence >10 percent) adverse reactions reported with Prolia in patients with bone loss receiving androgen deprivation therapy for prostate cancer or adjuvant aromatase inhibitor therapy for breast cancer are arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials.

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.

Important EU Safety Information
The most common (≥1 percent) adverse reactions in clinical trials with Prolia in patients with osteoporosis and breast or prostate cancer patients receiving hormone ablation were urinary tract infection, upper respiratory tract infection, sciatica, cataracts, constipation, abdominal discomfort, rash, eczema, pain in extremity and musculoskeletal pain. Skin infections (predominantly cellulitis) leading to hospitalization were reported more frequently in the Prolia group compared with placebo (0.4 percent vs. 0.1 percent) in postmenopausal osteoporosis studies. In breast and prostate cancer studies, serious adverse reactions of skin infection were similar in the Prolia and placebo groups (0.6 percent vs. 0.6 percent). In a Phase 3 placebo-controlled clinical trial in patients with prostate cancer receiving androgen deprivation therapy (ADT), an imbalance in cataract adverse events was observed with Prolia compared with placebo (4.7 percent vs. 1.2 percent). No imbalance in cataract adverse events was observed in postmenopausal women with osteoporosis or in women undergoing aromatase inhibitor therapy for nonmetastatic breast cancer.

Prolia may rarely lead to hypocalcemia. Prolia is contraindicated in patients with hypocalcaemia, and pre-existing hypocalcemia must be corrected by adequate intake of calcium and vitamin D before initiating therapy. Patients with severe renal impairment or receiving dialysis are at greater risk of developing hypocalcemia. In the post-marketing setting, rare cases of severe symptomatic hypocalcemia have been predominantly reported in patients at increased risk of hypocalcaemia, with most cases occurring in the first weeks of initiating therapy. Osteonecrosis of the jaw (ONJ) has been reported rarely in clinical studies in patients receiving denosumab at a dose of 60 mg every 6 months for osteoporosis. In the osteoporosis clinical trial program, atypical femoral fractures were reported rarely in patients treated with Prolia. In the post-marketing setting, rare events of drug-related hypersensitivity, including anaphylactic reaction, have been reported in patients receiving Prolia. Hypersensitivity to the active substance or any of the excipients is a contraindication for Prolia.

Prolia is not recommended for use in pregnant women.

Denosumab Commercialization Collaboration
Amgen and Daiichi Sankyo Company, Limited have a collaboration and license agreement for the development and commercialization of denosumab in Japan.

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 Sept. 15, 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.

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