New Data Show Greater Bone Mineral Density Gains With Prolia® (Denosumab) Compared With Zoledronic Acid

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Results From Study in Women With Postmenopausal Osteoporosis Previously Treated With Oral Bisphosphonates Presented at ASBMR

THOUSAND OAKS, Calif., Oct. 11, 2015 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced findings from a randomized, double-blind, double-dummy, multicenter Phase 4 study showing that Prolia® (denosumab) achieved greater gains in bone mineral density (BMD) than the intravenous bisphosphonate zoledronic acid in postmenopausal women with osteoporosis following previous treatment with oral bisphosphonates. The findings were presented today at the American Society for Bone and Mineral Research (ASBMR) 2015 Annual Meeting in Seattle.

"Despite the availability of newer therapies like denosumab, bisphosphonates are commonly used first-line to treat osteoporosis," said lead investigator Paul Miller, M.D., medical director of the Colorado Center for Bone Research, Lakewood, Colo. "Our findings showed that denosumab provides significantly greater bone mineral density increases than zoledronic acid."

The 12-month study (NCT01732770) included 643 women 55 years or older who had postmenopausal osteoporosis (BMD T-score –2.5 or less at the lumbar spine, total hip, or femoral neck) and had been taking oral bisphosphonate therapy for two or more years. The women were randomized 1:1 to receive either subcutaneous denosumab (60 mg) every six months plus intravenous placebo once yearly (denosumab group, 321 participants), or intravenous zoledronic acid (5 mg) once yearly plus subcutaneous placebo every six months (zoledronic acid group, 322 participants). The change from baseline in lumbar spine BMD at 12 months – the primary endpoint – in the denosumab group was significantly greater than that in the zoledronic acid group: 3.2 percent vs. 1.1 percent, respectively (p<0.0001).

The denosumab group also had significantly greater improvements than the zoledronic acid group in secondary and exploratory study endpoints, including BMD changes in the total hip (1.9 percent vs. 0.6 percent [p<0.0001]), femoral neck (1.2 percent vs. -0.1 percent [p<0.0001]), and 1/3 radius (0.6 percent vs. 0 percent [p<0.0184]).

"These findings add to the evidence supporting Prolia as an important therapeutic option for women with postmenopausal osteoporosis, especially those who have failed bisphosphonate treatment," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "Our continued research in this innovative antiresorptive reinforces Amgen's commitment to bone biology and understanding the value Prolia brings to treating osteoporosis in postmenopausal women at high risk for fracture."

In the study, no new safety signals were identified. The two study groups had similar incidences of overall adverse events (AEs), serious AEs, AEs leading to discontinuation, and fatal AEs. Three events consistent with the definition of atypical femoral fracture were observed, including two in the denosumab group and one in the zoledronic acid group. There were no cases of osteonecrosis of the jaw (ONJ), hypocalcemia, or delayed fracture healing.

About Osteoporosis
Excessive bone loss can lead to a condition called osteoporosis, which significantly increases a person's risk for fracture. Women specifically can lose up to 20 percent of their bone mass in the five to seven years after menopause,[1] and up to half of all women over the age of 50 will have an osteoporosis-related fracture in their lifetime.[2] Postmenopausal osteoporosis, the most common form of the disease,[3] is a condition that weakens bones over time, making them thinner, more brittle, and more likely to break.[1]

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 also indicated in the U.S. 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.

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.)
Prolia is contraindicated in patients with hypocalcemia. Preexisting 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.

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

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 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.

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®.

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 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.

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.

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.

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

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 consequences, including ONJ, atypical fractures, and delayed fracture healing.

The most common adverse reactions (>5 percent 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 percent 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 percent in the placebo group and 4.8 percent in the Prolia® groups. In men with osteoporosis, new malignancies were reported in no patients in the placebo group and 4 (3.3 percent) patients in the Prolia® group. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

The Prolia Postmarketing Active Safety Surveillance Program is available to collect information from prescribers on specific adverse events. Please see https://www.proliasafety.com/ or call 18007726436 for more information.

For more information, please see the Prolia 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 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 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 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 Oct. 11, 2015, 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. Our efforts to integrate the operations of companies we have acquired may not be successful. We may experience difficulties, delays or unexpected costs and not achieve anticipated benefits and savings from our ongoing restructuring plan. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or their ability to pay a dividend or repurchase our common stock.

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References

[1] American College of Preventative Medicine. *Osteoporosis: A Resource from the American College of Preventative Medicine*. 2009. Available https://c.ymcdn.com/sites/www.acpm.org/resource/resmgr/timetools-files/osteoporosisclinicalreferenc.pdf. Accessed on March 5, 2015.
[2] National Osteoporosis Foundation. *What Women Need to Know*. Available http://nof.org/articles/235. Accessed March 5, 2015.
[3] American Academy of Orthopaedic Surgeons. *Position Statement: Osteoporosis/Bone Health in Adults as a National Public Health Priority*. December 2014. Available http://www.aaos.org/about/papers/position/1113.asp. Accessed on March 5, 2015.

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