Amgen And UCB Announce Positive Top-Line Results From The Phase 3 Study Of Romosozumab In Postmenopausal Women With Osteoporosis

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FRAME Study Met All Primary Endpoints by Reducing the Incidence of New Vertebral Fracture Through 12 and 24 Months

THOUSAND OAKS, Calif. and BRUSSELS, Feb. 22, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) and UCB (Euronext Brussels: UCB) today announced top-line results from the Phase 3 placebo-controlled FRActure study in postmenopausal woMen with ostEoporosis (FRAME). These data showed FRAME met the co-primary endpoints by reducing the incidence of new vertebral fracture through months 12 and 24 in postmenopausal women with osteoporosis treated with romosozumab. The study also met the secondary endpoint of reducing the incidence of clinical fractures (composite of vertebral and non-vertebral fractures) in postmenopausal women with osteoporosis through 12 months. However, the secondary endpoint of reducing the incidence of non-vertebral fractures through months 12 and 24 was not met.

"A vertebral fracture due to osteoporosis can be a life-altering event, and the risk of these kinds of fractures will be a growing burden as our society ages," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "These data show that romosozumab reduced new vertebral fracture risk as soon as 12 months."

Results from the FRAME study showed that women receiving subcutaneous injection of romosozumab monthly experienced a statistically significant 73 percent reduction in the relative risk of a vertebral (spine) fracture through 12 months compared to those receiving placebo. The effect size persisted after both groups were transitioned to denosumab through the second year of treatment. Specifically, through month 24, romosozumab followed by denosumab reduced the relative risk of new vertebral fracture by a statistically significant 75 percent compared to placebo followed by denosumab. Additionally, patients receiving romosozumab experienced a statistically significant 36 percent reduction in the relative risk of a clinical fracture through 12 months compared to those receiving placebo.

"These data are encouraging and in meeting the co-primary endpoints of this study, romosozumab has shown to be effective in reducing the incidence of new vertebral fractures at months 12 and 24 and for clinical fractures as early as 12 months," said Professor Dr. Iris Loew-Friedrich, chief medical officer and executive vice president, UCB. "Deeper understanding of the results will help us to sharpen the profile of romosozumab in postmenopausal women with osteoporosis."

The percentage of patients with adverse events and serious adverse events in the 12-month double-blind period and 24-month study period were balanced overall between the treatment groups. In the initial 12-month treatment period, the most commonly reported adverse events in both arms (greater than 10 percent) were arthralgia, nasopharyngitis and back pain. Injection site reactions were reported in 5.2 percent of patients in the romosozumab treatment group and 2.9 percent in the placebo group during the 12-month period. Most injection site reactions were reported as mild in severity. Substudies evaluating hearing loss and worsening of knee osteoarthritis showed no difference between the treatment groups. There were two positively adjudicated events of osteonecrosis of the jaw in the romosozumab treatment group, one after completing romosozumab dosing and the other after completing romosozumab treatment and receiving the initial dose of denosumab. There was one positively adjudicated event of atypical femoral fracture after three months of romosozumab treatment.

FRAME is a Phase 3 multi-center, international, randomized, double-blind, placebo-controlled, parallel-group study to assess the efficacy and safety of romosozumab treatment in postmenopausal women with osteoporosis. The study evaluated 12 months of romosozumab treatment versus placebo followed by 12 months of open-label denosumab treatment for both arms.The purpose of this study was to determine if treatment with romosozumab is effective in reducing the risk of fracture in women with postmenopausal osteoporosis through months 12 and 24.

Further analysis of the Phase 3 FRAME study data is ongoing and will be submitted to a future medical conference and for publication. UCB and Amgen plan to discuss these results with global regulators in anticipation of a potential filing in 2016.

About Romosozumab

Romosozumab is an investigational bone-forming monoclonal antibody and is not approved by any regulatory authority for the treatment of osteoporosis. It is designed to work by inhibiting the protein sclerostin, and has a dual effect on bone, both increasing bone formation and decreasing bone breakdown. Romosozumab is being studied for its potential to reduce the risk of fractures in an extensive global Phase 3 program. This program includes two large fracture trials comparing romosozumab to either placebo or active comparator in more than 10,000 postmenopausal women with osteoporosis. Amgen and UCB are co-developing romosozumab.

About the FRAME study

FRAME is a multi-center, international, randomized, double-blind, placebo-controlled, parallel-group study in postmenopausal women with osteoporosis, defined as low bone mineral density at the total hip or femoral neck. The study evaluated the effectiveness of romosozumab treatment, compared with placebo, in reducing the risk of new vertebral fractures through 12 months. The study also further evaluated if romosozumab treatment for 12 months followed by denosumab treatment for 12 months, compared with placebo followed by denosumab treatment, was effective in reducing the risk of new vertebral fractures through 24 months. In addition, clinical fracture (a composite endpoint of symptomatic vertebral and non-vertebral fractures) risk reduction, non-vertebral fracture (fractures outside of the spine, excluding sites that are not considered osteoporotic, fractures due to high trauma or pathologic fractures) risk reduction and other endpoints were assessed at 12 and 24 months.

7,180 patients were randomized 1:1 to receive either 210 mg romosozumab subcutaneous (SC) monthly (QM) or placebo SC QM for the 12-month double-blind study period. After the placebo-controlled study period, patients entered the open-label phase where all patients received 60 mg denosumab SC every six months (Q6M) for 12 months, while remaining blinded to initial treatment. An additional 12 month extension period of open-label 60 mg denosumab SC Q6M is currently ongoing.

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 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.

Important Safety Information (U.S.)

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.

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.

Osteonecrosis of the jaw (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% 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® groups. 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. 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 1-800-772-6436 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 – Amgen

This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen 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. 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 its 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 Feb. 21, 2016, 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 Amgen projects. 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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints Amgen has selected. In addition, the length of time that it takes for Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expect similar variability in the future. Amgen develops 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 Amgen may have believed at the time of entering into such relationships. Also, Amgen or others could identify safety, side effects or manufacturing problems with Amgen's products after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. In addition, Amgen's business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Amgen performs a substantial amount of its manufacturing activities at a few key manufacturing facilities and also depends on third parties for a portion of its manufacturing activities, and limits on supply may constrain sales of certain Amgen products and its product candidate development.

In addition, sales of Amgen 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. Government and others' regulations and reimbursement policies as well as political and public scrutiny may affect the development, usage and pricing of Amgen's products. In addition, Amgen competes with other companies with respect to many of its marketed products as well as for the discovery and development of new products. Amgen believes that some of its newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Amgen's products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with its products. Amgen expects to face increasing competition from biosimilars. In addition, while Amgen routinely obtains patents for products and technology, the protection of its products offered by patents and patent applications may be challenged, invalidated or circumvented by competitors and there can be no guarantee of Amgen's ability to obtain or maintain patent protection for its products or product candidates or to prevail in intellectual property litigation. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of its existing products. Amgen's stock price may be volatile and may be affected by actual or perceived market opportunity, competitive position, and success or failure of its products or product candidates. Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's business and results of operations. Amgen's efforts to acquire other companies or products and to integrate the operations of companies it has acquired may not be successful. Amgen may not be able to access the capital and credit markets on terms that are favorable to Amgen, or at all. Amgen's business performance could affect or limit the ability of its Board of Directors to declare a dividend or its ability to pay a dividend or repurchase common stock.

The scientific information discussed in this news release related to Amgen's product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates.

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 8500 people in approximately 40 countries, the company generated revenue of € 3.3 billion in 2014. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

Forward looking statements – UCB

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. 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 information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.

Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.

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