



## Results From Phase 3 FRAME Study Of Romosozumab Showed Significant Reductions In Both New Vertebral And Clinical Fractures In Postmenopausal Women With Osteoporosis

September 18, 2016

### FRAME Data Simultaneously Published in New England Journal of Medicine and Presented at ASBMR Showed Treatment With Romosozumab Significantly Reduced New Vertebral and Clinical Fractures Through 12 Months Significant Bone Mineral Density Gains Shown at Six and 12 Months at the Lumbar Spine, Total Hip and Femoral Neck Bone Mineral Density Continued to Increase and Vertebral Fracture Risk Reduction Persisted With the Transition From Romosozumab to Denosumab Through 24 Months

THOUSAND OAKS, Calif. and BRUSSELS, Sept. 18, 2016 /PRNewswire/ -- Amgen (NASDAQ: AMGN) and UCB (Euronext Brussels: UCB) today announced findings from the FRAME study showing that the investigational agent romosozumab significantly reduced the incidence of new vertebral fractures in postmenopausal women with osteoporosis through 12 and 24 months, meeting the study's co-primary endpoints. The results from the Phase 3 study, the first to evaluate fracture risk reduction as early as one year as a primary endpoint, were published in the *New England Journal of Medicine* (NEJM) and presented today in an oral session at the Annual Meeting of the American Society for Bone Mineral Research (ASBMR) in Atlanta. Romosozumab works by binding and inhibiting the activity of the protein sclerostin, and as a result, has a dual effect on bone, both increasing bone formation and decreasing bone breakdown.

Experience the interactive Multimedia News Release here: <https://www.multivu.com/players/English/74140512-amgen-postmenopausal-osteoporosis-study>.

"Treatment data show that only one in five women who have experienced an osteoporotic fracture are started on treatment for the disease<sup>1</sup>, despite the fact that patients who experience an osteoporotic fracture are twice as likely to suffer a future fracture<sup>2</sup>," said study lead author Felicia Cosman, M.D., medical director of the Clinical Research Center at Helen Hayes Hospital and professor of medicine at Columbia University College of Physicians and Surgeons in New York. "The FRAME results demonstrate that romosozumab, with its dual effect of increasing bone formation and decreasing bone resorption, has the potential to reduce the risk of new vertebral and clinical fractures within 12 months, in addition to showing improvements in bone mass, with sustained benefits upon transition to denosumab, thereby addressing a critical treatment need for patients at increased risk of fracture."

FRAME (FRActure study in postmenopausal woMen with ostEoporosis), which enrolled 7,180 women, showed that those randomly assigned to receive a monthly subcutaneous 210 mg dose of romosozumab experienced a statistically significant 73 percent reduction in the relative risk of a new vertebral (spine) fracture through 12 months, the first co-primary endpoint, compared to those receiving placebo (fracture incidence 0.5 percent versus 1.8 percent, respectively [ $p<0.001$ ]). Of interest, the data showed that by six months, new vertebral fractures occurred in 14 romosozumab and 26 placebo patients, and between six to 12 months, fractures occurred in two additional romosozumab patients versus 33 additional placebo patients.

For those patients who received romosozumab in year one, fracture risk reduction persisted through month 24 after both groups transitioned to denosumab treatment in the second year of the study; there was a statistically significant 75 percent reduction in the risk of vertebral fracture at month 24 (the other co-primary endpoint) in patients who received romosozumab followed by denosumab versus placebo followed by denosumab (fracture incidence 0.6 percent versus 2.5 percent, respectively [ $p<0.001$ ]). In the second year of the study, new vertebral fractures occurred in five patients who transitioned from romosozumab to denosumab and 25 patients who transitioned from placebo to denosumab.

When looking at clinical fractures, which encompass all symptomatic fractures (both non-vertebral and painful vertebral fractures), patients receiving romosozumab experienced a statistically significant 36 percent reduction in the relative risk of a clinical fracture, a secondary endpoint, through 12 months compared to those receiving placebo (fracture incidence 1.6 percent versus 2.5 percent, respectively [ $p=0.008$ ]). A 33 percent reduction in relative risk of clinical fracture was observed through 24 months after patients transitioned from romosozumab to denosumab compared to patients transitioning from placebo to denosumab (nominal  $p=0.002$ , adjusted  $p=0.096$ ).

Romosozumab resulted in a 25 percent reduction compared to placebo in the relative risk of non-vertebral fractures through month 12, another secondary endpoint, but the reduced risk was not statistically significant (fracture incidence 1.6 percent versus 2.1 percent, respectively, [ $p=0.096$ ]). For the non-vertebral fracture endpoint, the overall fracture incidence in the study was lower than expected (2.1 percent in the placebo group in year one versus an expected rate of 3.5 percent).

In a sub-study of 126 subjects, romosozumab increased bone mineral density with gains of 9.7 percent and 4.7 percent from baseline by six months at the lumbar spine and total hip, respectively, and gains of 13.3 percent and 6.8 percent at 12 months (all comparisons versus placebo  $p<0.001$ ). Bone mineral density continued to increase in the romosozumab group after transitioning to denosumab, reaching 17.6 percent and 8.8 percent increases from baseline at the lumbar spine and total hip, respectively, at 24 months ( $p<0.001$  compared to placebo-to-denosumab group for all comparisons).

"We are pleased to see nearly 15 years of sclerostin antibody research reinforced with these Phase 3 data. Romosozumab, with its dual effect as a bone builder and anti-resorptive, has the potential to play a distinct and important role in the treatment of women with postmenopausal osteoporosis at increased risk of fracture," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "These positive FRAME study results are the basis of our Biologics Licensing Application that we submitted to the FDA in July, and we look forward to working with regulatory authorities to help make this potential treatment option available to patients."

"Osteoporotic fractures are common, resulting in far-reaching consequences for individuals and their families, as well as for society as a whole," said Dr. Pascale Richetta, head of bone and executive vice president, UCB. "To reduce the growing global burden of this prevalent chronic disease, more decisive steps need to be taken now for identifying, diagnosing and appropriately treating people with osteoporosis at an increased risk of fracture."

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. Injection site reactions, mostly mild in severity, 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. 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. Adjudicated serious cardiovascular events and cardiovascular deaths were balanced between treatment groups.

#### **About Romosozumab**

Romosozumab is an investigational bone-forming monoclonal agent and is not approved by any regulatory authority for the treatment of osteoporosis. It is designed to work by inhibiting the activity of 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 multicenter, 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 which encompasses all symptomatic fractures, both non-vertebral and painful 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 indicated 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 postmenopausal women with osteoporosis, Prolia reduces the incidence of vertebral, nonvertebral, and hip fractures.

Prolia is indicated 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 indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia also reduced the incidence of vertebral fractures.

Prolia is indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

#### **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=7,808) 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 [www.proliasafety.com](http://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 the Amgen and UCB Collaboration**

Since 2004, Amgen and UCB have been working together under a collaboration and license agreement to research, develop and market antibody products targeting the protein sclerostin. As part of this agreement, the two companies continue to collaborate on the development of romosozumab for the treatment of osteoporosis. This gene-to-drug project demonstrates how Amgen and UCB are joining forces to turn genetic discoveries into new medicine, turning conceptual science into a reality.

### **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](http://www.amgen.com) and follow us on [www.twitter.com/amgen](https://www.twitter.com/amgen).

### **About UCB**

UCB, Brussels, Belgium ([www.ucb.com](http://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 7,700 people in approximately 40 countries, the company generated revenue of € 3.9 billion in 2015. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB\_news

### **Forward-Looking Statements – Amgen**

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 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 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 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. 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 expects similar variability in the future. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints Amgen has selected. 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 relationship. Also, Amgen or others could identify safety, side effects or manufacturing problems with its products after they are on the market.

Amgen's results may be affected by its 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 its products and global economic conditions. In addition, sales of Amgen's 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, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen or others could identify safety, side effects or manufacturing problems with its 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 it and the U.S. government, Amgen could become subject to significant sanctions. Further, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors, or Amgen may fail to prevail in present and future intellectual property litigation. Amgen performs a substantial amount of its commercial 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 of its current products and product candidate development. 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. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third-party suppliers. 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 its business and results of operations. Amgen's efforts to acquire other companies or products and to integrate the operations of companies Amgen has acquired may not be successful. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all. Amgen is increasingly dependent on information technology systems, infrastructure and data security. Amgen's stock price may be volatile and may be affected by a number of events. Amgen's business performance could affect or limit the ability of the Amgen Board of Directors to declare a dividend or its ability to pay a dividend or repurchase its common stock.

The scientific information discussed in this news release relating to new indications for Amgen's products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration 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.

### **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.

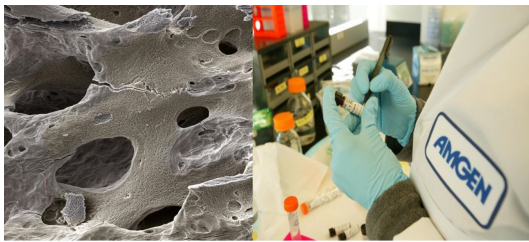
Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.

CONTACT: Amgen, Thousand Oaks  
Kristen Davis, 805-447-3008 (media)  
Kristen Neese, 805-313-8267 (media)  
Arvind Sood, 805-447-1060 (investors)

CONTACT: UCB, Brussels  
France Nivelles, Global Communications, UCB  
T +32.2.559.9178, [france.nivelles@ucb.com](mailto:france.nivelles@ucb.com)  
Laurent Schots, Media Relations, UCB  
T+32.2.559.92.64, [Laurent.schots@ucb.com](mailto:Laurent.schots@ucb.com)  
Antje Witte, Investor Relations, UCB  
T +32.2.559.94.14, [antje.witte@ucb.com](mailto:antje.witte@ucb.com)  
Isabelle Ghellynck, Investor Relations, UCB  
T+32.2.559.9588, [isabelle.ghellynck@ucb.com](mailto:isabelle.ghellynck@ucb.com)

1. Wilk A et al. Post-fracture pharmacotherapy for women with osteoporotic fracture: analysis of a managed care population in the USA. *Osteoporosis Int.* 2014;25(12):2777-2786.

2. International Osteoporosis Foundation. Stop at One. One Fracture Leads to Another. [http://share.iofbonehealth.org/WOD/2012/patient\\_brochure/WOD12-patient\\_brochure.pdf](http://share.iofbonehealth.org/WOD/2012/patient_brochure/WOD12-patient_brochure.pdf). Accessed August 29, 2016.



## Postmenopausal Osteoporosis Fact Sheet

### OVERVIEW

Osteoporosis, meaning "porous bone," is a disease characterized by weak bones and is caused by excessive bone loss.<sup>1</sup> Postmenopausal osteoporosis, the most common form of the disease, affects many women after menopause as their ability to form new bone cannot counter balance the rate at which bone is being removed.<sup>2,3</sup> Osteoporosis weakens bones over time, making them thinner, more brittle and more likely to break.<sup>1</sup> Women can lose up to 20 percent of their bone mass in the five to seven years after menopause.<sup>4</sup> When bones become weak and fragile, even a slight bump or fall from standing height can lead to a broken bone.<sup>5</sup> A fracture can be a life-changing event, making it harder to get around and do things independently.<sup>6</sup>

Osteoporosis affects approximately 200 million people worldwide,<sup>7,8</sup> and roughly 30 percent of all postmenopausal women in the United States and Europe have this disease.<sup>9</sup> The World Health Organization has officially declared osteoporosis a public health crisis,<sup>10,11</sup> and the International Osteoporosis Foundation urges governments around the globe to make osteoporosis a healthcare priority.<sup>12</sup> Worldwide, it is estimated one in three women over the age of 50 will experience an osteoporotic fracture.<sup>13,14</sup>

### RISK FACTORS

Everyone has cells that remove bone (osteoclasts) and other cells that rebuild bone (osteoblasts).<sup>15</sup> When women develop postmenopausal osteoporosis, bone-removing cells cause them to lose bone at a rate that is too fast.<sup>3,4</sup> The result is thinner, weaker bones that can break more easily.<sup>1</sup> Once an initial fracture has happened, the chances of another are much higher.<sup>16</sup> Those who experience an osteoporotic fracture are twice as likely to suffer a future fracture.<sup>16</sup> And while these patients may be at highest risk within the first 12 to 24 months following the initial event,<sup>17,25</sup> data show that one in three older women will fracture again within five years.<sup>26</sup>

There is a lot of information that can help a woman's healthcare provider assess her fracture risk. Understanding these risk factors can be helpful as there may be actions one can take to reduce the likelihood of developing osteoporosis, and therefore fractures. Key risk factors for developing osteoporosis may include:<sup>27</sup>

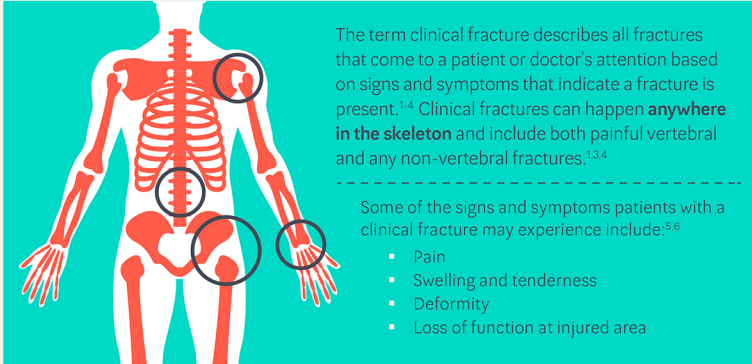
- Advanced age
- Low body mass index (BMI)
- Previous fracture
- Frequent falls
- Family history of osteoporosis
- Cigarette smoking
- Menopause
- Low calcium intake
- Low vitamin D level
- Alcohol

### FAST FACTS

- Women can lose up to 20 percent of their bone mass in the five to seven years after menopause.<sup>4</sup>
- Every three seconds, someone around the world breaks a bone because of osteoporosis.<sup>1</sup>
- In the U.S., osteoporotic fractures occur more frequently than myocardial infarction, stroke or breast cancer.<sup>38</sup>
- People who experience an osteoporotic fracture are twice as likely to suffer a future fracture.<sup>16</sup>
- A fracture can be a life-changing event, making it harder to get around and do things independently.<sup>6</sup>

# Clinical Fractures:

## What do they mean for patients living with osteoporosis?



The term clinical fracture describes all fractures that come to a patient or doctor's attention based on signs and symptoms that indicate a fracture is present.<sup>1-4</sup> Clinical fractures can happen **anywhere in the skeleton** and include both painful vertebral and any non-vertebral fractures.<sup>3,4</sup>

Some of the signs and symptoms patients with a clinical fracture may experience include:<sup>5,6</sup>

- Pain
- Swelling and tenderness
- Deformity
- Loss of function at injured area



A clinical fracture can be a life-changing event, making it harder to get around and do things independently.<sup>7</sup>

Annually, osteoporosis causes



The clinical burden of osteoporosis is evidenced by hospitalizations and emergency room visits resulting from clinical fractures.<sup>8,9-11</sup>

Beyond the physical impact of clinical fractures, these injuries are also associated with societal cost burden.



This may include both direct medical costs as well as indirect economic costs, such as a person's productivity and a caregiver's time.<sup>12-16</sup>



Once a person suffers from an initial fracture, the chances of another are **MUCH HIGHER**.<sup>17</sup>

After a clinical fracture, **ONE IN THREE OLDER WOMEN** will sustain a second fracture within the next five years.<sup>18,19</sup>



Clinical fractures at one site **CAN INCREASE THE RISK** for a future fracture at a different place in the body.<sup>20</sup>

### REFERENCES

- Cummings SR, Black DM, Thompson DE, et al. for the Fracture Intervention Trial Research Group. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures. *JAMA*. 1998;280:2077-2082.
- Kanis JA, Johnell O, Oden A, et al. The risk and burden of vertebral fractures in Sweden. *Osteoporos Int*. 2004;15:20-28.
- Office of the Surgeon General (US). Bone Health and Osteoporosis: A Report of the Surgeon General. Rockville (MD): Office of the Surgeon General (US); 2004. Available at: <http://www.nrcslm.nih.gov/book/BNM4533/>. Accessed August 26, 2016.
- van Heerden S, Cals J, Kessels F, Brink P, Dinant GJ, Geusens P. Risk of new clinical fractures within 3 years following a fracture. *Osteoporos Int*. 2005;15:548-54.
- American Academy of Orthopedic Surgeons. Fractures (Broken Bones). Available at: <http://orthoinfo.aaos.org/topic.cfm?topicID=00798>. Accessed August 26, 2016.
- National Health Service. How do I know if I've broken a bone? Available at: <http://www.nhs.uk/cho/pages/1050.aspx?ontologyid=72>. Accessed August 26, 2016.
- International Osteoporosis Foundation. The Global Burden of Osteoporosis: A Fact Sheet. Available at: <https://bonehealth.org/sites/default/files/media/PDF/FactSheet2020enr/2014-factsheet-osteoporosis-14.pdf>. Accessed August 26, 2016.
- Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int*. 2006;17:726-33.
- Singer A, Escudé A, Spangler L, et al. Burden of illness for osteoporotic fractures compared with other serious diseases among postmenopausal women in the United States. *Mayo Clin Proc*. 2014;89:53-62.
- Tarrale J-E, Hopkins RB, Leslie WD, et al. The burden of illness of osteoporosis in Canada. *Osteoporos Int*. 2012;22:2559-2603.
- Tajiri SS, Dabell E, Smith W, Arora T, Curtis JR, Saeg KH, et al. Death, disability, and institutionalization following hip fracture. *J Geriatr A Res Sci Med Sci*. 2014;69:246-253.
- Burgin R, Dawson-Hughes B, Salomon DH, Wong JB, King A, Tosteson A. Incidence and economic burden of osteoporosis-related fractures in the United States, 2005-2025. *J Bone Miner Res*. 2007;22:455-475.
- Watts SJ, Alameiri-Ostom J, Sanders RA. Osteoporosis Costing All Australians: A New Burden of Disease Analysis - 2012 to 2022. *Diets, Australia: Osteoporosis Australia*. 2013.
- Herrin ED, Sveinbom A, Vengelić M, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. A report prepared in collaboration with the International Osteoporosis Foundation (IOF) and the European Federation of Pharmaceutical Industry Associations (EFPIA). *Arch Osteoporos*. 2013;8(1-2):136-15.
- Pike C, Birbaumer HG, Schiller M, Sharma H, Burgin R, Edgett ET. Direct and indirect costs of non-vertebral fracture patients with osteoporosis in the US. *Pharmacoeconomics*. 2010;28:955-959.
- Song X, Shi H, Basamirav E, et al. Cost burden of second fracture in the US health system. *Bone*. 2011;48:608-616.
- International Osteoporosis Foundation. Stop at One: One Fracture Leads to Another. [http://share.iofbonehealth.org/WOD/2012/patient\\_brochure/WODD-patient\\_brochure.pdf](http://share.iofbonehealth.org/WOD/2012/patient_brochure/WODD-patient_brochure.pdf). Accessed August 22, 2016.
- Balastramanian A, Zhang J, Chen L, et al. High Risk of Second Fracture within 1, 2, 3 years after Prior Fracture among Women 65 years or Older. Accepted Abstract #2232. ASBMR Annual Meeting, Atlanta, GA, Sept. 10-15, 2016.
- Center JR, Blau D, Nguyen TV, Eisman JA. Risk of subsequent fracture after low-trauma fracture in men and women. *JAMA*. 2002;287(16):387-394.
- Banach S, Saeg KH, Adachi JD, et al. Previous fractures at multiple sites increase the risk for subsequent fractures: the Global Longitudinal Study of Osteoporosis in Women. *J Bone Miner Res*. 2012;27:645-653.



HQ/0816/RHZ/00038



To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/results-from-phase-3-frame-study-of-romosozumab-showed-significant-reductions-in-both-new-vertebral-and-clinical-fractures-in-postmenopausal-women-with-osteoporosis-300329792.html>

SOURCE Amgen