UCB News

ASBMR 2022: 3D modelling of hip DXA scans in postmenopausal women with osteoporosis reveals superior improvements in bone density of romosozumab versus controls

- Post-hoc analyses of the FRAME, ARCH and the STRUCTURE phase 3 trials using 3D modelling techniques showed significant cortical and trabecular bone improvements during the first year in romosozumab-treated patients.
- Romosozumab-treated patients achieved greater increases in cortical volumetric BMD (CvBMD), cortical thickness (Cth), cortical surface BMD (CsBMD) and trabecular volumetric BMD (TvBMD) than comparator groups, from as early as Month 6 through to Month 12.
- Data further demonstrated that patients at high risk of fracture may benefit the most from treatment with romosozumab first, followed by an antiresorptive.
- Additional data offered new insights into neurological factors contributing to fracture risk, the impact of the COVID pandemic and subsequent public health lockdowns on the existing treatment and care gaps, and the use of artificial intelligence in osteoporosis screening.

Brussels (Belgium), 9 September 2022 – 07:00 (CEST) – UCB and Amgen, global biopharmaceutical companies, today presented abstracts of three post-hoc analyses focusing on 3D modelling techniques that highlight significant cortical and trabecular bone improvements in patients treated with romosozumab. The data were presented along with additional 17 abstracts, at the American Society for Bone and Mineral Research (ASBMR) 2022 Annual Congress, taking place from 9th – 12th September in Austin, Texas, USA.

DXA-based modelling enables estimation of cortical and trabecular bone parameters comparable to QCT measurements and generates outputs to visualize and monitor osteoporosis (OP) treatment. In

both analyses, Lewiecki et al. used DXA-based modelling of the hip to assess 3D bone changes and map the distribution of changes in bone parameters over time in patients from FRAME, ARCH and STRUCTURE.[1]

In the first abstract, Lewiecki et al. looked at 3D modelling from hip DXA scans in postmenopausal women with osteoporosis who received oral bisphosphonate therapy for ≥3 years and ALN for ≥1 year prior to screening, and were randomized to ROMO or a comparator (STRUCTURE: teriparatide [TPTD]) for 12 months. The analysis found greater increases in CvBMD, Cth, CsBMD and TvBMD from as early as Month 6 following treatment with ROMO vs TPTD, with additional gains observed through to Month 12. The results also showed TPTD treatment led to a loss in CvBMD, Cth and CsBMD.[2]

Another abstract by Lewiecki et al. reported the results of a post-hoc analysis from the FRAME and ARCH studies. Postmenopausal women with osteoporosis were randomized to romosozumab 210 mg monthly (ROMO) or a comparator (FRAME: PBO; ARCH: alendronate [ALN] 70 mg) for 12 months. After 12 months, all patients received denosumab (DMAB) in FRAME or ALN in ARCH. 3D modelling from hip DXA scans found that at Month 12, treatment with ROMO vs PBO in FRAME and ROMO vs ALN in ARCH resulted in greater increases in cortical volumetric bone mineral density (CvBMD), cortical thickness (Cth), cortical surface BMD (CsBMD) and trabecular volumetric BMD (TvBMD). At month 24, the cumulative gains in CvBMD, Cth, CsBMD and TvBMD were greater in the ROMO/DMAB vs PBO/DMAB sequence ($P<0.001$) and in the ROMO/ALN vs ALN/ALN sequence ($P<0.05$).[1] This data further corroborates the Cosman et al. and McClung et al. studies that showed greater BMD gains, reduced new vertebral fracture incidence and lower incidence of clinical, non-vertebral and hip fractures with ROMO/DMAB treatment, and significant improved bone microarchitecture with ROMO/ALN treatment, respectively.[3,4]

Osteoporosis is the most common chronic metabolic bone disease.[5] Characterised by compromised bone strength, the condition causes approximately 9 million fractures each year.[5,6] Fragility fractures can result in significant burden on a person's life, often making everyday activities such as eating, dressing, shopping or driving difficult.[7]

"As people are living longer, the burden of fragility fractures due to osteoporosis requires effective addressing. So we are proud to communicate additional data supporting romosozumab as a bone forming option for postmenopausal women with severe osteoporosis at high risk of fracture," said Emmanuel Caeymaex, Executive Vice President, Immunology Solutions & Head of US, UCB. "ASBMR 2022 provides an integral forum for clinicians and scientists around the world to come together and share the latest breakthroughs and innovations and so we at UCB are proud to be participating with

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a wealth of scientific research this year. Our goal is to ensure osteoporosis care is a priority now and in the future, so we can continue to improve patient outcomes."

During ASBMR 2022, UCB and Amgen showcased their commitment to the screening, treatment, and management of osteoporosis with the presentation of a total of 19 abstracts.

UCB & Amgen abstracts:

- **One Year of Romosozumab Followed by One Year of Denosumab Compared With Two Years of Denosumab: BMD and Fracture Results From the FRAME and FRAME Extension Studies.** F. Cosman, M. Oates, D. Betah, S. Ferrari, J. Timoshanko, Z. Wang, M. McClung
- **Trends in Osteoporosis Care Patterns during the COVID-19 Pandemic in Alberta, Canada.** D.L. Kendler, J.P. Brown, A.G. Juby, P. Schneider, R. Wani, M. Packalen, S. Avcil, S. Li, M.S. Farris, E. Graves, S. McMullen, T. Oliveira
- **Current trends in osteoporosis epidemiology and the widening treatment gap among commercially-insured postmenopausal women in the United States (US).** M. Kim, P. Samai, M. Phelan, M. McDermott, C. Deignan, T. Lin, M.A. Brookhart
- **Cortical and trabecular bone improvements with romosozumab followed by denosumab or alendronate assessed using 3D modeling from DXA images.** E.M. Lewiecki, D. Betah, L. Humbert, C. Libanati, M. Oates, Y. Shi, R. Winzenrieth, S. Ferrari, F. Omura
- **Comparison of romosozumab and teriparatide effects on cortical and trabecular bone using 3D modeling from DXA images in postmenopausal women transitioning from bisphosphonate therapy.** E.M. Lewiecki, D. Betah, L. Humbert, C. Libanati, M. Oates, Y. Shi, R. Winzenrieth, S. Ferrari, F. Omura
- **Clinical Characteristics, Including History of Myocardial Infarction and Stroke, Among US PMO Women Initiating Treatment with Romosozumab and Other Antiosteoporosis Therapies.** T. Lin, Y. Liu, T. Arora, M. Oates, C. Deignan, Z. Yu, J.R. Curtis
- **Effect of Romosozumab on Bone Microarchitecture as Assessed by Tissue Thickness–Adjusted Trabecular Bone Score in Postmenopausal Women with Osteoporosis: Results from the ARCH Study.** M.R. McClung, D. Betah, B.Z. Leder, D.L. Kendler, M. Oates, J. Timoshanko, Z. Wang
- **Romosozumab Efficacy in Postmenopausal Women Without Prior Fracture Who Fulfill AACE Criteria for Osteoanabolic Therapy: Post-Hoc Analysis of Clinical Trial Data.** M. McClung, D. Betah, C. Deignan, Y. Shi, J. Timoshanko, F. Cosman

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- **Crystal Bone: Validation of a Novel AI/ML Algorithm in the Optum Reliant dataset to Identify Patients at Risk of Osteoporotic Fracture in the Next 2 Years.** E. Mody, R. Yood, C. Deignan, T. Rosenflanz, P. Zhang, T. Kelley, N. Payne, C. Andersen
- **Crystal Bone: Validation of a Novel AI/ML Algorithm in the Stanford Health Care dataset to Identify Patients at Risk of Osteoporotic Fracture in the Next 2 Years.** D.E. Sellmeyer, C. Deignan, T. Rosenflanz, Y. Nazarenko, P. Zhang, C. Andersen
- **One- and five-year survival after fragility fracture: Real-world retrospective matched-cohort study in Ontario, Canada.** G. Vincent, J.D. Adachi, E. Schemitsch, J. Tarride, M. Luen, R.J. Wani, J.P. Brown
- **The Impact of Osteoporotic Fractures on Activities of Daily Living and the Indirect Economic Measures in Five Countries.** E. Yeh, O. Rajkovic-Hooley, M. Silvey, W.S. Ambler, R. Pinedo-Villanueva, N. Harvey, A. Moayyeri

Research Collaboration abstracts supported by UCB and Amgen:

- **Gradients of risk of clinical risk factors for hip and vertebral fracture depend on age and are typically larger at younger age.** K. Engelke, C.C. Glüer, M. Kistler, F. Thomasius, P. Hadji, B. Schweikert, C. Libanati, A. Moayyeri
- **Retrospective Standalone Performance Testing of a Machine Learning Algorithm for Opportunistically Detecting Vertebral Fractures on Chest and Abdomen CT images in a Chinese population.** J. Nicolaes, Y. Liu, P. Huang, Y. Zhao, L. Wang, A. Yu, J. Dunkel, C. Libanati, X. Cheng
- **Evaluation of Romosozumab's Effects on Bone Marrow Adiposity in Postmenopausal Osteoporotic Women: Results from The FRAME Bone Biopsy Sub-Study.** P. Chavassieux, J.P. Roux, C. Libanati, Y Shi, R. Chapurlat
- **Neurological Clinical Risk Factors For Fracture – an underappreciated domain: ICD Code-Based Analysis of a German Health Insurance Database.** F. Thomasius, K. Engelke, P. Hadji, M. Kistler, B. Schweikert, A. Moayyeri, C. Libanati, C.C. Glüer
- **Gradients of risk of clinical risk factors for hip and vertebral fracture are generally larger in men than in women: results from a large health insurance database.** C.C. Glüer, K. Engelke, M. Kistler, F. Thomasius, P. Hadji, B. Schweikert, A. Moayyeri, C. Libanati
- **Inhibition/deletion of Wise (Sostdc1) potentiates cortical bone building effects of Sost deficiency.** R.B. Choi, G.G. Loots, A.G. Robling (abstract #XX)
- **Nmp4 Underlies the Treatment Plateaus of Osteoanabolics.** C. Korff, E.G. Atkinson, D.J. Horan, M. Adaway, A.G. Robling, J.P. Bidwell

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About the study methodology and patient population

FRAME and ARCH (Lewiecki et al.)

Postmenopausal women with osteoporosis were randomized to romosozumab (ROMO) 210 mg monthly or comparator (FRAME: PBO; ARCH: alendronate [ALN] 70mg) for 12 months. After 12 months all patients received denosumab (DMAB) in FRAME or ALN in ARCH. For each study, data from a subset of 200 randomly selected women per treatment group who had total hip DXA scans at baseline (BL), month (M) 12, and M24 and had provided consent for future research were included in the analysis. Percentage change from BL to M12 and M24 in cortical volumetric BMD (CvBMD), cortical thickness (Cth), cortical surface BMD (CsBMD), and trabecular vBMD (TvBMD) were evaluated. Percentage changes were assessed by repeated measures model adjusting for baseline covariates.

STRUCTURE (Lewiecki et al.)

Postmenopausal women with osteoporosis who had received oral bisphosphonate (BP) therapy for ≥3 years and ALN for ≥1 year prior to screening were then randomized 1:1 to receive open-label ROMO or teriparatide (TPTD) for 12M. Data from women who had total hip DXA scans at baseline (BL), M6, and M12 and had provided consent for future research were included in this analysis. Data from 308 women from STRUCTURE (ROMO, 160; TPTD, 148) who had evaluable 3D assessments at BL, M6, and M12 were analyzed. Percentage change from BL to M6 and M12 in cortical vBMD (CvBMD), cortical thickness (Cth), cortical surface BMD (CsBMD), and TvBMD were evaluated. Percentage changes were assessed by repeated measures model adjusting for BL covariates.

About EVENITY®▼ (romosozumab)[8]

Romosozumab is a bone-forming monoclonal antibody. It is designed to work by inhibiting the activity of sclerostin, which simultaneously results in increased bone formation and to a lesser extent decreased bone resorption. The romosozumab development program includes 19 clinical studies that enrolled approximately 14,000 patients. EVENITY has been studied for its potential to reduce the risk of fractures in an extensive global phase 3 program that included two large fracture trials comparing romosozumab to either placebo or active comparator in over 11,000 postmenopausal women with osteoporosis. Amgen and UCB are co-developing romosozumab. ▼This product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Important Safety Information about EVENITY® (romosozumab) in the EU/EEA

In the EU, Romosozumab is indicated for treatment of severe osteoporosis in postmenopausal women at high risk of fracture. **Contraindications**: Romosozumab is contraindicated in patients who are allergic to romosozumab or any of the excipients, who have low levels of calcium in the blood (hypocalcaemia), or who have a history of myocardial infarction (heart attack) or stroke**. Myocardial infarction or stroke**: Heart attack and stroke have been reported in patients receiving Romosozumab in randomised controlled trials (uncommon). Treatment with Romosozumab should not be initiated in patients with a history of heart attack or stroke. When determining whether to use Romosozumab for an individual patient, the presence of risk factors for cardiovascular problems, including established

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cardiovascular disease, high blood pressure, high blood fat levels, diabetes, smoking or kidney problems, should be evaluated. Romosozumab should only be used if the prescriber and patient agree that the benefit outweighs the risk. If a patient experiences a myocardial infarction or stroke during therapy, treatment with Romosozumab should be discontinued. **Hypocalcaemia**: Transient hypocalcaemia has been observed in patients receiving Romosozumab. Hypocalcaemia should be corrected prior to initiating therapy with Romosozumab and patients should be monitored for signs and symptoms of hypocalcaemia. If any patient presents with suspected symptoms of hypocalcaemia during treatment, calcium levels should be measured. Patients should be adequately supplemented with calcium and vitamin D. Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29ml/min/1.73m2) or receiving dialysis are at greater risk of developing hypocalcaemia and the safety data for these patients are limited. Calcium levels should be monitored in these patients. **Hypersensitivity**: Clinically significant hypersensitivity reactions, including angioedema, erythema multiforme, and urticaria occurred in the Romosozumab group in clinical trials. If an anaphylactic or other clinically significant allergic reaction occurs, appropriate therapy should be initiated and use of Romosozumab should be discontinued. **Osteonecrosis of the Jaw**: Osteonecrosis of the jaw (ONJ) has been reported rarely in patients receiving Romosozumab. The following risk factors should be considered when evaluating a patient's risk of developing ONJ: (1) potency of the medicinal product that inhibits bone resorption (the risk increases with the antiresorptive potency of the compound), and cumulative dose of bone resorption therapy, (2) cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection), smoking, (3) concomitant therapies: corticosteroids, chemotherapy, angiogenesis inhibitors, radiotherapy to head and neck, (4) poor oral hygiene, periodontal disease, poorly fitting dentures, history of dental disease, invasive dental procedures e.g. tooth extractions. All patients should be encouraged to maintain good oral hygiene and receive routine dental check-ups. Dentures should fit correctly. Patients under dental treatment, or who will undergo dental surgery (e.g. tooth extractions) whilst being treated with Romosozumab should inform their doctor about their dental treatment and inform their dentist that they are receiving Romosozumab. Patients should immediately report any oral symptoms such as dental mobility, pain or swelling or non-healing of sores or pus discharge during treatment with Romosozumab. Patients who are suspected of having or who develop ONJ while receiving Romosozumab should receive care by a dentist or an oral surgeon with expertise in ONJ. Discontinuation of Romosozumab therapy should be considered until the condition resolves and contributing risk factors are mitigated where possible**. Atypical Femoral Fractures**: Atypical low-energy or low trauma fracture of the femoral shaft, which can occur spontaneously, has been reported rarely in patients receiving Romosozumab. Any patient who presents with new or unusual thigh, hip, or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patient presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of Romosozumab therapy should be considered, based on an individual benefit-risk assessment. **Adverse Reactions**: The most common adverse reactions were nasopharyngitis (13.6%) and arthralgia (12.4%). Common adverse reactions included hypersensitivity, sinusitis, rash, dermatitis, headache, neck pain, muscle spasms and injection site reactions (most frequent injection site reactions were pain and erythema). Uncommon adverse reactions were urticaria, hypocalcaemia, stroke, myocardial infarction and cataract. Finally, rare side effects were serious allergic reactions which caused swelling of the face, throat, hands, feet, ankles or lower legs (angioedema) and acute skin eruption (erythema multiforme).

EVENITY® is a registered trademark of the UCB Group of Companies.

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 8 000 people operating in more than 40 countries, the company generated revenue of €5.3 billion in 2020. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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 translate a genetic discovery into a new medicine, turning conceptual science into a reality.

Forward looking statements

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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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