UCB News

UCB Presents New Findings Advancing Patient Care for Chronic Inflammatory Diseases and Osteoporosis at 2017 ACR/ARHP Annual Meeting

Key data focus on inflammatory and osteoporosis in patient populations with unmet needs including women of childbearing age and others:

- The results from the first-of-its-kind CRIB study demonstrate minimal placental transfer of CIMZIA® during pregnancy;an additional presentation highlighting positive results from the largest published cohort of pregnant women exposed to an anti-TNF
- Presentation on opioid prescribing trends for ankylosing spondylitis (AS), often in lieu of targeted therapies such as anti-TNFs, highlights potential gaps in awareness and care
- Additional presentations highlight findings from preclinical studies on the contribution of IL-17F to inflammation and the effects of dual neutralization of IL-17A and IL-17F with bimekizumab in disease-relevant models
- Multiple studies find fracture risk reduced with EVENITY™[1] (romosozumab) in postmenopausal women with osteoporosis

Brussels, Belgium – 6 November – UCB, a global biopharmaceutical company focusing on immunology, neurology, and bone treatment and research, will present findings from 14 separate abstracts at the 2017 American College of Rheumatology/Association for Rheumatology Health Professionals (ACR/ARHP) Annual Meeting in San Diego, CA (3 – 8 November 2017). These data will highlight some of the latest research on CIMZIA® (certolizumab pegol) and several investigational treatments, which collectively address serious unmet treatment needs among women of childbearing age and other populations with chronic inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), as well as osteoporosis.

Data highlights include findings from CRIB, a first-of-its-kind prospective pharmacokinetic study, demonstrating minimal placental transfer from mother to infant of CIMZIA during pregnancy. A separate poster presentation on the pregnancy outcomes of over 530 women exposed to CIMZIA during pregnancy did not reveal an increased risk of major malformations or an increased risk of fetal death related to CIMZIA treatment for chronic inflammatory diseases, compared to the US general population.

Data regarding the overuse of opioids in the treatment of AS when anti-TNFs may be indicated will also be presented. Study findings suggest that opioids are vastly overprescribed as a treatment for pain associated with AS, often in lieu of more effective treatments such as anti-TNFs and non-steroidal anti-inflammatory drugs (NSAIDs). As such, many patients are left with suboptimal disease management, and increased awareness of treatment options among prescribers and patients is indicated.

“UCB’s 14 data presentations at ACR/ARHP 2017 illustrate both the breadth and depth of sustained, long-term research that is at the core of our commitment to patients with unique needs and

[1] The trade name EVENITY™ is provisionally approved for use by the U.S. Food and Drug Administration and the European Medicines Agency

undertreated serious diseases. Our work embraces a growing number of diagnoses and patients who do not fall within existing treatment practices, and we will go as far as necessary to improve these patients' experience," Emmanuel Caeymaex, Head of Immunology and Executive Vice President at UCB. "Ongoing evidence supporting CIMZIA's use in women of childbearing age, many of whom often lack treatment options for their inflammatory diseases, and promising findings from our investigational programs for bimekizumab and romosozumab, give us great hope at UCB because they mean important potential new treatment options for patients."

Other CIMZIA findings include phase 3 data on rapid onset of response among RA patients who are not responsive to methotrexate and cost and utilization data for RA patients, as well as sustained improvement of enthesitis in axSpA patients over four years of treatment.

Data on UCB's pipeline demonstrate that, in addition to IL-17A, IL-17F also contributes to inflammation in disease-relevant models. Results also show that selective dual neutralization of both IL-17A and IL-17F with the monoclonal IgG1 antibody, bimekizumab, suppresses inflammation to a greater extent than IL-17A inhibition alone, supporting the potential of this novel approach for the management of immune mediated inflammatory diseases. Other studies on the investigational bone-forming monoclonal antibody, romosozumab, found a reduced risk of bone fracture in postmenopausal women with osteoporosis.

Following is a guide to the UCB-sponsored data presentations:

Presentations on CIMZIA® in Approved Indications:

Rheumatoid Arthritis

[1030]: Healthcare Service Utilization and Costs of Certolizumab Pegol Versus Infliximab Treatment in Patients with Rheumatoid Arthritis
Tkacz, J. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Health Services Research Poster II: Osteoarthritis and Rheumatoid Arthritis; ACR Poster Session B

[2451]: Rapid Onset of Response Observed with Certolizumab Pegol in Rheumatoid Arthritis Patients with Inadequate Response to Methotrexate: Efficacy and Safety Results of a Randomized, Double-Blind, Placebo-Controlled Phase 3 Study
Zhanguo, L. et al.

- Date/Time: Tuesday November 7; 9:00 AM – 11:00 AM PST
- Session Title/Info: Rheumatoid Arthritis – Small Molecules, Biologics and Gene Therapy Poster III: Efficacy and Safety of Originator Biologics and Biosimilars; ACR Poster Session C

Ankylosing Spondylitis (AS)

[1527]: Do TNF Inhibitors Alter the Natural History of Ankylosing Spondylitis By Impacting the Incidence and Prevalence of Comorbidities and Extra-Articular Manifestations?
Deodhar, A. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II; ACR Poster Session B

[1548]: Opioid Use in Patients with Ankylosing Spondylitis
Sloan, V. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II; ACR Poster Session B

Presentations on Investigational Studies of CIMZIA®:

Women of Childbearing Age

[1809]: Lack of Placental Transfer of Certolizumab Pegol during Pregnancy: Results from a Prospective, Postmarketing, Multicenter, Pharmacokinetic Study
Chakravarty, E. et al.

- Date/Time: Monday November 6; 2:30 PM – 4:00 PM PST
- Session Title/Info: Reproductive Issues in Rheumatic Disorders; ACR Concurrent Abstract Session

[1309]: Characteristics and Outcomes of Prospectively Reported Pregnancies Exposed to Certolizumab Pegol from a Safety Database
Clowse, M. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Reproductive Issues in Rheumatic Disorders Poster; ACR Poster Session B

Axial Spondyloarthritis (axSpA)

[1515]: Improvements in Enthesitis Scores with Certolizumab Pegol Treatment in Males and Females with Active Axial Spondyloarthritis Are Maintained to Week 204
Dougados, M. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Spondyloarthropathies and Psoriatic Arthritis – Clinical Aspects and Treatment Poster II; ACR Poster Session B

Presentations on UCB's Investigational Pipeline:

Romosozumab

[1886]: Continued Fracture Risk Reduction after 12 Months of Romosozumab Followed By Denosumab through 36 Months in the Extension of the Phase 3 Fracture Study in Postmenopausal Women with Osteoporosis
Lewiecki, M. et al.

- Date/Time: Monday November 6; 4:30 PM – 6:00 PM PST
- Session Title/Info: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis; ACR Concurrent Abstract Session

[1213]: Prediction Model for the Two-Year Risk of Fracture Among Older US Women
Balasubramanian, A. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster II; ACR Poster Session B

[318]: A Randomized Alendronate-Controlled Trial of Romosozumab: Results of the Phase 3 Active-Controlled Fracture Study in Postmenopausal Women with Osteoporosis at High Risk
Saag, K. et al.

- Date/Time: Sunday November 5; 9:00 AM – 11:00 AM PST
- Session Title/Info: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I; ACR Poster Session A

[319]: The Placebo-Controlled Fracture Study in Postmenopausal Women with Osteoporosis: The Foundation Effect of Rebuilding Bone with One Year of Romosozumab Leads to Continued Lower Fracture Risk after Transition to Denosumab
Cosman, F. et al.

- Date/Time: Sunday November 5; 9:00 AM – 11:00 AM PST
- Session Title/Info: Osteoporosis and Metabolic Bone Disease – Clinical Aspects and Pathogenesis Poster I; ACR Poster Session A

<u>Bimekizumab</u>

[1571]: Bimekizumab Dual Inhibition of IL-17A and IL-17F Provides Evidence of IL-17F Contribution to Chronic Inflammation in Disease-Relevant Cells
Maroof, A. et al.

- Date/Time: Monday November 6; 9:00 AM – 11:00 AM PST
- Session Title/Info: Spondyloarthropathies and Psoriatic Arthritis – Pathogenesis, Etiology Poster II; ACR Poster Session B

[73]: Regulation of Th17 Cell Responses By IL-25
Maroof, A. et al.

- Date/Time: Sunday November 5; 9:00 AM – 11:00 AM PST

- Session Title/Info: Cytokines, Mediators, Cell-Cell Adhesion, Cell Trafficking and Angiogenesis Poster I: The Variable World of Intercellular Signalling; ACR Poster Session A

[1936]: Bimekizumab Blocks T Cell-Mediated Osteogenic Differentiation of Periosteal Stem Cells: Coupling Pathological Bone Formation to IL-17A and IL-17F Signaling
Roberts, S. et al.

- Date/Time: Tuesday November 7; 9:00 AM – 11:00 AM PST
- Session Title/Info: Biology and Pathology of Bone and Joint Poster II; ACR Poster Session C

About Cimzia® In the US
Cimzia® is the only Fc-free, PEGylated anti-TNF (Tumor Necrosis Factor). Cimzia® has a high affinity for human TNF-alpha, selectively neutralizing the pathophysiological effects of TNF-alpha.

Cimzia® is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis, adults with active psoriatic arthritis (PsA), and adults with active ankylosing spondylitis (AS). In addition, it is indicated for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy. See important safety information including risk of serious bacterial, viral and fungal infections and tuberculosis below.

Important Safety Information about Cimzia® in the US

Risk of Serious Infections and Malignancy
Patients treated with Cimzia® are at an increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Cimzia® should be discontinued if a patient develops a serious infection or sepsis. Reported infections include:

- **Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before Cimzia® use and during therapy. Treatment for latent infection should be initiated prior to Cimzia® use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.**

The risks and benefits of treatment with Cimzia® should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Cimzia®, including

the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which Cimzia® is a member. Cimzia® is not indicated for use in pediatric patients.

Patients treated with Cimzia® are at an increased risk for developing serious infections involving various organ systems and sites that may lead to hospitalization or death. Opportunistic infections due to bacterial, mycobacterial, invasive fungal, viral, parasitic, or other opportunistic pathogens including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, legionellosis, listeriosis, pneumocystosis and tuberculosis have been reported with TNF blockers. Patients have frequently presented with disseminated rather than localized disease.

Treatment with Cimzia® should not be initiated in patients with an active infection, including clinically important localized infections. Cimzia® should be discontinued if a patient develops a serious infection or sepsis. Patients greater than 65 years of age, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants (e.g., corticosteroids or methotrexate) may be at a greater risk of infection. Patients who develop a new infection during treatment with Cimzia® should be closely monitored, undergo a prompt and complete diagnostic workup appropriate for immunocompromised patients, and appropriate antimicrobial therapy should be initiated. Appropriate empiric antifungal therapy should also be considered while a diagnostic workup is performed for patients who develop a serious systemic illness and reside or travel in regions where mycoses are endemic.

Malignancies

During controlled and open-labeled portions of Cimzia® studies of Crohn's disease and other diseases, malignancies (excluding non-melanoma skin cancer) were observed at a rate of 0.5 per 100 patient-years among 4,650 Cimzia®-treated patients versus a rate of 0.6 per 100 patient-years among 1,319 placebo-treated patients. In studies of Cimzia® for Crohn's disease and other investigational uses, there was one case of lymphoma among 2,657 Cimzia®-treated patients and one case of Hodgkin lymphoma among 1,319 placebo-treated patients. In Cimzia® RA clinical trials (placebo-controlled and open label), a total of three cases of lymphoma were observed among 2,367 patients. This is approximately 2-fold higher than expected in the general population. Patients with RA, particularly those with highly active disease, are at a higher risk for the development of lymphoma. The potential role of TNF blocker therapy in the development of malignancies is not known.

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blocking agents (initiation of therapy ≤18 years of age), of which Cimzia® is a member. Approximately half of the cases were lymphoma (including Hodgkin's and non-Hodgkin's lymphoma), while the other cases represented a variety of different malignancies and included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

Cases of acute and chronic leukemia have been reported with TNF-blocker use. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for developing leukemia.

Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma that has a very aggressive disease course and is usually fatal, have been reported in patients treated with TNF blockers, including Cimzia®. The majority of reported TNF blocker cases occurred in adolescent and young adult males with Crohn's disease or ulcerative colitis. Almost all of these patients had received treatment with the immunosuppressants azathioprine and/or 6-mercaptopurine (6-MP) concomitantly with a TNF blocker at or prior to diagnosis. Carefully assess the risks and benefits of treatment with Cimzia®, especially in these patient types.

Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-antagonists, including Cimzia®. Periodic skin examinations are recommended for all patients, particularly those with risk factors for skin cancer.

Heart Failure
Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. Cimzia® has not been formally studied in patients with CHF. Exercise caution when using Cimzia® in patients who have heart failure and monitor them carefully.

Hypersensitivity
Symptoms compatible with hypersensitivity reactions, including angioedema, dyspnea, hypotension, rash, serum sickness, and urticaria, have been reported rarely following Cimzia® administration. Some of these reactions occurred after the first administration of Cimzia®. If such reactions occur, discontinue further administration of Cimzia® and institute appropriate therapy.

Hepatitis B Reactivation
Use of TNF blockers, including Cimzia®, has been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. Some cases have been fatal. Test patients for HBV infection before initiating treatment with Cimzia®. Exercise caution in prescribing Cimzia® for patients identified as carriers of HBV, with careful evaluation and monitoring prior to and during treatment. In patients who develop HBV reactivation, discontinue Cimzia® and initiate effective anti-viral therapy with appropriate supportive treatment.

Neurologic Reactions
Use of TNF blockers, including Cimzia®, has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disease, including multiple sclerosis, and with peripheral demyelinating disease, including Guillain-Barré syndrome. Rare cases of neurological disorders, including seizure disorder, optic neuritis, and peripheral neuropathy have been reported in patients treated with Cimzia®. Exercise caution in considering the use of Cimzia® in patients with these disorders.

Hematologic Reactions
Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia (e.g., leukopenia, pancytopenia, thrombocytopenia) has been infrequently reported with Cimzia®. Advise all patients to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pallor) while on Cimzia®. Consider discontinuation of Cimzia® therapy in patients with confirmed significant hematologic abnormalities.

Drug Interactions
An increased risk of serious infections has been seen in clinical trials of other TNF blocking agents used in combination with anakinra or abatacept. Formal drug interaction studies have not been performed with rituximab or natalizumab; however, because of the nature of the adverse events seen with these combinations with TNF blocker therapy, similar toxicities may also result from the use of Cimzia® in these combinations. Therefore, the combination of Cimzia® with anakinra, abatacept, rituximab, or natalizumab is not recommended. Interference with certain coagulation assays has been detected in patients treated with Cimzia®. There is no evidence that Cimzia® therapy has an effect on in vivo coagulation. Cimzia® may cause erroneously elevated aPTT assay results in patients without coagulation abnormalities.

Autoimmunity
Treatment with Cimzia® may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. Discontinue treatment if symptoms of lupus-like syndrome develop.

Immunizations
Do not administer live vaccines or live-attenuated vaccines concurrently with Cimzia®.

Adverse Reactions
In controlled Crohn's clinical trials, the most common adverse events that occurred in ≥5% of Cimzia® patients (n=620) and more frequently than with placebo (n=614) were upper respiratory infection (20% Cimzia®, 13% placebo), urinary tract infection (7% Cimzia®, 6% placebo), and arthralgia (6% Cimzia®, 4% placebo). The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 8% for Cimzia® and 7% for placebo.

In controlled RA clinical trials, the most common adverse events that occurred in ≥3% of patients taking Cimzia® 200 mg every other week with concomitant methotrexate (n=640) and more frequently than with placebo with concomitant methotrexate (n=324) were upper respiratory tract infection (6% Cimzia®, 2% placebo), headache (5% Cimzia®, 4% placebo), hypertension (5% Cimzia®, 2% placebo), nasopharyngitis (5% Cimzia®, 1% placebo), back pain (4% Cimzia®, 1% placebo), pyrexia (3% Cimzia®, 2% placebo), pharyngitis (3% Cimzia®, 1% placebo), rash (3% Cimzia®, 1% placebo), acute bronchitis (3% Cimzia®, 1% placebo), fatigue (3% Cimzia®, 2% placebo). Hypertensive adverse reactions were observed more frequently in patients receiving Cimzia® than in controls. These adverse reactions occurred more frequently among patients with a baseline history of hypertension and among patients receiving concomitant corticosteroids and non-steroidal anti-inflammatory drugs. Patients receiving Cimzia® 400

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mg as monotherapy every 4 weeks in RA controlled clinical trials had similar adverse reactions to those patients receiving Cimzia® 200 mg every other week. The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 5% for Cimzia® and 2.5% for placebo.

The safety profile for patients with Psoriatic Arthritis (PsA) treated with CIMZIA® was similar to the safety profile seen in patients with RA and previous experience with Cimzia®.

The safety profile for AS patients treated with Cimzia® was similar to the safety profile seen in patients with RA.

For full prescribing information, please visit www.ucb.com

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

About Bimekizumab
Bimekizumab is an investigational humanized IgG1 monoclonal antibody rationally designed to potently and selectively neutralize the biological function of both IL-17A and IL-17F, two key pro-inflammatory cytokines. IL-17A and IL-17F are closely related cytokines that are co-expressed at sites of inflammation and both independently co-operate with other cytokines to mediate chronic inflammatory responses driving many severe skin and joint diseases. Dose-ranging studies for bimekizumab have also started. Bimekizumab is not approved by any regulatory authority worldwide.

About Romosozumab
Romosozumab is an investigational bone-forming monoclonal antibody that is not currently 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 resorption. 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.

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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 7500 people in approximately 40 countries, the company generated revenue of €4.2 billion in 2016. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

UCB Forward-Looking Statements
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.