UCB News

UCB Showcases the Depth of its Immunology Research and Commitment to Patients at EULAR 2019

- Three oral presentations on novel investigational molecule bimekizumab to show potential for improving disease activity and quality of life outcomes in patients with ankylosing spondylitis, and musculoskeletal and skin outcomes over 48 weeks in those with psoriatic arthritis
- Multiple presentations will highlight the value of CIMZIA® (certolizumab pegol) in the treatment of axial spondyloarthritis, including new data from a 52-week placebo-controlled study on the benefit of early intervention for rapid and durable symptom control in patients with non-radiographic axial spondyloarthritis
- Patient research demonstrating the need to educate and engage women with chronic inflammatory diseases about their disease state and family planning

Brussels, Belgium – 7 June 2019 – UCB, a global biopharmaceutical company, will present results from the clinical development program of the company's key pipeline molecule, bimekizumab – a novel humanized monoclonal IgG1 antibody that is thought to potently and selectively neutralizes both IL-17A and IL-17F cytokines – and the company's Fc-free anti-TNF treatment CIMZIA® (certolizumab pegol) at the Annual European Congress of Rheumatology (EULAR 2019), taking place in Madrid, June 12-15, 2019. These data underscore the company's commitment to advancing rheumatology science in order to transform the lives of patients living with chronic inflammatory diseases.

"At EULAR 2019, we are proud to present these positive findings on our pipeline molecule bimekizumab, while other studies reinforce the value of CIMZIA in a range of patients who have specific treatment requirements, particularly those with axial spondyloarthritis. UCB is committed to serving as partners in care, supporting patients and rheumatologists dealing with challenging treatment situations and improving the clinical understanding of their needs. Our aim is to bring real world value to patients with significant unmet needs," said Emmanuel Caeymaex, Head of Immunology and Executive Vice President, Immunology Patient Value Unit, UCB.

As part of the oral presentations, week 12 findings from a Phase 2b bimekizumab study demonstrating improvements in disease activity and patient-reported outcomes, such as pain, fatigue, function, morning stiffness, and quality of life (QoL) in patients with active ankylosing spondylitis (AS) will be presented.[i] Results from a 48-week Phase 2b randomized study in patients with psoriatic arthritis (PsA) will also be presented, supporting bimekizumab's long term efficacy and safety profile in this condition.[ii] A third presentation will provide further insight into the biology of IL-17A and IL-17F, supporting the value of dual neutralization of those cytokines as a targeted approach for suppression of inflammation.[iii]

CIMZIA data to be featured at EULAR 2019 include four new analyses from studies in patients with axial spondyloarthritis (axSpA). Important post-hoc results from the C-AXSPAND study will support the efficacy and safety of CIMZIA treatment in patients with non-radiographic axSpA, and show the benefit of early treatment.[iv] An interim analysis will be presented from C-OPTIMISE that demonstrated sustained remission during 48 weeks of CIMZIA treatment in patients with ankylosing spondylitis (AS) and non-radiographic axSpA.[v] Additionally, a new analysis from the RAPID-axSpA study confirms that CIMZIA treatment in axSpA

patients rapidly reduced active inflammation in the spine, which was sustained over 4 years and was associated with negligible increase in fatty lesions in the vertebral edges.[vi]

As part of UCB's commitment to ongoing patient value, the company will present findings from a survey of women in Europe and Asia-Pacific demonstrating a need to educate and engage women with chronic inflammatory disease around family planning issues, to allow them to make informed decisions with their physicians around their care.[vii]

In addition to the 12 data presentations, UCB will be sponsoring a satellite symposium highlighting the challenges that women with axSpA and PsA face, and the important role of shared decision making between patients and healthcare professionals when considering treatment options.

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

UCB Sponsored Symposia:

Considering the Patient Perspective: Challenges Facing Women with axSpA and PsA, I. van der Horst-Bruinsma, H. Marzo-Ortega, K. Anderson, L. Coates

- Date/Time: June 13, 2019: 8:15-9:30 CEST

Oral Presentations on Bimekizumab:

Dual neutralization of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and quality-of-life outcomes in patients with active ankylosing spondylitis: results from a Phase 2b, randomized, double-blind, placebo-controlled, dose-ranging study, D. van der Heijde, L. Gensler, A. Deodhar, X. Baraliakos, D. Poddubnyy, M. K. Farmer, D. Baeten, J. Coarse, M. Oortgiesen, M. Dougados

- Date/Time: June 14, 2019: 10:15-11:45 CEST

Dual neutralisation of IL-17A and IL-17F with bimekizumab in patients with active PsA: overall and TNF-inhibitor-naïve population results from a 48-week Phase 2b randomized study, C. Ritchlin, A. Kavanaugh, J. F. Merola, G. Schett, J. U. Scher, R. B. Warren, D. Assudani, T. Kumke, B. Ink, I. McInnes

- Date/Time: June 13, 2019: 10:15-11:45 CEST

Mucosal-associated invariant T (MAIT) cell-derived IL-17A and IL-17F production is IL-23-independent and biased towards IL-17F, S. Cole, C. Simpson, R. Okoye, M. Griffiths, D. Baeten, S. Shaw, A. Maroof

- Date/Time: June 14, 2019: 10:15-11:45 CEST

CIMZIA® Poster Presentations:

Earlier Treatment of Non-Radiographic Axial Spondyloarthritis with Certolizumab Pegol Results in Improved Clinical Outcomes, M. Rudwaleit, L. S. Gensler, A. Deodhar, J. Kay, W. P. Maksymowych, N. Haroon, R. Landewé, S. E. Auteri, N. de Peyrecave, T. Kumke, D. van der Heijde

- Date/Time: June 14, 2019: 11:45-13:30 CEST

Long-Term Certolizumab Pegol Treatment of Axial Spondyloarthritis is Associated with Rapid and Sustained Reduction of Active Inflammation and Minimal Structural Changes in the Spine: 4–Year MRI Results from Rapid-axSpA, X. Baraliakos, S. Kruse, S. E. Auteri, N. de Peyrecave, T. Nurminen, T. Kumke, B. Hoepken, J. Braun

- Date/Time: June 14, 2019: 11:45-13:30 CEST

Efficacy and Safety Outcomes in Patients with Axial Spondyloarthritis Treated with Certolizumab Pegol: Results from the 48–Week Run-In Part of C-OPTIMISE, R. Landewé, D. van der Heijde, M. Dougados, X. Baraliakos, F. Van den Bosch, K. Gaffney, N. de Peyrecave, L. Bauer, B. Hoepken, K. Thomas, L. S. Gensler

- Date/Time: June 14, 2019: 11:45-13:30 CEST

Body Mass Index and Systemic Corticosteroid Use as Indicators of Disease Burden and Their Influence on the Safety Profile of Certolizumab Pegol Across Indications, V. P. Bykerk, A. Blauvelt, J.R. Curtis, C. Gaujoux-Viala, T. K. Kvien, W. J. Sandborn, K. Winthrop, C. Popova, X. Mariette

- Date/Time: June 15, 2019: 10:30-12:00 CEST

UCB-Sponsored Data on Women with Chronic Rheumatic Diseases:

Perspectives of Women with Chronic Rheumatic Diseases on Their Journey to Motherhood: Comparison of Surveys from Asia-Pacific and Europe, Y. Tanaka, C. Barrett, Y. Hirano, K. Ikeda, K. Paizis, A. Sameshima, Y. Su, C. Saadoun, P.C. Wong

- Date/Time: June 15, 2019: 10:30-12:00 CEST

Abstract Book

Dual neutralisation of interleukin (IL)-17A and IL-17F with bimekizumab in moderate-to-severe plaque psoriasis: 60-week results from a randomised, double-blinded, Phase 2b extension study, A. Blauvelt, K. A. Papp, J. F. Merola, A. B. Gottlieb, N. Cross, C. Madden, M. Wang, C. Cioffi, C. E. M. Griffiths

Effectiveness and Safety of Certolizumab Pegol for the Treatment of Axial Spondyloarthritis in Real-World Clinical Practice in Europe: Results from a Prospective Non-Interventional 12-Month Cohort Study, X. Baraliakos, T. Witte, L. De Clerck, B. Frediani, E. Collantes-Estévez, G. Katsifis, B. VanLunen, E. Kleine, B. Hoepken, N. Goodson

Achievement of PASDAS Low Disease Activity and Very Low Disease Activity in Patients with Psoriatic Arthritis Treated with Certolizumab Pegol Over 4 Years and The Overlap with DAPSA and MDA Disease Activity Targets, L. C. Coates, J. F. Merola, O. FitzGerald, A. Kavanaugh, A. B. Gottlieb, W. Tillett, L. Bauer, B. Hoepken, T. Nurminen, P. J. Mease, P. Helliwell, D. van der Heijde

Family Planning in Chronic Rheumatic Diseases: Unmet Needs of Women and Men in Sweden, L. Alemo Munters, N. Holmen, S. Jansson

About Bimekizumab

Bimekizumab is an investigational novel humanized monoclonal IgG1 antibody that potently and selectively neutralizes both IL-17A and IL-17F, two key cytokines driving inflammatory processes. IL-17A and IL-17F have similar pro-inflammatory functions and independently cooperate with other inflammatory mediators to drive chronic inflammation and damage across multiple tissues.

Previous early phase clinical studies in psoriasis and psoriatic arthritis have suggested that bimekizumab's unique dual neutralization of both IL-17A and IL-17F may provide a new targeted approach for the treatment of immune-mediated inflammatory diseases.[viii,ix,x] Preclinical results in disease-relevant cells have shown that

neutralizing IL-17F and IL-17A reduces skin and joint inflammation, as well as pathological bone formation to an extent greater than inhibition of IL-17A alone.[ix,xi,xii]

The safety and efficacy of bimekizumab have not been established, and it is not approved by any regulatory authority worldwide.

About CIMZIA® in the EU/EEA

In the EU, CIMZIA® in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs (DMARDs) including MTX.

CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. CIMZIA in combination with MTX is also indicated for the treatment of severe, active and progressive RA in adults not previously treated with MTX or other DMARDs.

CIMZIA has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function, when given in combination with MTX.

CIMZIA, in combination with MTX, is also indicated for the treatment of active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate. CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate.

CIMZIA is also indicated in the EU for the treatment of adult patients with severe active axial spondyloarthritis (axSpA), comprising:

- Ankylosing spondylitis (AS) – adults with severe active AS who have had an inadequate response to, or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).
- Axial spondyloarthritis (axSpA) without radiographic evidence of AS – adults with severe active axSpA without radiographic evidence of AS but with objective signs of inflammation by elevated C-reactive protein (CRP) and/or Magnetic Resonance Imaging (MRI) who have had an inadequate response to, or are intolerant to NSAIDs.

CIMZIA is also indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

About CIMZIA® in Fertility, Pregnancy and Lactation in the EU/EEA

Women of childbearing potential

The use of adequate contraception should be considered for women of childbearing potential. For women planning pregnancy, continued contraception may be considered for 5 months after the last CIMZIA dose due to its elimination rate, but the need for treatment of the woman should also be taken into account (see below).

Pregnancy

Data from more than 500 prospectively collected pregnancies exposed to CIMZIA with known pregnancy outcomes, including more than 400 pregnancies exposed during the first trimester, does not indicate a malformative effect of CIMZIA. However, the available clinical experience is too limited to, with a reasonable certainty, conclude that there is no increased risk associated with CIMZIA administration during pregnancy.

Animal studies using a rodent anti-rat TNFα did not reveal evidence of impaired fertility or harm to the foetus. However, these are insufficient with respect to human reproductive toxicity. Due to its inhibition of TNFα, CIMZIA administered during pregnancy could affect normal immune response in the newborn.

CIMZIA should only be used during pregnancy if clinically needed. Non-clinical studies suggest low or negligible level of placental transfer of a homologue Fab-fragment of certolizumab pegol (no Fc region).

In a clinical study 16 women were treated with certolizumab pegol (200 mg every 2 weeks or 400 mg every 4 weeks) during pregnancy. Certolizumab pegol plasma concentrations measured in 14 infants at birth were Below the Limit of Quantification (BLQ) in 13 samples; one was 0.042 µg/ml with an infant/mother plasma ratio at birth of 0.09%. At Week 4 and Week 8, all infant concentrations were BLQ. The clinical significance of low levels certolizumab pegol for infants is unknown. It is recommended to wait a minimum of 5 months following the mother's last CIMZIA administration during pregnancy before administration of live or live-attenuated vaccines (e.g. BCG vaccine), unless the benefit of the vaccination clearly outweighs the theoretical risk of administration of live or live-attenuated vaccines to the infants.

Breastfeeding
In a clinical study in 17 lactating women treated with CIMZIA, minimal transfer of certolizumab pegol from plasma to breast milk was observed. The percentage of the maternal certolizumab pegol dose reaching an infant during a 24 hour period was estimated to 0.04% to 0.30%. In addition, since certolizumab pegol is a protein that is degraded in the gastrointestinal tract after oral administration, the absolute bioavailability is expected to be very low in a breastfed infant. Consequently, CIMZIA can be used during breastfeeding.

Important Safety Information about CIMZIA® in the EU/EEA
Cimzia® was studied in 4,049 patients with rheumatoid arthritis (RA) in controlled and open label trials for up to 92 months. The commonly reported adverse reactions (1-10%) in clinical trials with Cimzia® and post-marketing were viral infections (includes herpeszoster, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthaenia, leukopaenia (including lymphopaenia, neutropaenia), eosinophilic disorder, pain (any sites), pyrexia, sensory abnormalities, hypertension, pruritus (any sites), hepatitis (including hepatic enzyme increase), injection site reactions, and nausea. Serious adverse reactions include sepsis, opportunistic infections, tuberculosis (including miliary, disseminated and extrapulmonary), herpes zoster, lymphoma, leukaemia, solid organ tumours, angioneurotic oedema, cardiomyopathies (includes heart failure), ischemic coronary artery disorders, pancytopaenia, hypercoagulation (including thrombophlebitis, pulmonary embolism), cerebrovascular accident, vasculitis, hepatitis/hepatopathy (includes cirrhosis), and renal impairment/nephropathy (includes nephritis). In RA controlled clinical trials, 4.4% of patients discontinued taking Cimzia® due to adverse events vs. 2.7% for placebo.

Cimzia® is contraindicated in patients with hypersensitivity to the active substance or any of the excipients, active tuberculosis or other severe infections such as sepsis or opportunistic infections and moderate to severe heart failure.

Serious infections including sepsis, tuberculosis and opportunistic infections (e.g. histoplasmosis, nocardia, candidiasis) have been reported in patients receiving Cimzia®. Some of these events have been fatal. Monitor patients closely for signs and symptoms of infections including tuberculosis before, during and after treatment with Cimzia®. Treatment with Cimzia must not be initiated in patients with a clinically important active infection. If an infection develops, monitor carefully and stop Cimzia® until the infection is controlled. Before initiation of therapy with Cimzia®, all patients must be evaluated for both active and inactive (latent)

tuberculosis infection. If active tuberculosis is diagnosed prior to or during treatment, Cimzia® therapy must not be initiated and must be discontinued. If latent tuberculosis is diagnosed, appropriate anti-tuberculosis therapy must be started before initiating treatment with Cimzia®. Patients should be instructed to seek medical advice if signs/symptoms (e.g. persistent cough, wasting/weight loss, low grade fever, listlessness) suggestive of tuberculosis occur during or after therapy with Cimzia®.

Reactivation of hepatitis B has occurred in patients receiving a TNF-antagonist including Cimzia® who are chronic carriers of the virus (i.e. surface antigen positive). Some cases have had a fatal outcome. Patients should be tested for HBV infection before initiating treatment with Cimzia®. Carriers of HBV who require treatment with Cimzia® should be closely monitored and in the case of HBV reactivation Cimzia® should be stopped and effective anti-viral therapy with appropriate supportive treatment should be initiated.

TNF antagonists including Cimzia® may increase the risk of new onset or exacerbation of clinical symptoms and/or radiographic evidence of demyelinating disease, including multiple sclerosis; of formation of autoantibodies and uncommonly of the development of a lupus-like syndrome; of severe hypersensitivity reactions. If a patient develops any of these adverse reactions, Cimzia® should be discontinued and appropriate therapy instituted.

With the current knowledge, a possible risk for the development of lymphomas, leukaemia or other malignancies in patients treated with a TNF antagonist cannot be excluded. Rare cases of neurological disorders, including seizure disorder, neuritis and peripheral neuropathy, have been reported in patients treated with Cimzia®.

Adverse reactions of the haematologic system, including medically significant cytopaenia, have been 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 haematological abnormalities.

The use of Cimzia® in combination with anakinra or abatacept is not recommended due to a potential increased risk of serious infections. As no data are available, Cimzia® should not be administered concurrently with live vaccines. The 14-day half-life of Cimzia® should be taken into consideration if a surgical procedure is planned. A patient who requires surgery while on Cimzia® should be closely monitored for infections.

Cimzia® was studied in 325 patients with active axial spondyloarthritis (axSpA) and in 409 patients with psoriatic arthritis (PsA) for up to 4 years. The safety profile for axSpA and PsA patients treated with Cimzia® was consistent with the safety profile in RA and previous experience with Cimzia® .

Cimzia® was studied in 1112 patients with psoriasis in controlled and open-label studies for up to 18 months. The safety profile of Cimzia® 400 mg every 2 weeks and Cimzia® 200 mg every 2 weeks were generally similar.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision March 2019. https://www.ema.europa.eu/documents/product-information/cimzia-epar-product-information_en.pdf

For further information, UCB:

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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 in immunology and neurology. With 7,500 people in approximately 40 countries, the company generated revenue of € 4.6 billion in 2018. 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.

[i] van der Heidje D, et al. Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and quality of life outcomes in patients with active ankylosing spondylitis: results from a Phase 2b, randomised, double-blind, placebo controlled, dose-ranging study. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[ii] Ritchlin C, et al. Dual neutralisation of IL-17A and IL-17F with bimekizumab in patients with active PsA: overall and TNF-inhibitor naïve population results from 48-week Phase 2b randomised study. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[iii] Cole S, et al. Mucosal-associated invariant T (MAIT) cell-derived IL-17A and IL-17F production is IL-23-independent and biased towards IL-17F. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[iv] Rudwaleit M, et al. Earlier Treatment of Non-Radiographic Axial Spondyloarthritis with Certolizumab Pegol Results in Improved Clinical Outcomes. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[v] Landewé R, et al. Efficacy and Safety Outcomes in Patients with Axial Spondyloarthritis Treated with Certolizumab Pegol: Results from the 48-Week Run-In Part of C-OPTIMISE. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[vi] Baraliakos X, et al. Long-Term Certolizumab Pegol Treatment of Axial Spondyloarthritis is Associated with Rapid and Sustained Reduction of Active Inflammation and Minimal Structural Changes in the Spine: 4–Year MRI Results from Rapid-axSpA. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[vii] Tanaka Y, et al. Perspectives of Women with Chronic Rheumatic Diseases on Their Journey to Motherhood: Comparison of Surveys from Asia-Pacific and Europe. Abstract to be presented at EULAR 2019, 12-15 June, Madrid Spain.
[viii] Glatt S, Helmer E, Haier B, et al. First-in-human randomized study of bimekizumab, a humanized monoclonal antibody and selective dual inhibitor of IL-17A and IL-17F, in mild psoriasis. Br J Clin Pharmacol. 2017 May;83(5):991-1001. doi: 10.1111/bcp.13185. Epub 2017 Jan 10.
[ix] Papp K, Merola J, Gottlieb A, Griffiths C, Cross N, Peterson L, Cioffi C, Blauvelt A. Dual neutralization of both interleukin 17A and interleukin 17F with bimekizumab in patients with psoriasis: Results from BE ABLE 1, a 12-week randomized, double-blinded, placebo-controlled phase 2b trial. J Am Acad Dermatol. 2018 Aug;79(2):277-286.e10. https://www.ncbi.nlm.nih.gov/pubmed/29609013.
[x] Glatt S, Baeten D, Baker T, et al. Dual IL-17A and IL-17F neutralisation by bimekizumab in psoriatic arthritis: evidence from preclinical experiments and a randomized placebo-controlled clinical trial that IL-17F contributes to human chronic tissue inflammation. Ann Rheum Dis. 2018;77:523-532.
[xi] Shah M, Maroof A, Al-Hosni R, Gikas P, Gozzard N, Shaw S, Roberts S. Bimekizumab Blocks T Cell-Mediated Osteogenic Differentiation of Periosteal Stem Cells: Coupling Pathological Bone Formation to IL-17A and IL-17F Signaling [abstract]. Arthritis Rheumatol. 2017; 69 (suppl 10).
[xii] Maroof A, Okoye R, Smallie T, et al. Bimekizumab dual inhibition of IL-17A and IL-17F provides evidence of IL-17F contribution to chronic inflammation in disease-relevant cells. Ann Rheum Dis. 201706;76 (suppl.2):213-213.