UCB receives positive EU CHMP opinion for CIMZIA® (certolizumab pegol) to treat severe, active and progressive rheumatoid arthritis in DMARD-naïve patients

- Decision provides new option for adults with rheumatoid arthritis (RA) who have not been treated with methotrexate or other disease-modifying anti-rheumatic drugs (DMARD-naïve)
- European Commission decision expected in Q1 2016

Brussels, Belgium – 20 November, 2015 – UCB has announced that the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending extending the European Union marketing authorization for the use of CIMZIA® in the treatment of severe, active and progressive RA in DMARD-naïve adult patients.

The positive opinion was based on period 1 of UCB's Phase 3 C-EARLY™ study, which found that adding CIMZIA® to optimized methotrexate achieved statistically significant sustained remission and inhibition of radiographic progression (change from baseline in van der Heijde modified total Sharp score) at week 52 in DMARD-naïve patients with early, active RA.[1]

"Evidence suggests that early assessment, recognition and treatment of RA symptoms are associated with less joint destruction in the long-term and higher chances of achieving remission. Our C-EARLY research also supports this early window of opportunity for treating patients and has demonstrated that CIMZIA® can provide clinical benefit and improve outcomes for an important subset of RA patients – those who are DMARD-naïve with prognostic factors of severe disease progression, within a year of diagnosis. We are thrilled that the CHMP decision brings us one step closer to bringing CIMZIA® to these patients," said Emmanuel Caeymaex, Head, Immunology Patient Value Unit, UCB.

The evaluation for an extension of indication is reviewed by CHMP as a Type II variation. At the end of the evaluation, the CHMP issues a scientific opinion with respect to extension of indication. This scientific opinion is then passed on to the European Commission, which has the ultimate authority for granting the marketing authorization within approximately two months after receipt of the CHMP opinion.

About C-EARLY™

The C-EARLY™ study is a phase 3, multi-center, randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of certolizumab pegol (CZP) in combination with optimized methotrexate (MTX) for the treatment of DMARD-naïve adult patients with early, active RA.[1,2] Optimized MTX was the dose escalation of MTX by 5mg every two weeks up to the highest dose the patient could tolerate, but no more than 25mg per week, by week 8 and maintained to week 52 of the study.

In the study, 879 patients with early, active RA (<1 year since diagnosis; fulfilling the 2010 ACR/EULAR classification criteria) who were DMARD-naïve and had at least moderate disease

activity (DAS28[ESR] ≥3.2) were randomized to either CZP plus methotrexate MTX (n=660) or placebo plus optimized MTX (n=219) for 52 weeks.[1] Ninety-five percent of the patients in the study had high disease activity, with a DAS28[ESR] > 5.1.

The primary endpoint of the study was sustained remission (DAS28[ESR] <2.6 at both Weeks 40 and 52). The key secondary endpoint was sustained low disease activity (DAS28[ESR] ≤3.2 at both Weeks 40 and 52). Other key secondary endpoints included proportion of patients with ACR50 response, change from baseline in HAQ-DI and inhibition of radiographic progression (change from baseline in van der Heijde modified total Sharp score) at week 52.[1]

For all patients in the study, MTX therapy was initiated with 10mg weekly and increased to 25mg after 6-8 weeks, if well tolerated. At least 15mg weekly of MTX had to be taken to remain in the study.

The study showed that, after 52 weeks, treatment with CZP plus optimized MTX resulted in more patients in sustained remission and low disease activity, greater improvements in the signs and symptoms of rheumatoid arthritis including physical function, and inhibition of structural damage compared with optimized MTX treatment alone. No new safety signals for CZP were reported.[1]

Secondary results from the C-EARLY™ study showed that patients treated with CZP plus MTX had greater improvements at one year in pain, disease activity, fatigue and health related quality of life, improved workplace and household productivity, and reduced need for assistance with regular activities compared to patients receiving placebo and optimized MTX.[2,3]

Results from the C-EARLY study were recently presented as a poster presentation at the European League Against Rheumatism Annual Congress (EULAR 2015) in Rome, Italy, June 10-13, and as an oral presentation at the American College of Rheumatology (ACR) 2015 Annual Scientific Meeting, in San Francisco, CA, November 6-11.

About CIMZIA®

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, in combination with methotrexate (MTX), is indicated for:

- the treatment of moderate to severe, active rheumatoid arthritis (RA) in adult patients when the response to disease-modifying antirheumatic drugs (DMARDs) including MTX, has been inadequate. Cimzia can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate

About CIMZIA® in the EU/EEA[4]

In the EU, CIMZIA in combination with methotrexate (MTX) is indicated in Rheumatoid Arthritis (RA) for:

- the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs (DMARDs) including MTX.[4] CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. 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.
- 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 methotrexate or when continued treatment with methotrexate is inappropriate.[3]

CIMZIA is also indicated in the EU for the treatment of adult patients with axial spondyloarthritis (axSpA), comprising:[4]

- 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.[4]

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 herpes, 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, 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 or moderate-to-severe heart failure.

Serious infections including sepsis, tuberculosis and opportunistic infections 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® if infection becomes serious. 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; 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 hematologic system, including medically significant cytopaenia, have 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 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) in a placebo-controlled clinical trial for up to 30 months and in 409 patients with psoriatic arthritis (PsA) in a placebo-controlled clinical trial for up to 30 months. The safety profile for axSpA and PsA patients treated with CIMZIA® was consistent with the safety profile in RA and previous experience with CIMZIA®.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision 16th December 2014. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf

References

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EARLY randomized, double-blind, controlled phase 3 study. Presented at the American College of Rheumatology (ACR) 2015 Annual Scientific Meeting; abstract # 968
2. Bykerk, V, Bingham, C, Burmester, G-R et al. Reduction of Disease Burden on Workplace and Household Productivity Following 52 Weeks of Treatment with Certolizumab Pegol in Combination with Methotrexate in DMARD-Naïve Patients with Active, Severe, Progressive Rheumatoid Arthritis. Presented at the American College of Rheumatology (ACR) 2015 Annual Scientific Meeting; abstract # 2736
3. Emery, P, Bingham, C, Burmester, G-R et al. Improvements in patient-reported outcomes and workplace and household productivity following 52 weeks of treatment with certolizumab pegol in combination with methotrexate in DMARD-naïve early rheumatoid arthritis patients: results from the C-EARLY randomized, double-blind, controlled phase 3 study. Presented at the European League Against Rheumatism (EULAR) 2015 Congress; abstract # SAT0165
4. CIMZIA® EU Summary of Product Characteristics. Accessed 26th February 2015 from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf

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About UCB

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Forward looking statements - UCB

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