Cimzia® (certolizumab pegol) Data Showed Broad and Rapid Relief From Burden of Symptoms In Rheumatoid Arthritis Patients

- **Rapid, sustained and clinically meaningful improvement in wide-ranging patient-reported outcomes (PROs), including pain and quality of life, were seen in patients following treatment with Cimzia® over 24 weeks[1]**
- **Patients treated with Cimzia® who achieved response by week 12 had a greater chance of achieving long-term clinical outcomes, compared to patients who do not respond to treatment by week 12[1]**

BRUSSELS, BELGIUM, 9th May - UCB announced results from a post hoc analysis of the RAPID 2 study, published in the *Annals of Rheumatic Diseases,* which showed Cimzia®, the only approved PEGylated anti-TNF, plus methotrexate (MTX) provided rapid relief from a broad range of symptoms associated with the burden of moderate to severe active rheumatoid arthritis (RA). Those adult patients treated with Cimzia® that achieved early responses were found to have an increased chance of achieving longer-term outcomes.[1]

"These data show that when administered with methotrexate, certolizumab pegol offers rapid relief across a broad range of rheumatoid arthritis symptoms and that relatively few patients need to be treated before at least one patient reports clinical benefits from the positive relief the treatment provides" said lead investigator Dr Vibeke Strand, Adjunct Clinical Professor in the Division of Immunology and Rheumatology, at Stanford University, California. "By assessing patient-reported outcomes at early-stages of treatment we are able to predict late-stage clinical outcomes and treatment benefits for patients, providing great reassurance to both patients and their healthcare professionals."

PROs were secondary efficacy endpoints in RAPID 2 and were used to measure the impact of treatment with certolizumab pegol versus placebo. Number needed to treat (NNT) analysis was used in these post hoc analyses to interpret the PRO results. The NNT determines the number of patients that need to be treated in order to obtain the benefit of interest in one additional patient; therefore, small NNTs indicate favourable treatment effects. NNTs and minimum clinically important differences (MCIDs, which determine clinically meaningful improvements) were evaluated.[1]

In the RAPID 2 study, patients with active RA (by 1987 American College of Rheumatology [ACR] classification criteria) with inadequate responses to MTX therapy were randomised to receive certolizumab pegol (400mg at weeks 0, 2 and 4 followed by 200mg or 400mg every two weeks*) plus MTX, or placebo together with MTX for 24 weeks.[1] The primary outcome measure was ACR 20 response at week 24.

At week 24, significantly more patients in the certolizumab pegol treatment groups reported improvements ≥ MCID in all six PROs (pain, fatigue, patient's global assessment of disease (PtGA), physical function by HAQ, and HRQOL by SF-36 physical and mental

* In the EU, the approved maintenance dose regimen is 200mg every two weeks. In the US, the approved maintenance dose regimen is 200mg every two weeks or 400mg every 4 weeks can be considered

component summary scores). The beneficial effects of certolizumab pegol were similar between the 200mg and 400mg dose levels with no significant difference between treatment groups in any PROs.[1]

Furthermore, at week 24, 63% of certolizumab pegol 200mg treated patients reported clinically meaningful improvements in ≥ 1 PRO compared with 13% in placebo groups, and approximately 23% of all certolizumab pegol treated patients reported clinically meaningful improvements in all six PROs compared with 3% in placebo groups.[1]

The NNT for reported changes ≥ MCID in all six PROs was approximately five patients, and these results showed the highest correlation between pain, PtGA and fatigue. The NNT for reported changes ≥ MCID in up to five PROs was 2-3.[1]

Improvements ≥ MCID in pain were investigated to predict outcomes at week 24. Those patients achieving pain MCID by week 12 were more likely to have better outcomes than those who did not achieve MCID at week 12. Additionally, a comparison of week 6 and 12 responders, showed approximately 27% of patients who reported improvements ≥ MCID in pain at week 6 achieved low disease activity (LDA) at week 24, compared with 16% of week 12 responders.[1]

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Cimzia® (certolizumab pegol) in European Union / EEA important safety information
Cimzia® was studied in 2367 patients with RA in controlled and open label trials for up to 57 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), asthenia, leukopaenia (including lymphopaenia, neutropaenia), eosinophilic disorder, pain (any sites), pyrexia, sensory abnormalities, hypertension, pruritis (any sites), hepatitis (including hepatic enzyme increase), injection site reactions. Serious adverse reactions include sepsis, opportunistic infections, tuberculosis, herpes zoster, lymphoma, leukaemia, solid organ tumours, angioneurotic edema, 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, 5% of patients discontinued taking Cimzia® due to adverse events vs. 2.5% 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, moderate to severe heart failure.

Before initiation of Cimzia®, evaluate patients for both active or inactive (latent) tuberculosis infection. Monitor patients for the development of signs and symptoms of infection during and after treatment with Cimzia®. If an infection develops, monitor carefully, and stop Cimzia® if infection becomes serious.

TNF blockers including Cimzia® may increase the risk: of reactivation of Hepatitis B Virus (HBV) in patients who are chronic carriers of the virus; 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 cytopenia, 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 or attenuated 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.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision February 2011.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf

About CIMZIA®

Cimzia® is the only PEGylated anti-TNF (Tumor Necrosis Factor). Cimzia® has a high affinity for human TNF-alpha, selectively neutralizing the pathophysiological effects of TNF-alpha. Over the past decade, TNF-alpha has emerged as a major target of basic research and clinical investigation. This cytokine plays a key role in mediating pathological inflammation, and excess TNF-alpha production has been directly implicated in a wide variety of diseases. The U.S. Food and Drug Administration (FDA) has approved Cimzia® 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 and for the treatment of adults with moderately to severely active rheumatoid arthritis. Cimzia® in combination with MTX, is approved in the EU for the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying antirheumatic drugs (DMARDs) including MTX. Cimzia® can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. UCB is also developing Cimzia® in other autoimmune disease indications. Cimzia® is a registered trademark of UCB PHARMA S.A.

About UCB

UCB, Brussels, Belgium (www.ucb.com) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing more than 9000 people in over 40 countries, UCB produced revenue of EUR 3.22 billion in 2010. UCB is listed on Euronext Brussels (symbol: UCB).

Forward-looking statements

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different 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, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.

References:

1. *Strand, V. et al. Certolizumab pegol plus methotrexate provides broad relief from the burden of rheumatoid arthritis: analysis of patient-reported outcome from the RAPID 2 trial; Annals of Rheumatic Diseases; DOI:10.1136/ard.2010.143586; http://ard.bmj.com/content/early/2011/03/17/ard.2010.143586.full*