Novel ACR hybrid score in rheumatoid arthritis applied for the first time to data from the RAPID 1 study with Cimzia® (certolizumab pegol)

- **American College of Rheumatology (ACR) hybrid score associated with greater sensitivity for measuring treatment response in rheumatoid arthritis (RA) compared to traditional ACR20/50/70 measures**
- **A post-hoc analysis of the RAPID 1 study showed majority of improvement in ACR hybrid scores was achieved before 12 weeks and was maintained up to week 52[1]**

BRUSSELS, BELGIUM, 16th May – The ACR hybrid score, a new measure of response to RA treatment recently developed by the American College of Rheumatology, demonstrated improved sensitivity compared to traditional ACR responses, according to recently published results in *Arthritis Care & Research*.[1] Traditional ACR20/50/70 and DAS28 scores were compared to the ACR hybrid score in a post-hoc analysis of the RAPID 1 study, the first clinical trial data to be analysed using the ACR hybrid score.[1]

"The ACR hybrid score suggested similar results to other standard outcome measures, in that certolizumab pegol treated patients had significantly higher improvement in signs and symptoms of RA over placebo", said Dr R.F. van Vollenhoven from the Karolinska Institute in Stockholm, Sweden and lead author of the publication. "These results are of interest because the ACR hybrid score may represent a more sensitive and accurate measure of RA treatment response than the current accepted standard and could be considered as a valuable primary end point in future clinical trials."

The ACR hybrid score combines conventional ACR20/50/70 scores with the mean percent change in all 7 ACR core components, providing a percent improvement from baseline on a continuous scale.[1] The post hoc analysis of the ACR hybrid scores were from RAPID 1 (Rheumatoid Arthritis PreventIon of structural Damage), a phase III double-blind placebo-controlled trial designed to establish the efficacy and tolerability of certolizumab pegol together with methotrexate (MTX), in the treatment of active RA in patients who did not adequately respond to conventional treatment.[2]

The use of the ACR hybrid score was evaluated relative to other measures of response, including the ACR20/50/70 response rates and changes in DAS28 (disease activity score), and analyses differences between active treatment and placebo, elements that may be underestimated using ACR20/50/70 response criteria.[1] By also incorporating worsening disease activity, the ACR hybrid score may provide a better evaluation of the treatment's effect on overall change in disease activity.[1]

Results from this post hoc analysis suggest that certolizumab pegol plus MTX conferred significantly greater benefit than placebo plus MTX regardless of measures according to ACR20 responder rates, ACR hybrid scores and mean changes from baseline in the DAS28.[1] By all three measures, in some patients responses to certolizumab pegol plus MTX were significantly greater by week 1, continued to improve through the first 12 weeks of treatment, and were sustained to study at week 52.[1] Of the certolizumab pegol plus

MTX treated patients, 258 out of 392 (65.8%) and 172 out of 392 (43.9%) had ACR20 and ACR50 responses respectively.[1]

The data published were from the RAPID 1 study - the co-primary end points were ACR20 score at week 24 and change in mTSS (modified Total Sharp Score) at week 52.[2] The post hoc analysis focused on patients who received MTX and either 200mg subcutaneously or placebo every 2 weeks for 52 weeks accounting for 393 patients in the ITT population (30 patients were excluded due to nonimputable data).[2]

For further Information:
Scott Fleming, Global Communications Manager – Immunology
T +44 770.277.7378, scott.fleming@ucb.com

Andrea Levin, Senior PR Manager, US Communications and Public Relations
T +1 770 970 8352, andrea.Levin@ucb.com

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. *van Vollenhoven, RF. et al. American College of Rheumatology Hybrid Analysis of Certolizumab Pegol plus Methotrexate in Patients with Active Rheumatoid Arthritis: Data from a 52-week Phase III trial; Arthritis Care Res; DOI: 10.1002/acr.20331; Vol.63, No.1, January 2011, p128-134*
2. *Keystone E et al. Certolizumab pegol Plus Methotrexate Is Significantly More Effective Than Placebo Plus Methotrexate in Active Rheumatoid Arthritis. Arthritis & Rheumatism. Vol. 58, No. 11, November 2008, pp 3319-3329 DOI 10.1002/art.23964*