Cimzia® studies show significant clinical benefits for mono- and combination therapy in patients with rheumatoid arthritis

- **FAST 4WARD showed monotherapy Cimzia® 400 mg, dosed every four weeks, provided significant and effective clinical benefits compared to placebo**
- **RAPID 2 trial showed Cimzia®, together with *methotrexate* (MTX), achieved significant reduction in signs, symptoms and progression of rheumatoid arthritis**

Brussels, Belgium, November 18, 2008 at 7:00 AM (CET) – UCB today announced the results of two phase III studies, published in the Annals of the Rheumatic Diseases Online, showing Cimzia® (*certolizumab pegol*), the only PEGylated anti-TNFα (Tumour Necrosis Factor alpha), provided significant clinical benefits as monotherapy, and in combination with *methotrexate*, in adults with active rheumatoid arthritis (RA).

The six month FAST 4WARD study met primary and secondary endpoints*, and showed 400 mg *certolizumab pegol*, given every four weeks as subcutaneous monotherapy, significantly reduced signs, symptoms and pain associated with RA, and improved physical function, compared to patients treated with placebo ($p<0.001$).

"The positive outcomes of the FAST 4WARD study are exciting and demonstrate the potential for *certolizumab pegol* as a future therapy dosed every four weeks for patients with rheumatoid arthritis. While the RAPID studies have shown the benefits of *certolizumab pegol* as combination therapy, this is the first phase III trial to show a clinical benefit as monotherapy which becomes important when patients must discontinue treatment due to tolerability issues with conventional treatments, or have contraindications." said Professor Roy Fleischmann, University of Texas Southwestern Medical Centre, Dallas.

Meeting the primary endpoint*, patients treated with *certolizumab pegol* demonstrated significantly superior ACR20 response rates at Week 24 versus those on placebo ($p<0.001$: 45.5% versus 9.3%). The response to treatment was rapid and significant with more than one third (36.7%) of patients on *certolizumab pegol* achieving an ACR20 response as early as Week 1 of treatment, compared to less than 10 per cent on placebo ($p<0.05$), which was sustained throughout the study.

Patients on *certolizumab pegol* also reported clinically significant improvements in physical function (HAQ-DI) from Week 1 through to week 24, relative to placebo ($p<0.001$), consistent with significantly reduced pain scores (VAS) and disease activity (DAS28-3) ($p<0.001$).

In the study, serious adverse events (SAEs) occurred 2.8% and 7.2% of patients in the placebo and the *certolizumab pegol* groups, respectively. Reported SAEs included infections and benign tumours. The majority of AEs reported in both treatment groups were mild to moderate. The most commonly occurring AEs were headache, nasopharyngitis, and upper respiratory tract infections, diarrhea and sinusitis. The

incidence of injection site pain (1.8%) and discontinuations due to AEs (4.5%) were low in the *certolizumab pegol* group.

A second six month study called RAPID 2**, published this week, showed treatment with *certolizumab pegol*, together with *methotrexate* (MTX), significantly improved the clinical signs and symptoms of RA, inhibited progression of disease, and improved physical function in adult patients with active disease.

"The RAPID 2 study is important in demonstrating the benefits of *certolizumab pegol* in reducing the pain and symptoms of rheumatoid arthritis, and in helping to prevent joint damage associated with this debilitating condition in patients with active disease," said lead author Professor Josef Smolen, Division of Rheumatology, Medical University of Vienna.

"These findings expand data from RAPID 1 and its extension study presented at the 2008 American College of Annual Scientific Meeting which showed the long-term benefits of *certolizumab pegol* in providing relief of symptoms, improving productivity and quality of life and lessening fatigue," said Professor Smolen.

In the RAPID 2 study, patients were randomly allocated to receive one of three treatment regimens: *certolizumab pegol* 400 mg at Weeks 0, 2 and 4, then 200 mg every two weeks; *certolizumab pegol* 400 mg every 2 weeks; or placebo every 2 weeks, together with MTX.

In RAPID 2, patients treated with Cimzia® (200 mg or 400 mg), together with MTX, showed significantly superior ACR20 responses as early as Week 1, compared to patients treated with placebo and MTX ($p<0.01$), which were sustained throughout the study ($p<0.001$).

Patients in both *certolizumab pegol* treatment arms reported clinically significant improvements in physical function (HAQ-DI) from week 1, compared to placebo versus MTX, with improvements in quality of life sustained up to Week 24 ($p<0.001$). In addition, *certolizumab pegol*, inhibited progression of structural joint damage, with significantly smaller mean change from baseline in modified Total Sharp Score (TSS) at week 24, compared to MTX alone ($p<0.001$).

There were no statistically significant differences in clinical efficacy on primary or secondary end points between the 200 mg and 400 mg *certolizumab pegol* treatment arms.

The simultaneous studies, RAPID 2 and RAPID 1***, are the first large, placebo-controlled Phase III trials demonstrating the efficacy and tolerability of *certolizumab pegol* in the treatment of RA, as part of clinical trials programme involving more than 2,300 patients.

The most commonly reported SAEs were infections (including tuberculosis) and malignancies (including lymphoma). The most commonly reported AEs were headache, nasopharyngitis, and upper respiratory tract infections. Pooled safety data from both studies showed that the incidence of injection site pain (n=<3 new cases /100 patient years) and discontinuations due to adverse events (AEs) were low in the *certolizumab pegol* group.

The U.S. Food and Drug Administration (FDA) accepted a Biologics License Application for Cimzia® for the treatment of adult patients with active RA in February 2008. UCB

submitted a Marketing Authorisation Application to the European Medicines Agency in June 2008 requesting the approval of Cimzia® as a subcutaneous treatment for adults with moderate to severe active RA.

About FAST 4WARD (Study 011)

*The 24-week FAST 4WARD (e**F**fic**A**cy and **S**afety of cer**T**olizumab pegol – **4** **W**eekly dos**A**ge in **R**heumatoi**D** arthritis, Study O11) was designed to evaluate the efficacy and tolerability of certolizumab pegol 400 mg as monotherapy. The phase III randomised, double-blind, placebo-controlled trial involved 220 adult patients with active RA who had previously failed at least one disease-modifying anti-rheumatic drug (DMARD). Patients were randomised to receive either 400 mg certolizumab pegol subcutaneously every four weeks (n=111), or placebo - sorbitol (n=109). Patients were assessed for improvement in signs and symptoms of RA. FAST 4WARD met its primary endpoint ACR20 response rate at Week 24, and secondary endpoints including ACR50 and ACR70 responder rates. Patients who received certolizumab pegol experienced clinically and statistically significant improvements in all ACR components at Week 24 compared to those on placebo (p<.05).*

About RAPID 2

This Phase III double-blind placebo-controlled trial, involving 619 patients with active adult-onset RA was designed to evaluate the efficacy and tolerability of subcutaneous (SC) liquid certolizumab pegol (200 and 400 mg) together with MTX every 2 weeks compared to placebo together with MTX in patients with active RA despite ≥ 6 months treatment with MTX. Patients were randomly allocated to receive one of three treatment regimens: 246 patients received certolizumab pegol (liquid formulation) 400 mg and at Weeks 0, 2 and 4, then 200 mg every two weeks; 246 patients received certolizumab pegol (liquid formulation) 400 mg every 2 weeks; 127 patients received placebo every 2 weeks. RAPID 2 met its primary endpoint ACR20 response rate at Week 24, and secondary endpoints: change from baseline in mTSS, ACR 50 and ACR 70 responses at Week 24. Significantly more patients in the certolizumab pegol 200 and 400 mg groups achieved an ACR20 response versus placebo (p≤ 0.001); rates were 57.3%, 57.6%, and 8.7%, respectively. Certolizumab pegol 200 and 400 mg also significantly inhibited radiographic progression; mean changes from baseline in mTSS at Week 24 were 0.2 and –0.4, respectively, versus 1.2 for placebo (rank analysis p≤ 0.01). Certolizumab pegol treated patients reported rapid and significant improvements in physical function versus placebo (p≤ 0.001).

About RAPID 1

The Phase III double-blind placebo-controlled trial, involving 982 adults, was designed to establish the efficacy and tolerability of certolizumab pegol together with MTX, in the treatment of active RA in patients who did not adequately respond to conventional treatment. Patients were randomly allocated to receive one of three treatment regimens: 393 patients received certolizumab pegol 400 mg and at Weeks 0, 2 and 4, then 200 mg every two weeks; 390 patients received certolizumab pegol 400 mg every 2 weeks; 199 patients received placebo every 2 weeks. RAPID 1 met co-primary endpoints: ACR20 response rate at Week 24 and change from baseline in mTSS at Week 52.

About CIMZIA®

Cimzia® is the only PEGylated anti-TNF (Tumour Necrosis Factor). Cimzia® has a high affinity for human TNF-alpha, selectively neutralising 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 moderate to severe active disease who have had an inadequate response to conventional therapy. Cimzia® was approved in Switzerland for induction of a clinical response and for the maintenance of a clinical response and remission in patients with active Crohn's disease who have not responded adequately to conventional treatment in September 2007. UCB is also developing Cimzia® in rheumatoid arthritis and other autoimmune disease indications. Cimzia ® is a registered trademark of UCB S.A.

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About UCB

UCB, Brussels, Belgium (www.ucb-group.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 around 12 000 people in over 40 countries, UCB achieved revenue of 3.6 billion euro in 2007. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statement

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.