Moderate to severe rheumatoid arthritis patients treated with Cimzia® (certolizumab pegol) showed improved quality of life, reduction in fatigue and pain as reported in RAPID 1 study

- Patients treated with Cimzia® (certolizumab pegol) plus methotrexate (MTX) reported reductions in fatigue and pain from week 1 through to week 52
- Patients treated with Cimzia plus MTX reported improvements in physical function from week 1 through to week 52
- Patients treated with Cimzia plus MTX reported improvements in health-related quality of life (HRQoL) at the first assessment (week 12) and sustained up to week 52

Brussels, BELGIUM, December 8th, 2009 – UCB today announced new published data, in the online edition of Arthritis Research & Therapy, demonstrated that Cimzia®, the only approved PEGylated anti-TNF, plus methotrexate (MTX) provided rapid and sustained improvements in physical function, health related quality of life (HRQoL) as measured by short form 36 (SF-36), as well as reduced fatigue and arthritis pain. These improvements in patient-reported outcomes were statistically significant and clinically meaningful from the first post-baseline assessments through to the end of the study period at 1 year.

“The management of rheumatoid arthritis is an important partnership between patients and clinicians, and patient-reported outcomes make an essential contribution towards assessing a treatment’s overall effectiveness,” said Dr. Vibeke Strand, Adjunct Clinical Professor, Division of Immunology/Rheumatology of Stanford University School of Medicine, and lead author. “These new results demonstrate that the benefits of certolizumab pegol extend beyond those of clinical efficacy already demonstrated in RAPID 1 into areas that are more relevant and meaningful to patients on a daily basis.”

Following treatment with Cimzia plus MTX, patients reported improvements, as measured by SF-36, in HRQoL at week 12 with significant improvements in both the physical and mental component scores of HRQoL (as assessed by SF-36). More specifically, energy (vitality) and emotional state (mental health) domain scores approached age and gender adjusted norms of the U.S population, and a significant improvement in SF-36 mental component summary (MCS) scores was observed with Cimzia plus MTX in this trial. Improvements in the SF-36 physical and mental component summaries and in all eight domains were statistically significant from first post-baseline measurement and sustained to week 52.

Statistically significant and clinically meaningful reductions in fatigue were reported by more patients treated with Cimzia plus MTX than placebo plus MTX throughout the study. At week 1, mean changes from baseline in fatigue assessment scale (FAS) were -1.3 and -1.2 for the Cimzia 200mg and 400mg plus MTX compared with -0.5 for the placebo plus MTX group and by the end of the study (week 52), mean changes from baseline were -2.6, -2.5 and -0.8, respectively. At week 52, 48.9% and 48.6% of Cimzia 200mg and
400mg-treated patients reported clinically significant reductions in fatigue compared with only 12.6% of placebo-treated patients.

Statistically significant improvements in physical function as assessed by HAQ-DI were also reported by Cimzia treated patients. By the end of study at week 52, mean scores were 1.1 for both treatment groups, compared with baseline scores of 1.7. Significantly more Cimzia plus MTX-treated patients than placebo plus MTX-treated patients reported clinically meaningful HAQ-DI improvements throughout the trial.

Cimzia treated patients also reported significant improvements from baseline in pain (as measured by the visual analogue scale) and global assessment of disease activity evident at week 1 and sustained through week 52. Significantly more Cimzia plus MTX-treated patients than placebo plus MTX-treated patients reported clinically meaningful reductions in pain and improvements in global assessment of disease activity throughout the trial.

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IMPORTANT SAFETY INFORMATION

Risk of Serious Infections and Malignancy

Patients treated with CIMZIA are at an increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. CIMZIA should be discontinued if a patient develops a serious infection or sepsis. Reported infections include:

- Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before CIMZIA use and during therapy. Treatment for latent infection should be initiated prior to CIMZIA use.
- Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.
- Bacterial, viral and other infections due to opportunistic pathogens.

The risks and benefits of treatment with CIMZIA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with CIMZIA, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA is a member. CIMZIA is not indicated for use in pediatric patients.

Serious and sometimes fatal infection due to bacterial, mycobacterial, invasive fungal, viral or other opportunistic pathogens has been reported in patients receiving TNF-blocking agents. Among opportunistic infections, tuberculosis, histoplasmosis, aspergillosis, candidiasis, coccidioidomycosis, listeriosis, and pneumocystosis were the most common. Treatment with CIMZIA should not be initiated in patients with an active infection, including clinically important localized infections. CIMZIA should be discontinued if a patient develops a serious infection or sepsis. Patients who develop a new infection during treatment with CIMZIA should be closely monitored, undergo a prompt and complete diagnostic workup appropriate for immunocompromised patients, and appropriate antimicrobial therapy should be initiated. Appropriate empiric antifungal therapy should also be considered while a diagnostic workup is performed for patients who develop a serious systemic illness and reside or travel in regions where mycoses are endemic.

Malignancies

During controlled and open-labeled portions of CIMZIA studies of Crohn’s disease and other diseases, malignancies (excluding non-melanoma skin cancer) were observed at a rate of 0.5 per 100 patient-years among 4,650 CIMZIA-treated patients versus a rate of 0.6 per 100 patient-years among 1,319 placebo-treated patients.
In studies of CIMZIA for Crohn’s disease and other investigational uses, there was one case of lymphoma among 2,657 CIMZIA-treated patients and one case of Hodgkin lymphoma among 1,319 placebo-treated patients. In CIMZIA RA clinical trials (placebo-controlled and open label) a total of three cases of lymphoma were observed among 2,367 patients. This is approximately 2-fold higher than expected in the general population. Patients with RA, particularly those with highly active disease, are at a higher risk for the development of lymphoma. The potential role of TNF blocker therapy in the development of malignancies is not known.

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blocking agents (initiation of therapy ≤18 years of age), of which CIMZIA is a member. Approximately half of the cases were lymphoma (including Hodgkin's and non-Hodgkin's lymphoma, while the other cases represented a variety of different malignancies and included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

Cases of acute and chronic leukemia have been reported with TNF-blocker use. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for developing leukemia.

Heart Failure
Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. CIMZIA has not been formally studied in patients with CHF. Exercise caution when using CIMZIA in patients who have heart failure and monitor them carefully.

Hypersensitivity
Symptoms compatible with hypersensitivity reactions, including angioedema, dyspnea, hypotension, rash, serum sickness, and urticaria, have been reported rarely following CIMZIA administration. If such reactions occur, discontinue further administration of CIMZIA and institute appropriate therapy.

Hepatitis B Reactivation
Use of TNF blockers, including CIMZIA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. Some cases have been fatal. Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating CIMZIA therapy. Exercise caution in prescribing CIMZIA for patients identified as carriers of HBV, with careful evaluation and monitoring prior to and during treatment. In patients who develop HBV reactivation, discontinue CIMZIA and initiate effective anti-viral therapy with appropriate supportive treatment.

Neurologic Reactions
Use of TNF blockers, including CIMZIA, has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of demyelinating disease. Rare cases of neurological disorders, including seizure disorder, optic neuritis, and peripheral neuropathy have been reported in patients treated with CIMZIA. Exercise caution in considering the use of CIMZIA in patients with these disorders.

Hematologic Reactions
Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia (e.g., leukopenia, pancytopenia, thrombocytopenia) has 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 hematologic abnormalities.

Drug Interactions
An increased risk of serious infections has been seen in clinical trials of other TNF blocking agents used in combination with anakinra or abatacept. Formal drug interaction studies have not been performed with rituximab or natalizumab; however because of the nature of the adverse events seen with these combinations with TNF blocker therapy, similar toxicities may also result from the use of CIMZIA in these combinations. Therefore, the combination of CIMZIA with anakinra, abatacept, rituximab, or natalizumab is not recommended. Interference with certain coagulation assays has been detected in patients treated with CIMZIA. There is no evidence that CIMZIA therapy has an effect on in vivo coagulation. CIMZIA may cause erroneously elevated aPTT assay results in patients without coagulation abnormalities.

Autoimmunity
Treatment with CIMZIA may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. Discontinue treatment if symptoms of lupus-like syndrome develop.

Immunizations
Do not administer live vaccines or attenuated vaccines concurrently with CIMZIA.

Adverse Reactions
In controlled Crohn’s clinical trials, the most common adverse events that occurred in ≥5% of CIMZIA patients (n=620) and more frequently than with placebo (n=614) were upper respiratory infection (20% CIMZIA, 13% placebo), urinary tract infection (7% CIMZIA, 6% placebo), and arthralgia (6% CIMZIA, 4% placebo). The
proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 8% for CIMZIA and 7% for placebo.

In controlled RA clinical trials, the most common adverse events that occurred in ≥ 3% of patients taking CIMZIA 200 mg every other week with concomitant methotrexate (n=640) and more frequently than with placebo with concomitant methotrexate (n=324) were upper respiratory tract infection (6% CIMZIA, 2% placebo), headache (5% CIMZIA, 4% placebo), hypertension (5% CIMZIA, 2% placebo), nasopharyngitis (5% CIMZIA, 1% placebo), back pain (4% CIMZIA, 1% placebo), pyrexia (3% CIMZIA, 2% placebo), pharyngitis (3% CIMZIA, 1% placebo), rash (3% CIMZIA, 1% placebo), acute bronchitis (3% CIMZIA,1% placebo), fatigue (3% CIMZIA, 1% placebo). Hypertensive adverse reactions were observed more frequently in patients receiving CIMZIA than in controls. These adverse reactions occurred more frequently among patients with a baseline history of hypertension and among patients receiving concomitant corticosteroids and non-steroidal anti-inflammatory drugs. Patients receiving CIMZIA 400mg as monotherapy every 4 weeks in RA controlled clinical trials had similar adverse reactions to those patients receiving CIMZIA 200mg every other week. The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 5% for CIMZIA and 2.5% for placebo.

Please see full prescribing information at www.cimzia.com/pi.aspx

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 RAPID 1
RAPID 1 is a Phase III double-blind placebo-controlled trial, involving 982 adults, that 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. Significantly more patients in the certolizumab pegol 200 mg and 400 mg groups achieved an ACR20 response versus placebo (p ≤ 0.001); rates at Week 24 were 58.8%, 60.8%, and 13.6%, respectively, and remained significant at Week 52 (p ≤ 0.001). Certolizumab pegol 200 mg and 400 mg also significantly inhibited radiographic progression; mean changes from baseline in mTSS at Week 52 were 0.4 and 0.2, respectively, versus 2.8 for placebo (rank analysis p ≤ 0.001). Certolizumab pegol treated patients reported rapid, significant and clinically meaningful improvements in physical function versus placebo (p ≤ 0.001).

All patient-reported outcomes assessed in the RAPID 1 trial were secondary endpoints. These PROs included evaluations of concepts such as HRQoL, fatigue and the patient-reported components of the ACR core set criteria (physical function, arthritis pain and patient’s global assessment of disease activity). HRQoL was assessed using the Short-Form 36-Items (SF-36) health survey. Fatigue (weariness, tiredness) was evaluated using the Fatigue Assessment Scale (FAS), a numeric rating scale (NRS) from 0 to 10 with higher scores indicating greater fatigue. Physical function was assessed by the Health Assessment Questionnaire-Disability Index (HAQ-DI), evaluating eight activities of daily living. Patient’s arthritis pain and patient’s global assessment of disease activity (PtGA) were evaluated using visual analog scales (VAS).

Short-Form 36 –Items (SF-36)
A health survey measurement to assess eight domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health, scored 0 to 100, with higher scores indicating better HRQoL.
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 approximately 10,000 people in over 40 countries, UCB generated revenue of EUR 3.6 billion in 2008. 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.

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