Axial spondyloarthritis patients treated with certolizumab pegol reported improvements in pain, fatigue and physical function, and increased workplace and household productivity

- **RAPID™-axSpA study highlights burden of axial spondyloarthritis (axSpA) and a similarly high burden for ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) patients**
- **Patients with axSpA reported a high burden on workplace and household productivity with on average >1 week of paid work and 2-3 weeks of household duties or social activities affected per month, at study baseline**
- **AS and nr-axSpA patients treated with certolizumab pegol reported rapid improvements in pain, fatigue and physical function vs. placebo**
- **AS and nr-axSpA patients treated with certolizumab pegol reported improvements in workplace and household productivity, as well as increased participation in social and daily activities vs. placebo**
- **Certolizumab pegol is not approved for the treatment of axSpA. UCB filed certolizumab pegol with global regulatory authorities earlier this year for the treatment of active axSpA**

**Slough (UK), June 14th 2013,** – UCB today announced new data from the RAPID™-axSpA study showing that the disease burden of axial spondyloarthritis (axSpA) on household and workplace productivity was high at study baseline as reported by the overall study population, with a similarly high burden reported by patients with ankylosing spondylitis (AS) and axSpA without definitive radiographic evidence of AS (nr-axSpA). The data was presented at the European League Against Rheumatism (EULAR) 2013 Congress in Madrid, Spain.

AxSpA is a form of spondyloarthritis that affects mainly the spine and sacroiliac joints, and includes both AS and nr-axSpA patients. Data from the phase 3 study showed that certolizumab pegol rapidly improved multiple patient reported outcomes such as total back pain and fatigue vs. placebo with similar improvements in both AS and nr-axSpA populations. Patients treated with certolizumab pegol also reported improved workplace and household productivity and increased participation in social and daily activities vs. placebo with similar improvements in both AS and nr-axSpA patients.

"RAPID™-axSpA is the first Phase 3 study of an anti-TNF to include axSpA patients both with and without radiographic evidence of structural damage to the sacroiliac joints," said Professor Désirée van der Heijde, Professor of Rheumatology at Leiden University Medical Center, the Netherlands. "The baseline study results show that axSpA patients who do not have radiographic structural damage have a similar burden of disease as AS patients. There is a need for effective treatments to help prevent work losses and days missed from
family, social and leisure activities to reduce the individual and economic burden of the disease.”

The RAPID™-axSpA study is an ongoing Phase 3, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of certolizumab pegol in patients with active axSpA. Patients (n=325) were randomized 1:1:1 to placebo, or 400 mg certolizumab pegol at week 0, 2 and 4 loading dose followed by either 200 mg certolizumab pegol every two weeks or 400 mg certolizumab pegol every four weeks. The primary endpoint of the RAPID™-axSpA study was ASAS20 at week 12 and clinical improvements in ASAS20 responses were statistically significant in both dosing arms vs. placebo (p<0.05). Adverse events (AEs) occurred in 70.4% of certolizumab pegol (combined dose) treated patients vs 62.6% for placebo, with serious AEs occurring in 4.7% vs 4.7% and serious infections in 1.1% vs 0%.

Abstract title: High economic burden of axial spondyloarthritis related to paid work and household productivity at baseline in the RAPID-axSpA study: differences and similarities between ankylosing spondylitis and non-radiographic axial spondyloarthritis

At baseline 69.2% of axSpA patients, 67.4% of AS patients and 71.4% of nr-axSpA patients were employed outside the home. A high burden of axSpA on workplace and household productivity was reported with a similarly high burden of disease in AS and nr-axSpA sub-populations.

On average, at study baseline, patients reported that axSpA affected more than one week of paid work and 2-3 weeks of household duties or social activities over the previous month. Household productivity losses were 2-3 times higher in non-employed and disease work-disabled patients compared to employed patients. At study baseline 39.1% of the axSpA patients reported that they needed regular assistance from relatives, friends or paid caregivers in their usual activities (42.1% in AS vs. 35.4% in nr-axSpA). These patients also reported higher losses at workplace and within the household compared to those who did not require regular assistance.

Abstract title: Rapid improvements in patient-reported outcomes with certolizumab pegol in patients with axial spondyloarthritis, including ankylosing spondylitis: 24-week results of RAPID-axSpA study

Both dosing regimens of certolizumab pegol rapidly improved patient-reported outcomes (total back pain, fatigue, physical function, ankylosing spondylitis quality of life) in the axSpA study population vs. placebo (week 24 mean change from baseline; p < 0.05). Spinal pain was improved as early as day 2 after initiation of certolizumab pegol compared to placebo.

Improvements in total back pain, fatigue and quality of life were similar in nr-axSpA and AS patients treated with both dosing regimens of certolizumab pegol vs. placebo (p<0.05). In patients treated with certolizumab pegol, improvements in physical function and sleep were greater in patients with nr-axSpA than AS compared with placebo, and nr-axSpA patients were more likely to reach population norms for SF-36.

Abstract title: Improvements in work and household productivity after 24 weeks of certolizumab pegol in treatment of axial spondyloarthritis patients, including patients with ankylosing spondylitis: results of RAPID-axSpA study

Compared to placebo, employed patients treated with certolizumab pegol reported less work days lost per month with improvements reported as early as week 4 and maintained to week 24 (mean 2.3 days at baseline (BL) and 1.1 at week 24 for 200 mg certolizumab pegol every 2 weeks, 1.4 days at BL and 0.6 at week 24 for 400 mg certolizumab pegol every 4 weeks vs. 2.4 days at BL and 2.0 at week 24 for placebo). Patients in both
certolizumab pegol arms also reported less work days with reduced productivity per month from week 4 to week 24.

Compared to placebo, patients treated with certolizumab pegol reported fewer days missed of household work per month with improvements reported as early as week 4 and maintained to week 24 (mean 5.8 days at BL and 2.3 at week 24 for 200 mg certolizumab pegol every 2 weeks, 4.7 days at BL and 2.2 at week 24 for 400 mg certolizumab pegol every 4 weeks vs 6.9 days at BL and 5.6 at week 24 for placebo). Patients also reported fewer days missed of family/social/leisure activities per month (mean 4.4 days missed at BL and 1.1 at week 24 for 200 mg certolizumab pegol every 2 weeks, 3.6 days missed at BL and 1.9 at week 24 for 400 mg certolizumab pegol every 4 weeks vs. 5.3 days missed at BL and 3.0 at week 24 for placebo).

Similar improvements with certolizumab pegol were reported in the AS and nr-axSpA populations.

In the EU, certolizumab pegol in combination with methotrexate (MTX) is approved for the treatment of moderate to severe active rheumatoid arthritis in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs including MTX. Certolizumab pegol can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. 

Certolizumab pegol is not approved for the treatment of axSpA. In February 2013, UCB filed with the EU regulatory authorities to extend the marketing authorization for certolizumab pegol to the treatment of active axSpA.
**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. 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. 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.

**Cimzia® (certolizumab pegol) EU/EEA Important Safety Information**

Cimzia® was studied in 4,049 patients with 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 (including herpes, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthenia, leucopaenia (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, pancytopenia, 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.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision 25th April 2013.


References

1. van der Heijde, D., Purcaru, O., Kavanaugh, A. High economic burden of axial spondyloarthritis related to paid work and household productivity at baseline in the RAPID-axSpA study: differences and similarities between ankylosing spondylitis and non-radiographic axial spondyloarthritis. Presented at the European League Against Rheumatism (EULAR) 2013 Congress. Abstract # FR10439.


3. van der Heijde, D., Braun, J., Rudwaleit, M. et al. Improvements in work and household productivity after 24 weeks of certolizumab pegol in treatment of axial spondyloarthritis patients, including patients with ankylosing spondylitis: results of RAPID-axSpA study. European League Against Rheumatism (EULAR) 2013 Congress. Abstract # OP0107


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About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With 9000 people in approximately 40 countries, the company generated revenue of EUR 3.4 billion in 2012. 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. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially 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, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.

Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical