# Astellas and UCB announce approval of Cimzia® (certolizumab pegol) in Japan for the treatment of adult patients with rheumatoid arthritis

**Tokyo, Japan and Brussels, Belgium, 25th December, 2012 –** Astellas Pharma Inc. ("Astellas";Tokyo:4503; President and CEO: Yoshihiko Hatanaka) and UCB S.A. ("UCB"; Brussels, Belgium, CEO: Roch Doliveux, "UCB Japan": Tokyo, Japan, President and Representative Director: Joel Peterson) today announced that UCB Japan has received marketing approval from the Japanese Ministry of Health, Labor and Welfare (MHLW) for Cimzia® (INN;certolizumab pegol). Cimzia®, under joint development in Japan, has been approved as a 200 mg syringe for subcutaneous (s.c) injection for the treatment of adult patients with rheumatoid arthritis (RA) who have had an inadequate response to conventional treatment (including inhibition of progression of bone structural damage).[1]

Cimzia® is the only PEGylated Fc-free anti-TNF. In Japanese clinical trials, improvements in the signs and symptoms of rheumatoid arthritis were observed in adult patients one week after administration of certolizumab pegol with or without methotrexate (MTX), in accordance with the criteria of the American College of Rheumatology.[2,3] Improvements were also observed in physical function as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI) criteria.[2,3] The progression of joint damage, as measured by change in Van der Heijde modified Total Sharpe Score (mTSS), was inhibited by certolizumab pegol when given with and without MTX.[2,3] The safety profile of certolizumab pegol in the Japanese clinical trials was consistent with the safety profile reported in previous studies of certolizumab pegol in rheumatoid arthritis.[4]

Certolizumab pegol is designed in the form of a prefilled syringe to facilitate self-administration by RA patients, once trained by their healthcare professional. For adult patients 400 mg s.c. should be administered at Weeks 0, 2, and 4, followed by 200 mg every 2 weeks. For maintenance dosing, 400mg every 4 weeks s.c. can be considered.[1]

Certolizumab pegol is currently commercialized in over 30 countries in such regions as Europe and the United States.[5] In January 2012 Astellas and UCB entered into the agreement to jointly develop and commercialize certolizumab pegol for rheumatoid arthritis in Japan. Under the terms of this agreement UCB will manufacture and supply the product for commercialization and Astellas will exclusively manage distribution and sales. In January 2012, UCB Japan filed an application for marketing approval for certolizumab pegol in Japan. Astellas will make a payment to UCB for the marketing authorization milestone which has already been included in the full-year business forecasts for the current fiscal year (ending March 2013 for Astellas).

Astellas and UCB believe that by launching certolizumab pegol in the Japanese market they will be able to provide RA patients with a new treatment option and contribute further to treatment of the disease.

**Product Summary**

| | |
|---|---|
| Product name: | Cimzia® 200 mg Syringe for S.C. Injection |
| Generic name: | Certolizumab Pegol |
| Indication: | Treatment of rheumatoid arthritis not responding to conventional therapy (including inhibition of progression of bone structural damage) |
| Dosage regimen: | Usually, for adult patients, Certolizumab pegol should be administered subcutaneously at 400 mg at Weeks 0, 2, and 4, followed by 200 mg every 2 weeks. For maintenance dosing, 400mg every 4 weeks s.c. can be considered. |

**About RA**

RA is a progressive disease which causes chronic inflammation of the joints.[6] It generally affects joints in the body such as hands, wrists, feet and ankles, however the systemic nature of the condition means that it can also affect the body as a whole, including internal organs and the vascular system.[6,7] It is estimated that 0.65 million people live with RA in Japan and over 23 million globally.[8,9] Prevalence is not split evenly between genders, since women are three times more likely to be affected than men.[7] Although RA can affect people of all ages, the onset of the disease usually occurs between 40-60 years of age.[7]

**About CIMZIA® in the EU**

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) in EU/ 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 and nausea. 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 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 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 hematological 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 June 2012.

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

**References**


1. Cimzia® Japanese Prescribing Information
2. Yamamoto K, Takeuchi T, Yamanaka H et al. Efficacy and Safety of Certolizumab Pegol Plus Methotrexate in Japanese Rheumatoid Arthritis Patients With an Inadequate Response to Methotrexate. 2011 American College of Rheumatology annual meeting. Poster #1218
3. Yamamoto K, Takeuchi T, Yamanaka H et al. Efficacy and Safety of Certolizumab Pegol Without Methotrexate Co-Administration in Japanese Patients With Active Rheumatoid Arthritis. 2011 American College of Rheumatology annual meeting. Poster #1220
4. UCB data on file
5. UCB data on file
6. Ruderman E and Tambar S. (2012) Rheumatoid Arthritis. *American College of Rheumatology*. Available at http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.pdf#toolbar=1. Accessed November 2012.
7. Panayi G. (03 October 2011) What is RA? *National Rheumatoid Arthritis Society*. Available at http://www.nras.org.uk/about_rheumatoid_arthritis/what_is_ra/what_is_ra.aspx. Accessed November 2012.
8. Miyasaka N, Rheumatoid Arthritis; Internal Medicine 9th Edition generally edited by Tsuneaki, S, Yazaki, Y, Asakura Publishing, Co., Ltd., 1053-1057.
9. Mathers C, Doris MF, Boerma JT. The global burden of disease: 2004 update. World Health Organization, 2008. Available at http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html. Accessed November 2012.



***For further information UCB***

*Eimear O Brien, Director, Brand Communications*

*T +32.2.559.9271, eimear.obrien@ucb.com*

*Antje Witte, Investor Relations UCB*
*T +32.2.559.9414, antje.witte@ucb.com*

*France Nivelle, Global Communications, UCB*
*T +32.2.559.9178, france.nivelle@ucb.com*

*Laurent Schots, Media Relations, UCB*

*T +32.2.559.9264, laurent.schots@ucb.com*

***For further information Astellas Pharma Inc.***

*Corporate Communications, Astellas Pharma Inc.*

*Tel: +81-3-3244-3201*

*Fax: +81-3-5201-7473*

*http://www.astellas.com/en/*


***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 more than 8 500 people in about 40 countries, the company generated revenue of EUR 3.2 billion in 2011. UCB is listed on Euronext Brussels (symbol: UCB).*

***About Astellas Pharma Inc.***

*Astellas Pharma Inc., located in Tokyo, Japan, is a pharmaceutical company dedicated to improvingthe health of people around the world through the provision of innovative and reliable pharmaceutical products. Astellas has approximately 17,000 employees worldwide. The organization is committed to becoming a global category leader in Urology, Immunology (including Transplantation) and Infectious Diseases, Oncology, Neuroscience and Diabetes DM Complications and Kidney Diseases. For more information on Astellas Pharma Inc., please visit the company Website at www.astellas.com/en.*

***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 pricing and reimbursement.*