UCB Announces Filing Acceptance with the China Food and Drug Administration for CIMZIA® (certolizumab pegol) for the Treatment of Moderate-to-Severe Rheumatoid Arthritis

Brussels, Belgium – 30 March, 7:00 CEST – UCB, a global biopharmaceutical company, today announced the submission of an application for an Import Drug License to the Chinese Food and Drug Administration (CFDA) for the approval of CIMZIA® (certolizumab pegol) to treat moderate-to-severe rheumatoid arthritis (RA). The submission is based on results from two Phase 3 clinical trials, RAPID-C and RAPID-C open-label extension (OLE), which evaluated the efficacy and safety of CIMZIA plus methotrexate (MTX) in Chinese adults with moderate-to-severe active rheumatoid arthritis who had previously experienced inadequate response to MTX. Results concluded that patients experienced greater improvement in relief of the signs and symptoms of RA when CIMZIA was used in combination with MTX, compared with MTX alone.[i]

While rheumatic diseases are typically less common in Asia than in other parts of the world, RA has a prevalence of 0.41% in China (0.69% in women and 0.11% in men), indicating a need for effective treatment options.[ii] The results of the RAPID-C and RAPID-C OLE trials demonstrate the potential value of CIMZIA for Chinese patients.[iii] In addition, due to its unique Fc-free molecular structure, CIMZIA is the only anti-TNF that has robust evidence from conception to late pregnancy and lactation.[iv]

“This submission reflects UCB’s commitment to bringing our innovative scientific research and treatment solutions to patients with challenging chronic inflammatory diseases like rheumatoid arthritis who are in need. The research we have conducted to support this submission represents a focused approach to identifying options for Chinese patients, whose special treatment needs have not always been thoroughly understood. Combined with our commitment to research and improving patient experience in China and across the globe, today is an important step forward for the treatment of this debilitating condition,” said Emmanuel Caeymaex, Executive Vice President, Immunology Patient Value Unit, UCB.

About RAPID-C
The RAPID-C study enrolled 430 patients, including patients both with and without prior treatment experience with biologic products. Patients were randomized to either 400 mg at weeks 0, 2, and 4 followed by 200 mg every two weeks, or placebo every two weeks. CIMZIA demonstrated statistically significant improvements in the primary endpoint compared to placebo. The primary endpoint was the percentage of patients who achieved a 20% or greater disease improvement from baseline as measured by the American College of Rheumatology response (ACR20) at week 24. Additionally, all secondary endpoint analyses supported the primary results. The secondary endpoints included ACR50 and ACR70 response at week 24, as well as change from Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 24.

About RAPID-C OLE
The RAPID-C OLE study continued to assess the safety, tolerability, and efficacy of CIMZIA as additional medication to methotrexate (MTX) in Chinese patients from the RAPID-C study through week 52. Primary endpoints focused on the percentage of patients who experienced treatment-emergent adverse events (TEAE) or serious treatment-emergent serious events (SAE). The improvements observed during the RAPID-C study were maintained through 52 weeks of CIMZIA treatment. Overall, the safety profile in Chinese RA patients is consistent with that observed in

previous studies with CIMZIA and the RA indication, and in line with that expected in patients receiving anti-TNFα therapy.

This submission was also supported by the Phase 1 RA0045 clinical trial evaluating the pharmacokinetics and safety of CIMZIA in healthy Chinese subjects.

CIMZIA is not currently marketed in China.

About CIMZIA® in the EU/EEA
In the EU, CIMZIA® in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs (DMARDs) including MTX.

CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. CIMZIA in combination with MTX is also indicated for the treatment of severe, active and progressive RA in adults not previously treated with MTX or other DMARDs. CIMZIA has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function, when given in combination with MTX.

CIMZIA, in combination with MTX, is also indicated for the treatment of active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate. CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate.

CIMZIA is also indicated in the EU for the treatment of adult patients with severe active axial spondyloarthritis (axSpA), comprising:

- Ankylosing spondylitis (AS) – adults with severe active AS who have had an inadequate response to, or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).
- Axial spondyloarthritis (axSpA) without radiographic evidence of AS – adults with severe active axSpA without radiographic evidence of AS but with objective signs of inflammation by elevated C-reactive protein (CRP) and/or Magnetic Resonance Imaging (MRI) who have had an inadequate response to, or are intolerant to NSAIDs.

Important Safety Information about CIMZIA® in the EU/EEA
CIMZIA® was studied in 4,049 patients with rheumatoid arthritis (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 (includes herpes, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthaenia, leukopaenia (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, pancytopaenia, 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 haematologic 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.

CIMZIA® was studied in 325 patients with active axial spondyloarthritis (axSpA) in a placebo-controlled clinical trial for up to 30 months and in 409 patients with psoriatic arthritis (PsA) in a placebo-controlled clinical trial for up to 30 months. The safety profile for axSpA and PsA patients treated with CIMZIA® was consistent with the safety profile in RA and previous experience with CIMZIA®.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision December 2017.

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

CIMZIA® is a registered trademark of the UCB Group of Companies.

For further information, UCB:

Corporate Communications	Investor Relations	Brand Communications
France Nivelle, Global Communications, UCB T +32.2.559.9178, france.nivelle@ucb.com	Antje Witte, Investor Relations, UCB T +32.2.559.94.14, antje.witte@ucb.com	Andrea Levin Christopher, Immunology Communications, UCB T +1.404.483.7329 andrea.christopher@ucb.com
Laurent Schots, Media Relations, UCB T +32.2.559.92.64, laurent.schots@ucb.com	Isabelle Ghellynck T +32.2.559.9588 Isabelle.Ghellynck@ucb.com	

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 in immunology or neurology. With more than 7 500 people in approximately 40 countries, the company generated revenue of € 4.5 billion in 2017. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

Forward looking statements - UCB

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.

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[ii]RAPID-C OLE. Clinical Study Report. Data on File. UCB. 2018.
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[iv] Clowse ME, Förger F, Hawng C, et al. Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study. Ann Rheum Dis. 2017;0:1–7.