



New Data Showcases the Value of CIMZIA® (certolizumab pegol) in Patients with Psoriasis

- 96-week safety data from Phase 3 CIMPASI-1, CIMPASI-2 and CIMPACT studies confirm positive long-term safety profile of CIMZIA® (certolizumab pegol) in moderate-to-severe plaque psoriasis
- First presentation of nail disease data from Phase 3 psoriasis studies demonstrate that 66.2% of patients achieved total resolution of nail disease at week 48
- Dose escalation or continued treatment with 400mg of CIMZIA every two weeks were shown to be effective treatment strategies for psoriasis patients who do not adequately respond to initial treatment

Brussels, Belgium – 25 April 2019 – UCB, a global biopharmaceutical company, today announced new data supporting the long-term safety of CIMZIA® (certolizumab pegol), the only Fc-free, PEGylated anti-Tumor Necrosis Factor (TNF), in patients with moderate-to-severe plaque psoriasis, and new efficacy data for patients who show signs of psoriasis-related nail disease and those who had an inadequate early treatment response to CIMZIA. These findings are being presented at the 6th Congress of the Skin Inflammation & Psoriasis International Network (SPIN), in Paris, April 25-27, 2019.

“This new research demonstrates UCB’s ongoing commitment to delivering meaningful outcomes for psoriasis patients, where there is still significant unmet need. This includes patients with psoriatic nail disease and those who do not initially adequately respond to their treatment dose. The multitude of evidence from these ongoing trials complements data from across all areas of chronic inflammatory diseases to show the value of CIMZIA in treating different patient populations,” said Emmanuel Caeymaex, Head of Immunology and Executive Vice President at UCB.

Results include pooled 96-week safety data from the ongoing Phase 3 CIMZIA psoriasis trials, CIMPASI-1, CIMPASI-2 and CIMPACT,^{i,ii} confirming the long-term safety of CIMZIA in the treatment of psoriasis.ⁱⁱⁱ In the 995 patients treated with at least one dose of CIMZIA for up to 96 weeks, no new safety signals were observed and the safety profile was consistent with other anti-TNFs in psoriasis.ⁱⁱⁱ The overall incidence of adverse events of interest was low; observed incidence rates of adverse events after 16 weeks were comparable for CIMZIA and placebo and risk for adverse events did not appear to increase with longer exposure to CIMZIA up to 96 weeks.ⁱⁱⁱ

The impact of CIMZIA on nail disease in psoriasis patients was presented for the first time at SPIN.^{iv} While CIMZIA use in psoriatic arthritis (PsA) has demonstrated to be efficacious in nail disease,^v nail outcomes for CIMZIA in psoriasis have not previously been reported. Pooled 48-week data from CIMPASI-1 and CIMPASI-2 Phase 3 trials showed total nail disease resolution for approximately two-thirds (66.2%, n=133) of psoriasis patients with nail disease.^{iv} Results were consistent for patients on either CIMZIA dose regimen and CIMZIA demonstrated similar efficacy in treating nail disease in psoriasis patients with and without concomitant PsA.^{iv}

Finally, findings from the Phase 3 CIMPACT study demonstrated the efficacy of continued CIMZIA treatment for psoriasis patients who were partial responders (PASI \geq 50<75) or inadequately responded (did not achieve PASI75) in the first 16 weeks of treatment.^{vi} The results showed an important improvement in PASI75, PASI90 and PGA 0/1 response rates during an additional 32 weeks of treatment with 400mg of CIMZIA every two weeks both for patients who increased their dosing regimen from 200mg of CIMZIA or those who remained on the dose regimen of 400mg of CIMZIA every two weeks.^{vi} These data emphasize the importance of finding the right treatment regimen for individual psoriasis patients, and that CIMZIA is a potential effective long-term option for patients that inadequately responded in the first few months of their treatment.^{vi}

About CIMZIA in Psoriasis Safety Analysisⁱⁱⁱ

This new analysis pooled data from across CIMPASI-1, CIMPASI-2 and CIMPACT,^{i,ii} for patients receiving at least one dose of CIMZIA during the first 96 weeks of the studies, including initial, maintenance, and open-label periods. Adverse events were included if they occurred within 10 weeks of the last CIMZIA dose. Incidence rates of adverse events were calculated as incidence of new cases per 100 patient-years. At week 16, 59.8% of patients (n = 692) reported \geq 1 adverse event, including 56.2% and 63.4% of patients who received 200mg of CIMZIA or 400mg of CIMZIA every two weeks, respectively. This was similar to placebo patients, where 61.8% (n = 157) of patients reported \geq 1 adverse event. Risk did not appear to increase with longer exposure. Over 96 weeks, 82.4% of patients (n = 995) reported \geq 1 adverse event, including 70.8% and 74.3% of patients who received 200mg of CIMZIA or 400mg of CIMZIA every two weeks, respectively. These adverse event incidence rates for week 96 are at a lower level than those previously reported for week 48 and week 16.

About CIMZIA in Psoriatic Nail Disease Analysis^{iv}

This analysis included psoriasis patients enrolled in CIMPASI-1, CIMPASI-2 and CIMPACT Phase 3 trials who also had nail disease (modified Nail Psoriasis Severity Index (mNAPSI) score of greater than zero) at baseline.^{i,ii} Presence of concomitant PsA at baseline was self-reported. Resolution of nail disease (mNAPSI=0) and change from baseline (CFB) in mNAPSI were reported at week 48. Of the 133 patients that remained in the study at week 48, 66.2% achieved total resolution of nail disease (mNAPSI=0) with a mean CFB in mNAPSI of -4.4. Similar results were observed in patients with self-reported PsA (mNAPSI=69.0% [n=29]) and without PsA (mNAPSI=65.4% [n=104]).

About CIMZIA in psoriasis Continued Treatment Analysis^{vi}

This study evaluated the efficacy of continued CIMZIA treatment in psoriasis patients enrolled in the CIMPACT Phase 3 trial who showed an inadequate response (did not achieve a 75% improvement from baseline in PASI [PASI75]) after the first 16 weeks.ⁱⁱ At week 16, patients who previously were receiving 200mg or 400mg of CIMZIA every two weeks entered an open-label escape arm and received 400mg of CIMZIA every two weeks for 32 weeks. At week 48, the response rates in the proportion of patients who had an increase in their dose regimen from 200mg to 400mg of CIMZIA every two weeks were PASI75=61.2% (95% CI: 47.6–74.9%), PASI90=36.7% (95% CI: 23.2–50.2%), PGA0/1 (“clear” or almost clear)=46.9% (95% CI: 33.0–60.9%). For

patients who had continued at the 400mg of CIMZIA every two weeks dose regimen, week 48 response rates were PASI75=80.6% (95% CI: 67.6–93.5%), PASI90=44.4% (95% CI: 28.2–60.7%), PGA0/1=55.6% (95% CI: 39.3–71.8%).

About the CIMPASI-1, CIMPASI-2 and CIMPACT Phase 3 trials^{i,ii}

CIMPASI-1, CIMPASI-2 and CIMPACT Phase 3 trials each evaluate the efficacy and safety of CIMZIA in adult patients with moderate-to-severe plaque psoriasis. The three trials enrolled approximately 1,000 patients, including patients with and without prior treatment experience with biologic products. In these trials, adults with moderate-to-severe psoriasis for at least six months (PASI \geq 12, \geq 10% BSA, PGA \geq 3 on a 5-point scale) were randomized to 400mg of CIMZIA every 2 weeks, 200mg of CIMZIA every two weeks (with an initial loading dose of 400mg at week 0, 2 and 4), placebo, or etanercept at 50mg twice weekly (CIMPACT only).

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.

CIMZIA is also indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

About CIMZIA® in Fertility, Pregnancy and Lactation in the EU/EEA

Women of childbearing potential

The use of adequate contraception should be considered for women of childbearing potential. For women planning pregnancy, continued contraception may be considered for 5 months after the last CIMZIA dose due to its elimination rate, but the need for treatment of the woman should also be taken into account (see below).

Pregnancy

Data from more than 500 prospectively collected pregnancies exposed to CIMZIA with known pregnancy outcomes, including more than 400 pregnancies exposed during the first trimester, does not indicate a malformative effect of CIMZIA. However, the available clinical experience is too limited to, with a reasonable certainty, conclude that there is no increased risk associated with CIMZIA administration during pregnancy.

Animal studies using a rodent anti-rat TNF α did not reveal evidence of impaired fertility or harm to the foetus. However, these are insufficient with respect to human reproductive toxicity. Due to its inhibition of TNF α , CIMZIA administered during pregnancy could affect normal immune response in the newborn.

CIMZIA should only be used during pregnancy if clinically needed. Non-clinical studies suggest low or negligible level of placental transfer of a homologue Fab-fragment of certolizumab pegol (no Fc region).

In a clinical study 16 women were treated with certolizumab pegol (200 mg every 2 weeks or 400 mg every 4 weeks) during pregnancy. Certolizumab pegol plasma concentrations measured in 14 infants at birth were Below the Limit of Quantification (BLQ) in 13 samples; one was 0.042 μ g/ml with an infant/mother plasma ratio at birth of 0.09%. At Week 4 and Week 8, all infant concentrations were BLQ. The clinical significance of low levels certolizumab pegol for infants is unknown. It is recommended to wait a minimum of 5 months following the mother's last CIMZIA administration during pregnancy before administration of live or live-attenuated vaccines (e.g. BCG vaccine), unless the benefit of the vaccination clearly outweighs the theoretical risk of administration of live or live-attenuated vaccines to the infants.

Breastfeeding

In a clinical study in 17 lactating women treated with CIMZIA, minimal transfer of certolizumab pegol from plasma to breast milk was observed. The percentage of the maternal certolizumab pegol dose reaching an infant during a 24 hour period was estimated to 0.04% to 0.30%. In addition, since certolizumab pegol is a protein that is degraded in the gastrointestinal tract after oral administration, the absolute bioavailability is expected to be very low in a breastfed infant. Consequently, CIMZIA can be used during breastfeeding.

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 herpeszoster,

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 (including miliary, disseminated and extrapulmonary), 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 and moderate to severe heart failure.

Serious infections including sepsis, tuberculosis and opportunistic infections (e.g. histoplasmosis, nocardia, candidiasis) 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® until the infection is controlled. 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, including multiple sclerosis; 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 cytopenia, have been 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) and in 409 patients with psoriatic arthritis (PsA) for up to 4 years. The safety profile for axSpA and PsA patients treated with Cimzia® was consistent with the safety profile in RA and previous experience with Cimzia®.

Cimzia® was studied in 1112 patients with psoriasis in controlled and open-label studies for up to 18 months. The safety profile of Cimzia® 400 mg every 2 weeks and Cimzia® 200 mg every 2 weeks were generally similar.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision March 2019. https://www.ema.europa.eu/documents/product-information/cimzia-epar-product-information_en.pdf

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For further information, UCB:

Corporate Communications

France Nivelles,
Global Communications, UCB

T +32.2.559.9178,
france.nivelles@ucb.com

Laurent Schots,
Media Relations, UCB
T +32.2.559.92.64,
laurent.schots@ucb.com

Investor Relations

Antje Witte,
Investor Relations, UCB

T +32.2.559.94.14,
antje.witte@ucb.com

Brand Communications

Andrea Levin Christopher,
Immunology Communications, UCB

T +1.404.483.7329
andrea.christopher@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 and neurology. With 7,500 people in approximately 40 countries, the company generated revenue of € 4.6 billion in 2018. 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.

ⁱ Gottlieb AB, Blauvelt A, Thaçi D, *et al.* Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo controlled studies (CIMPASI-1 and CIMPASI-2). *JAAD* 2018;79:302-14.e6. doi:10.1016/j.jaad.2018.04.012

ⁱⁱ Lebwohl M, Blauvelt A, Paul C, *et al.* Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT). *JAAD* 2018;79:266-76.e5. doi:10.1016/j.jaad.2018.04.013

ⁱⁱⁱ Blauvelt A, Strober B, Langley R, *et al.* Safety of Certolizumab Pegol in Plaque Psoriasis: Pooled 96-Week Data from Three Phase 3, Multicenter, Randomized, Placebo-Controlled Studies (CIMPASI-1, CIMPASI-2 and CIMPACT). Abstract presented at SPIN 2019.

^{iv} Gottlieb AB, Thaçi D, Leonardi C, *et al.* Nail Outcome Improvements with Certolizumab Pegol in Moderate to Severe Plaque Psoriasis: Results from Phase 3 Trials. Abstract presented at SPIN 2019.

^v van der Heijde D, Deodhar A, FitzGerald O, *et al.* 4-year results from the RAPID-PsA phase 3 randomised placebo-controlled trial of certolizumab pegol in psoriatic arthritis. *RMD Open* 2018;4:e000582. doi:10.1136/rmdopen-2017-000582

^{vi} Augustin M, Lebwohl M, Piguat V, *et al.* Efficacy of Continued Certolizumab Pegol Treatment in Patients Who Inadequately Respond in the First 16 Weeks: Results from the CIMPACT Trial. Abstract presented at SPIN 2019.