UCB News

Arthritis & Rheumatology Publishes the First Randomized Placebo-Controlled Study Over 52 Weeks in Non-Radiographic Axial Spondyloarthritis Showing Positive Results for CIMZIA® (certolizumab pegol)

- Results from C-AXSPAND, the first 52-week placebo-controlled study in adult patients with non-radiographic axial spondyloarthritis (nr-axSpA), demonstrated the potential impact of CIMZIA® (certolizumab pegol) when added to common background medications
- The study met the primary endpoint, with 47.2% of CIMZIA patients demonstrating major improvement response in Ankylosing Spondylitis Disease Activity Score (ASDAS-MI) at Week 52 versus 7% of placebo patients
- Findings underscore the high disease burden of nr-axSpA and the limitations of the common medications available in the U.S. to control the disease

Brussels, Belgium – 11 March 2019 – UCB, a global biopharmaceutical company, announced detailed findings from the investigational study C-AXSPAND, the Phase 3, multi-center, double-blind, placebo-controlled study conducted over 52 weeks, demonstrating positive results for CIMZIA® (certolizumab pegol) in the treatment of non-radiographic axial spondyloarthritis (nr-axSpA) in patients with objective signs of inflammation despite the use of non-steroidal anti-inflammatory drugs (NSAIDs). Results published in *Arthritis & Rheumatology* reveal the study met its primary endpoint, with 47.2% of patients treated with CIMZIA demonstrating major improvement response in Ankylosing Spondylitis Disease Activity Score (ASDAS-MI) at week 52, compared to 7% of patients treated with placebo. The study also met ASAS40, an important secondary endpoint, with 47% of CIMZIA-treated patients achieving a 40% improvement in Ankylosing Spondylitis Assessment Score (ASAS40) compared to 11.4% of placebo-treated patients at week 12.

Nr-axSpA causes inflammatory back pain, prolonged and severe stiffness, fatigue, sleep disturbances, and reduced physical function for people living with this disease. The C-AXSPAND study was developed with a specific, controlled trial design in patients diagnosed with nr-axSpA with active disease and objective signs of inflammation despite the use of NSAIDs. The study is unique in that it used Ankylosing Spondylitis Disease Activity Score – Major Improvement (ASDAS-MI), a rigorous response threshold, and assessed the long-term efficacy of CIMZIA in a one-year, placebo-controlled trial. The first 52 weeks of the study have been completed and an additional two years of safety follow-up are ongoing. CIMZIA is not currently approved for the treatment of nr-axSpA by the U.S. Food and Drug Administration.

“These findings are particularly revealing because they highlight the importance of disease control for patients living with non-radiographic axial spondyloarthritis, for whom common medications may not adequately control active disease. CIMZIA has the potential to become a valuable option for patients with nr-axSpA and their rheumatologists,” said Emmanuel Caeymaex, Head of Immunology and Executive Vice President at UCB. “We are proud of our leadership in nr-axSpA and of our commitment to our patient value strategy, connecting patients to science to solutions.”

"People living with nr-axSpA experience a significant disease burden, as there are currently no treatment options approved for this patient population in the US. This is a painful, debilitating disease and people frequently go for years without receiving a proper diagnosis and effective treatment. The results from the C-AXSPAND study are uniquely impactful as they show that nr-axSpA does not improve spontaneously and the majority of patients do not typically experience relief with existing medications, such as NSAIDs or analgesics. These data will help inform and evolve the treatment landscape for nr-axSpA," said Dr. Atul Deodhar, MD, MRCP, FACP, FACR, Professor of Medicine, OHSU, and a lead investigator for the study.

To examine the efficacy and safety of CIMZIA in nr-axSpA, the C-AXSPAND Phase 3 trial randomized 317 adult patients to receive either CIMZIA or placebo plus common background medications, which included NSAIDs, corticosteroids, analgesics and slow-acting anti-rheumatic drugs. Clinical response was evaluated with a stringent primary outcome measure used for the first time in a clinical trial, ASDAS-MI, defined as an ASDAS decrease of at least two points from baseline or reaching lowest possible value at week 52. The ASDAS is a composite index to assess patient disease activity in axSpA through objective evidence of systemic inflammation, such as C-reactive protein (CRP), and patient-reported outcomes, such as back pain, duration of morning stiffness, patient global assessment of the disease, and peripheral pain/swelling.[i]

Patients in both the treatment and placebo groups remained on their background therapy for the duration of the study, which could be adjusted at any point. The safety profile was consistent with previous clinical trials of CIMZIA.

These findings were also presented at the American College of Rheumatology/Association of Rheumatology Health Professionals (ACR/ARHP) Annual Meeting on October 22, in Chicago, Illinois.

About Non-Radiographic Axial Spondyloarthritis (nr-axSpA) and Ankylosing Spondylitis (AS)

Non-radiographic axSpA and AS comprise the axial spondyloarthritis, or axSpA, spectrum of disease, which typically starts in patients under 45 years of age. Nr-axSpA and AS share similar symptomology and disease burden. In AS there is a definitive structural damage in the sacroiliac joints detectable by x-ray. In nr-axSpA, there is no definitive radiographic sacroiliitis, though more sensitive magnetic resonance imaging (MRI) testing may detect evidence of active sacroiliitis, visible as inflammation in the sacroiliac joints. Historically, nr-axSpA has not been well-recognized due to a lack of understanding of the disease history, progression, and prognosis, resulting in substantial diagnostic delay. As a result, nr-axSpA is often misdiagnosed and undertreated.

These patients face a significant disease burden whether they have nr-axSpA (i.e., no definitive evidence of sacroiliitis on x-ray) or AS (i.e., definitive evidence of sacroiliitis on x-ray). They often experience substantial inflammatory back pain, prolonged and severe stiffness, fatigue, sleep disturbances, reduced physical function, impaired quality of life, and impaired work and home productivity and social participation.[i]

Limited evidence exists regarding the exact prevalence of axSpA, though it is thought to impact a substantial proportion of the population. Recent data suggest that 0.5% to 1.4% of the adult population have axSpA, similar to the prevalence of rheumatoid arthritis, which is 0.5% to 1.0%.[ii,iii,iv]

About C-AXSPAND

C-AXSPAND is a multi-center, randomized, double-blind, parallel-group, 52-week study of certolizumab pegol (CZP) compared to placebo. The study randomized 317 adult patients with active axSpA without x-ray evidence of ankylosing spondylitis (AS). Patients needed to have objective evidence of inflammatory disease, defined as sacroiliitis on magnetic resonance imaging (MRI) and/or elevated C-reactive protein (CRP) levels. Patients must have had an inadequate response to, have a contraindication to, or have been intolerant to at least two non-steroidal anti-inflammatory drugs (NSAIDs). Inadequate response to an NSAID is defined as lack of response to at least 14 days of continuous NSAID therapy at the highest tolerated dose of the administered NSAID.

The primary objective of C-AXSPAND was to assess the safety and efficacy of CZP on the signs and symptoms of active axSpA in patients without x-ray evidence of AS. The primary endpoint assessed was ASDAS-MI response at Week 52. The secondary objectives of the study were to assess efficacy, safety, and tolerability, and to demonstrate the effect of CZP on health outcomes, disease activity, sacroiliac (SI) joint inflammation through MRI, and changes in concomitant and background medications.

Safety variables assessed in the study were adverse events, vital signs, physical examination, and measurements of laboratory parameters.

About CIMZIA® in the US

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.

CIMZIA® is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis, adults with active psoriatic arthritis (PsA), and adults with active ankylosing spondylitis (AS). CIMZIA is also indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

In addition, it is indicated for reducing signs and symptoms of Crohn's disease (CD) and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy. See important safety information including risk of serious bacterial, viral and fungal infections and tuberculosis below.

Important Safety Information about CIMZIA® in the US

CONTRAINDICATIONS

CIMZIA is contraindicated in patients with a history of hypersensitivity reaction to certolizumab pegol or to any of the excipients. Reactions have included angioedema, anaphylactoid reaction, serum sickness, and urticaria.

SERIOUS INFECTIONS

Patients treated with CIMZIA are at 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.

Discontinue CIMZIA if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before CIMZIA use and during therapy. Initiate treatment for latent TB 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. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

Carefully consider the risks and benefits of treatment with CIMZIA prior to initiating therapy in the following patients: with chronic or recurrent infection; who have been exposed to TB; with a history of opportunistic infection; who resided in or traveled in regions where mycoses are endemic; with underlying conditions that may predispose them to infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with CIMZIA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start CIMZIA during an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- If an infection develops, monitor carefully and initiate appropriate therapy.

MALIGNANCY

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.

- Consider the risks and benefits of CIMZIA treatment prior to initiating or continuing therapy in a patient with known malignancy.
- In clinical trials, more cases of malignancies were observed among CIMZIA-treated patients compared to control patients.
- In CIMZIA clinical trials, there was an approximately 2-fold higher rate of lymphoma than expected in the general U.S. population. Patients with rheumatoid arthritis, particularly those with highly active disease, are at a higher risk of lymphoma than the general population.
- Malignancies, some fatal, have been reported among children, adolescents, and young adults being treated with TNF blockers. Approximately half of the cases were lymphoma, while the rest were other types of malignancies, including rare types associated with immunosuppression and malignancies not usually seen in this patient population.
- Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including CIMZIA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis, and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. Carefully assess the risks and benefits of treating with CIMZIA in these patient types.
- Cases of acute and chronic leukemia were reported with TNF blocker use.

HEART FAILURE

- Worsening and new onset congestive heart failure (CHF) has been reported with TNF blockers. Exercise caution and monitor carefully.

HYPERSENSITIVITY

- Angioedema, anaphylactoid reaction, dyspnea, hypotension, rash, serum sickness, and urticaria have been reported following CIMZIA administration. If a serious allergic reaction occurs, stop CIMZIA and institute appropriate therapy. The needle shield inside the removable cap of the CIMZIA prefilled syringe contains a plastic derivative of natural rubber latex which may cause an allergic reaction in individuals sensitive to latex.

HEPATITIS B VIRUS REACTIVATION

- Use of TNF blockers, including CIMZIA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal.
- Test patients for HBV infection before initiating treatment with CIMZIA.

- Exercise caution in patients who are carriers of HBV and monitor them before and during CIMZIA treatment.
- Discontinue CIMZIA and begin antiviral therapy in patients who develop HBV reactivation. Exercise caution when resuming CIMZIA after HBV treatment.

NEUROLOGIC REACTIONS

- TNF blockers, including CIMZIA, have been associated with rare cases of new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, seizure disorder, optic neuritis, peripheral neuropathy, and Guillain-Barré syndrome.

HEMATOLOGIC REACTIONS

- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia has been infrequently reported with CIMZIA.
- Consider stopping CIMZIA if significant hematologic abnormalities occur.

DRUG INTERACTIONS

- Do not use CIMZIA in combination with other biological DMARDS.

AUTOIMMUNITY

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

IMMUNIZATIONS

- Patients on CIMZIA should not receive live or live-attenuated vaccines.

ADVERSE REACTIONS

- The most common adverse reactions in CIMZIA clinical trials (≥8%) were: upper respiratory infections (18%), rash (9%), and urinary tract infections (8%).

For full prescribing information, please visit www.ucb-usa.com.

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 TNFα 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 TNFα, 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 µg/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 andopen 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, 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 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 cytopaenia, 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® shouldnot 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 July 2018. https://www.ema.europa.eu/documents/product-information/cimzia-epar-product-information_en.pdf

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

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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 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.

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[i] UCB Clinical Study Protocol. PROTOCOL AS0006 (C-AXSPAND) AMENDMENT 4. Data on File.

[ii] Reveille JD (2012): Prevalence of axial spondylarthritis in the United States: estimates from a cross-sectional survey. Arthritis Care Res (Hoboken). 2012 Jun;64(6):905-10. doi: 10.1002/acr.21621. Epub 2012 Jan 24. Accessed at: https://www.ncbi.nlm.nih.gov/pubmed/22275150

[iii] Reveille JD, Weisman MH. (2013): The epidemiology of back pain, axial spondyloarthritis and HLA-B27 in the United States. Am J Med Sci. 2013 Jun;345(6):431-6. Accesed at: https://www.ncbi.nlm.nih.gov/pubmed/23841117

[iv] Strand et al paper (2013) : Prevalence of axial spondyloarthritis in United States rheumatology practices: Assessment of SpondyloArthritis International Society criteria versus rheumatology expert clinical diagnosis. Arthritis Care Res (Hoboken). 2013 Aug;65(8):1299-306. Accessed at: https://www.ncbi.nlm.nih.gov/pubmed/23436774