FOR EMEA MEDICAL AND TRADE MEDIA ONLY (EXCLUDING BENELUX AND UK)

Media Contact:
Kevin Veninga
Phone: +31 61526-8214
kveninga@its.jnj.com

Investor Contacts:
Chris DelOrefice
(732) 524-2955 (office)

Lesley Fishman
(732) 524-3922 (office)

THE EUROPEAN COMMISSION APPROVES EXPANDED USE OF JANSSEN'S STELARA® (USTEKINUMAB) FOR THE TREATMENT OF PAEDIATRIC PATIENTS WITH MODERATE TO SEVERE PLAQUE PSORIASIS

The expanded use of ustekinumab addresses a high unmet need among children with moderate to severe plaque psoriasis, aged 6–11 years old, for whom there are limited biologic treatment options

Beerse, Belgium, 23 January, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that the European Commission (EC) has approved the expanded use of STELARA® (ustekinumab) for the treatment of paediatric patients (ages 6–11) with moderate to severe plaque psoriasis. Ustekinumab was previously approved for use in adolescent and adult patients with plaque psoriasis, aged 12 years and older, and is now the first available biologic treatment in this patient population to selectively address the IL-23/IL-12 pathway, an important therapeutic target for the condition.[1]

In one third of the 14 million cases in Europe, psoriasis begins in childhood.[2,3] Psoriasis is an immune-mediated inflammatory disease that affects the skin,

resulting in areas of red or inflamed skin covered with silvery scales, which are known as plaques.[2] The condition can have a profound, long-term impact on the psychological health and overall quality of life for children.[3,4] The development of paediatric psoriasis is also associated with high incidence of low self-esteem, and it can have long-term ramifications into adulthood and beyond.[5]

"*This latest EC approval is a significant milestone for young children struggling to cope with the symptoms of psoriasis,*" said Lloyd Miller, Vice President, Immunodermatology Disease Area Leader, Janssen Research & Development, LLC. *"We're delighted that this therapy, which has a well-established safety and efficacy profile in adults with plaque psoriasis and other immune diseases, is now expanded to children as young as six who are living with this chronic disease."*

The EC approval is based on results from the Phase 3 CADMUS Jr study, building on the prior Phase 3 CADMUS study, which found ustekinumab improved the signs and symptoms of plaque psoriasis, as well as health-related quality of life (HrQOL), in paediatric patients aged six to 11 years old.[6,7,8,9,10] The primary endpoint was the proportion of patients who achieved a physician's global assessment (PGA) score of Cleared (0) or Minimal (1) at week 12. Secondary endpoints included the proportion of patients achieving improvements in psoriasis area and severity index of ≥75% (PASI 75), ≥90% (PASI 90), and change from baseline in Children's Dermatology Life Quality Index (CDLQI)* at week 12.[8]

In the study, 44 patients (aged 6–11 years) from nine countries were enrolled and treated with at least one injection of ustekinumab. At baseline, the mean duration of psoriasis was 3.5 (standard deviation 2.49) years. At week 12, subjects treated with ustekinumab showed clinically meaningful improvements in their psoriasis and HrQOL. At week 12, 77.3% (95% confidence interval [CI]: 62.2%, 88.5%) achieved PGA 0/1, 84.1% (95% CI: 69.9%, 93.4%) achieved PASI 75, and 63.6% (95% CI: 47.8%, 77.6%) achieved PASI 90. The mean change from baseline in CDLQI was -6.3 (95% CI: -8.29; -4.28, lower is better). All patients were followed for up to 52 weeks after the first administration of ustekinumab. Improvements in

PGA 0/1, PASI 75, PASI 90 and CDLQI were maintained through to week 52 (75.6%, 87.7%, 70.7%, and 58.3%, respectively).[6,7]

Safety data from CADMUS Jr were consistent with the known safety profiles reflected in respective current prescribing information labels and ustekinumab was generally well-tolerated by paediatric patients with plaque psoriasis. Overall, 34 patients had more than one adverse event (AE; [77.3%]) and three had more than one serious AE (6.8%). One patient had a serious infection (mononucleosis), 29 had infections (65.9%), and 12 had infections requiring treatment (27.3%). In general, the AEs and other safety data reported up to one year in two paediatric patient studies (CADMUS and CADMUS Jr) were similar to those seen in previous studies in adults with plaque psoriasis.[6,7,11,12,13]

This marketing authorisation follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), issued on 12 December 2019.

#ENDS#

Key definitions

*The Children's Dermatology Life Quality Index is a 10-item questionnaire designed to measure the impact of any skin disease on the lives of children. A score of 0–1 denotes no impact, whereas a score of ≥19 denotes an extremely large impact. A reduction in this score equates to a reduction in the impact on the life of the child.[14]

About psoriasis

What it is

Psoriasis is an immune-mediated inflammatory disease that manifests on the skin.[15] The most common form of psoriasis is plaque psoriasis, usually resulting in areas of red or inflamed skin covered with silvery scales, which are known as plaques.[16] The inconsistent nature of psoriasis means that even when plaques appear to subside, patients can have ongoing concerns over their return.[15]

Impact

Psoriasis can cause a great physical and psychological burden. Mental health issues are common among people with psoriasis, and the impact it can have on quality of life is comparable to diabetes and cancer.[4] Psoriasis is also associated with several comorbidities including psoriatic arthritis, cardiovascular diseases, metabolic syndrome, chronic obstructive pulmonary disorder (COPD) and osteoporosis.[17] In addition, many individuals are faced with social exclusion, discrimination and stigma because of their disease.[18] Children are a particularly vulnerable patient group, and studies show that psoriasis has a profoundly disruptive effect on forming social relationships and school life.[19]

About the CADMUS programme

CADMUS Jr is a Phase 3, multicentre, open-label study including 44 participants aged 6–11 years, which was initiated following the successful completion of the CADMUS study involving patients aged 12–17 years. The study included a single arm in which patients received one injection of ustekinumab subcutaneously on weeks 0, 4, 16, 28 and 40. The dose of ustekinumab administered was dependant on the weight of the participant, as follows: Participants weighing <60 kg received ustekinumab 0.75 mg/kg; participants weighing ≥60 kg to ≤100 kg received ustekinumab 45 mg; participants weighing >100 kg received ustekinumab 90 mg. Following completion of the week 52 visit, participants who had a beneficial response from ustekinumab treatment, as determined by the investigator, and who had not yet reached the age of 12 years or older in countries where marketing authorisation for ustekinumab has been granted for the treatment of psoriasis in adolescent participants (12–17 years), and who were willing to continue ustekinumab treatment, could enter the long-term extension (LTE) period (from week 56 through week 264) of the study. The study primarily concluded in December 2017 and the LTE period is ongoing.[8]

CADMUS is a Phase 3, multicentre, randomised, double-blind study including 110 participants aged 12–17 years. The study included three arms: the ustekinumab standard dosage arm, the ustekinumab half-standard dosage arm, and the placebo

arm. In the standard dosage arm (0.75 mg/kg, 45 mg, or 90 mg [based on body weight]), patients received one injection of ustekinumab subcutaneously on weeks 0, 4, 16, 28 and 40, and received one placebo injection subcutaneously on weeks 0 and 4 or week 12. In the half-standard dosage arm (0.375 mg/kg, 22.5 mg, or 45 mg [based on body weight]), patients received one injection of ustekinumab subcutaneously on weeks 0, 4, 16, 28 and 40, and received one placebo injection subcutaneously on weeks 0 and 4 or week 12. In the placebo arm, patients received one placebo injection subcutaneously on weeks 0 and 4 or week 12, followed by ustekinumab at half-standard or standard dosage at weeks 12, 16, 28, and 40. The study concluded in January 2014.[9]

The primary endpoint of both studies was the percentage of participants achieving a PGA score of Cleared (0) or Minimal (1) at week 12. Safety data from CADMUS Jr and CADMUS were consistent with the known safety profiles reflected in respective current prescribing information labels, and ustekinumab was generally well-tolerated by paediatric patients with plaque psoriasis. Overall for CADMUS Jr, 34 patients had more than one AE (77.3%) and three had more than one serious AE (6.8%). One patient had a serious infection (mononucleosis), 29 had infections (65.9%), and 12 had infections requiring treatment (27.3%). For CADMUS, 90 patients (81.8%) reported an AE, of which 34.5% reported nasopharyngitis, 12.7% reported an upper respiratory tract infection, and 8.2% reported pharyngitis. 74 (67.3%) reported an infection and two serious infections were reported (pyelonephritis and ear infection). In general, the AEs and other safety data reported up to 1 year in both paediatric patient studies were similar to those seen in studies in adults with plaque psoriasis.[6,7,10,11,12,13]

About STELARA® (ustekinumab)[6]

In the European Union (EU), ustekinumab is approved for the treatment of moderate to severe plaque psoriasis in children and adolescent patients aged six years and older who are inadequately controlled by or are intolerant to other systemic therapies or phototherapies, and is also approved for the treatment of moderate to severe plaque psoriasis in adults who failed to respond to, have a

contraindication to, or are intolerant to other systemic therapies including cyclosporine, methotrexate (MTX) or psoralen plus ultraviolet A. In addition to psoriasis, ustekinumab has also been approved for the treatment of three further immune-mediated conditions in the EU: psoriatic arthritis, Crohn's disease (CD) and ulcerative colitis (UC).

Ustekinumab is approved alone or in combination with MTX for the treatment of active psoriatic arthritis in adult patients when the response to previous non-biological disease-modifying antirheumatic drug therapy has been inadequate. Ustekinumab is also approved for the treatment of adults with moderately to severely active UC who have had an inadequate response with, or lost response to, or were intolerant to either conventional therapy or a biologic, or have medical contraindications to such therapies. Moreover, ustekinumab is approved for the treatment of adult patients with moderate to severe CD who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha antagonist, or have medical contraindications to such therapies.

The Janssen Pharmaceutical Companies of Johnson & Johnson maintain exclusive worldwide marketing rights to STELARA®.

Important safety information[6]

The most common AEs (>5%) in controlled periods of clinical studies with ustekinumab were nasopharyngitis and headache. Most were considered to be mild and did not necessitate discontinuation of study treatment. The most serious adverse reaction that has been reported for ustekinumab is serious hypersensitivity reactions, including anaphylaxis. The overall safety profile is similar for adult patients with psoriasis, psoriatic arthritis, CD and UC.

Please refer to the Summary of Product Characteristics for full prescribing information for ustekinumab:
https://www.ema.europa.eu/en/medicines/human/EPAR/stelara

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com/emea. Follow us at www.twitter.com/JanssenEMEA.

Janssen-Cilag International NV, the marketing authorisation holder for STELARA® in the EU, and Janssen Research & Development, LLC, are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

Cautions concerning forward-looking statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding development and potential availability in the EU of STELARA® (ustekinumab). The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialise, actual results could vary materially from the expectations and projections of Janssen-Cilag International NV, and any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or

regulatory action; changes in behaviour and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended 30 December, 2018, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

# # #

References

[1] Benson J, *et al*. Discovery and mechanism of ustekinumab. *MAbs* 2011;3:535–45.

[2] Ortonne J and Prinz J. Alefacept: A novel and selective biologic agent for the treatment of chronic psoriasis. *Eur J Dermatol* 2004;14:41–5.

[3] Bronckers I, *et al*. Psoriasis in children and adolescents: diagnosis, management and comorbidities. *Paediatr Drugs* 2015;17:373–84.

[4] Bajorek Z, *et al*. The impact of long term conditions on employment and the wider UK economy. *The Work Foundation* 2016. Available at: http://www.theworkfoundation.com/wp-content/uploads/2016/11/397_The-impact-of-long-term-conditions-on-the-economy.pdf. (last accessed January 2020).

[5] Salman A, *et al*. Impact of psoriasis in the quality of life of children, adolescents and their families: a cross-sectional study. *An Bras Dermatol* 2018;93:819–23.

[6] European Medicines Agency. STELARA Summary of product characteristics. 2020. Available at: https://www.medicines.org.uk/emc/product/4413/smpc. (last accessed January 2020).

[7] Phillip S, *et al*. Ustekinumab for the treatment of moderate-to-severe plaque psoriasis in paediatric patients. Presented at Skin Inflammation and Psoriasis International Network (SPIN), Paris, France, 25–27 April 2019 (poster abstract P025).

[8] ClinicalTrials.gov. An efficacy, safety, and pharmacokinetics study of subcutaneously administered ustekinumab in the treatment of moderate to severe chronic plaque psoriasis in pediatric participants greater than or equal to 6 to less than 12 years of age (CADMUS Jr). Identifier NCT02698475. Available at: https://clinicaltrials.gov/ct2/show/NCT02698475. (last accessed January 2020).

[9] ClinicalTrials.gov. A study of the safety and efficacy of ustekinumab in adolescent patients with psoriasis (CADMUS). Identifier NCT01090427. Available at: https://clinicaltrials.gov/ct2/show/NCT01090427. (last accessed January 2020).

[10] Landells I, *et al*. Ustekinumab in adolescent patients age 12 to 17 years with moderate-to-severe plaque psoriasis: Results of the randomized phase 3 CADMUS study. *J Am Acad Dermatol* 2015;43:594–603.

[11] Papp K, *et al*. Safety surveillance for ustekinumab and other psoriasis treatments from the Psoriasis Longitudinal Assessment and Registry (PSOLAR). *J Drugs Dermatol* 2015;14(7):706–14.

[12] Leonardi C, *et al*. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 76-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 1). *Lancet* 2008;371:1665–74.

[13] Papp K, *et al*. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet* 2008;371:1675–84.

[14] Cardiff University School of Medicine. Children's Dermatology Life Quality Index. Available at: https://www.cardiff.ac.uk/medicine/resources/quality-of-life-questionnaires/childrens-dermatology-life-quality-index. (last accessed January 2020).

[15] Clark RA. Resident memory T cells in human health and disease. *Sci Transl Med* 2015;7:269rv1.

[16] British Skin Foundation. Psoriasis. Available at: www.britishskinfoundation.org.uk/SkinInformation/AtoZofSkindisease/Psoriasis.aspx (last accessed January 2020).

[17] Nijsten T and Wakkee M. Complexity of the association between psoriasis and comorbidities. *J Invest Dermatol* 2009;129:1601–3.

[18] World Health Organization. Global Report on Psoriasis. 2016. Available at: apps.who.int/iris/bitstream/10665/204417/1/9789241565189_eng.pdf. (last accessed January 2020).

[19] De Jager M, *et al*. The burden of childhood psoriasis. *Pediatr Dermatol* 2011;28:736–7.