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**European Commission Approves Expanded Use of Janssen’s STELARA®  
(ustekinumab) for the Treatment of Moderately to Severely Active  
Ulcerative Colitis in the European Union**

**BEERSE, BELGIUM, 4 September, 2019** – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today that the European Commission (EC) has approved the expanded use of ustekinumab for the treatment of adults with moderately to severely active ulcerative colitis (UC), who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies.<sup>1</sup> Ustekinumab is the first available biologic treatment to selectively target the IL-12/IL-23 pathway, an important therapeutic target in UC.<sup>2</sup>

*“The devastating impact of ulcerative colitis on the lives of people with this condition is often underestimated. Typically, ulcerative colitis first presents in young adults at a time when they are still in education or starting their careers – often limiting their ability to achieve their personal goals,”* said Professor Silvio Danese\*, Head of the Inflammatory Bowel Diseases Centre at Humanitas Research Hospital, Milan, Italy. *“Whilst there is no cure yet for ulcerative colitis, treatments which can*

*help prevent the flare up of symptoms and allow people to get on with their lives are hugely important. For this reason, the approval of ustekinumab in ulcerative colitis is welcome news and will provide a valuable therapeutic option for both patients and their doctors."*

Affecting 2.6 million people in Europe, UC is a serious, chronic immune-mediated inflammatory disease of the large intestine.<sup>3</sup> Symptoms vary but may include abdominal cramps, bloody diarrhoea and fatigue, which can be painful, embarrassing and debilitating, placing a significant burden on people with the condition.<sup>4,5</sup> For up to two thirds of people with UC, current treatments are not completely successful or complications may arise.<sup>6,7,8,9</sup>

*"Today marks a significant milestone in the treatment of ulcerative colitis," said Jan Wehkamp, MD, Vice President, Gastroenterology Disease Area Leader, Janssen Research & Development, LLC. "Many hundreds of thousands of people in Europe struggle with one of the two types of inflammatory bowel disease – Crohn's disease and ulcerative colitis – and are in urgent need of effective treatment options. Ustekinumab has been available to people with Crohn's disease since it was approved in 2016, and thanks to the patients who enrolled in the UNIFI clinical trial programme and their willingness to participate, we are delighted it will now be available to people with ulcerative colitis, offering them a chance of durable remission and relief from the often painful and debilitating symptoms."*

The EC approval is based on data from the pivotal Phase 3 UNIFI trial programme – a programme that was split into an initial Induction study (UNIFI-I) of at least eight weeks, followed by a Maintenance study (UNIFI-M) of 44 weeks – both of which demonstrated ustekinumab's efficacy as a treatment option for patients with moderately to severely active UC who demonstrated an inadequate response to or were unable to tolerate conventional (i.e. corticosteroids or immunomodulators) or biologic (i.e. one or more tumour necrosis factor [TNF]-alpha antagonists and/or vedolizumab) therapies.<sup>10,11</sup>

Ustekinumab has demonstrated a consistent safety profile in UC where trials show the treatment is well tolerated. In the primary randomised population of the Induction and Maintenance studies, a similar proportion of patients in the ustekinumab and placebo groups experienced adverse events (AE), serious AEs, infections and serious infections through to week 44. During the Induction phase, one death from an oesophageal varices haemorrhage was reported, and no malignancies, opportunistic infections or tuberculosis were reported. During the Maintenance phase, no deaths and two malignancies other than non-melanoma skin cancer (NMSC) were reported (90 mg ustekinumab q8w: colon cancer [n=1]; 90 mg ustekinumab q12w: papillary renal cell carcinoma [n=1]). There was one patient-reported NMSC in the 90 mg ustekinumab q12w group (2 squamous cell carcinoma events).<sup>10,11</sup>

Marketing authorisation follows a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), issued on 25 July 2019.<sup>12</sup> Janssen announced the submission of a supplemental Biologics License Application (sBLA) to the US Food and Drug Administration (FDA) seeking approval of STELARA® (ustekinumab) for the treatment of adults with moderately to severely active ulcerative colitis in December 2018. The review is ongoing.

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\*Professor Danese is a paid consultant for Janssen. He has not been compensated for any media work.

### **About the UNIFI Programme**

UNIFI is a Phase 3 programme, designed to evaluate the safety and efficacy of ustekinumab induction and maintenance dosing for the treatment of moderately to severely active UC in adults who demonstrated an inadequate response to, or were unable to tolerate, conventional (i.e. corticosteroids, immunomodulators) or biologic (i.e. one or more TNF-alpha antagonists and/or vedolizumab) therapies. Both the Induction and Maintenance studies were randomised, double-blind,

placebo-controlled, parallel group, multicentre studies. The Induction study was of at least 8 weeks duration for participants, who were each administered a single IV ustekinumab infusion.<sup>10,11</sup>

Participants achieving clinical response in the Induction study were eligible to enter into the Maintenance study. The Maintenance study was 44 weeks in duration, representing a total treatment duration of 1 year. The primary endpoint of the Induction study was clinical remission at week 8, and the primary endpoint for the Maintenance study was clinical remission at week 44. After completion of the Maintenance study, eligible participants are continuing in a long-term extension study for an additional three years.<sup>10,11</sup>

In the Induction study, for the recommended dose of ustekinumab, 62 percent of patients were found to have achieved clinical response<sup>a</sup> compared with 31 percent of patients receiving placebo ( $p < 0.001$ ) at week 8.<sup>11</sup> As early as week 2 of the study, a higher proportion of patients who received a single IV infusion dose of ustekinumab had no bleeding or achieved normal stool frequency as compared with those randomised to placebo.<sup>1,11</sup> Full results of the Induction study were previously shared during a plenary session at the American College of Gastroenterology Annual Scientific Meeting and in a [press release](#) on 9 October, 2018.<sup>13</sup>

All patients who were randomised into the 44-week Maintenance study were induction responders to IV ustekinumab. Among patients subsequently randomised to receive subcutaneous ustekinumab (q8w or q12w), a significantly greater percentage achieved clinical remission vs initial responders randomised to placebo. The sustained effect of ustekinumab was also observed in those in the ustekinumab q8w and q12w groups compared to placebo (57.4 percent and 48.3 percent respectively, vs 35.4 percent,  $p < 0.001$  and  $p = 0.010$ , respectively), as measured by durable partial Mayo remission<sup>b</sup> (partial Mayo remission at  $\geq 80$  percent of all visits

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<sup>a</sup> Clinical response was defined as a decrease from baseline in the Mayo score by  $\geq 30$  percent and  $\geq 3$  points, with either a decrease from baseline in the rectal bleeding subscore  $\geq 1$  or a rectal bleeding subscore of 0 or 1.

<sup>b</sup> Partial Mayo remission = Mayo score  $\leq 2$ . The partial Mayo score includes stool frequency, rectal bleeding, and physician's global assessment subscores and ranges from 0 to 9.

and at the last visit).<sup>14</sup> Full results of the Maintenance study were previously presented during a plenary session at 14th Congress of the European Crohn's and Colitis Organisation and shared in a [press release](#) on 11 March, 2019.<sup>15</sup>

### **About ulcerative colitis (UC)**

UC affects up to 2.6 million people in Europe.<sup>3</sup> It is a chronic disease of the large intestine, also known as the colon, in which the lining becomes inflamed and develops tiny open sores, or ulcers, that produce pus and mucous. UC is the result of an abnormal response by the body's immune system. Symptoms vary, but may include loose and more urgent bowel movements, persistent diarrhoea, abdominal pain, bloody stools, loss of appetite, weight loss and fatigue.<sup>5</sup>

### **About STELARA® (ustekinumab)**<sup>16</sup>

In the European Union, ustekinumab is approved for the treatment of moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or psoralen plus ultraviolet A, and is also indicated for the treatment of moderate to severe plaque psoriasis in adolescent patients aged 12 years and older who are inadequately controlled by or are intolerant to other systemic therapies or phototherapies. In addition, 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. In November 2016, the EC approved ustekinumab for the treatment of adult patients with moderate to severe Crohn's disease 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**

Please refer to the full Summary of Product Characteristics for full prescribing information for ustekinumab:

<https://www.medicines.org.uk/emc/product/7638/smpc>

## **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](http://www.janssen.com/EMEA). Follow us at [www.twitter.com/JanssenEMEA](https://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 regulatory approvals and benefits of a new treatment option for 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](http://www.sec.gov), [www.jnj.com](http://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.

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