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News Release

Media contact:
Kevin Veninga
Mobile: +31 61526 8214
KVeninga@ITS.JNJ.com

Investor relations:
Chris DelOrefice
Office: +1 (732) 524-2955

Lesley Fishman/Jennifer McIntyre
Office: +1 (732) 524-3922

The Lancet Simultaneously Publishes Two Phase 3 Studies Detailing Comprehensive Efficacy and Safety of TREMFYA®▼ (guselkumab), a First-in-Class IL-23 p19 Subunit Inhibitor, in Psoriatic Arthritis

DISCOVER-1 and DISCOVER-2, totaling 1120 patients, are the first Phase 3 psoriatic arthritis studies evaluating this mechanism of action

Guselkumab is currently under review by the EMA for approval to treat adults with active psoriatic arthritis

It is estimated that up to a third of the 14 million people who are living with psoriasis in Europe will also develop psoriatic arthritis[1,2]

BEERSE, BELGIUM, April 6, 2020 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced that *The Lancet* has published comprehensive data from DISCOVER-1 and -2, two Phase 3 studies evaluating the safety and efficacy of TREMFYA® (guselkumab) for the treatment of adults with active psoriatic arthritis (PsA).[3,4] Guselkumab is a monoclonal antibody that selectively binds to the p19

subunit of interleukin (IL)-23 and inhibits its interaction with the IL-23 receptor. IL-23 is an important driver of the pathogenesis of inflammatory diseases such as psoriasis and PsA.[5] These are the first publications from a Phase 3 programme reporting safety and efficacy results in active PsA for an antibody with this mechanism of action. Guselkumab is currently not licensed for the treatment of PsA and is undergoing evaluation for this use by the European Medicines Agency (EMA).

Data from the two studies in the DISCOVER programme formed the basis of the validated filing on 11 October 2019, to the EMA in the European Union for approval of guselkumab for the treatment of adult patients with active PsA.[6] Primary endpoint results published in *The Lancet* complement the first presentation of data from the DISCOVER programme at the 2019 American College of Rheumatology and Association of Rheumatology Professionals Annual Meeting (ACR/ARP) in November 2019. DISCOVER-1 evaluated 381 participants with active PsA who had an inadequate response to standard therapies, including participants (~30 percent) previously treated with anti-tumour necrosis factor (TNF) alpha biologics.[3] DISCOVER-2 included 739 patients who were biologic-naïve and had an inadequate response to standard therapies.[4]

"Psoriatic arthritis is a complex disease and patients are looking for therapies that can address as many of their distressing symptoms as possible," said lead study investigator and author of the DISCOVER-2 study, Philip J. Mease[i], M.D., Swedish Medical Center/Providence St. Joseph Health and University of Washington in Seattle, Washington. "With varied endpoints addressing joint, skin, soft tissue inflammation and physical function, plus robust safety data, these publications in *The Lancet* demonstrate how guselkumab treats the multi-dimensional condition of PsA."

Results published in *The Lancet* show that, at week 24, the primary endpoints achieved statistical significance in both studies. Results of secondary endpoints were also reported.[3,4]

- **Joint symptoms:**
    - In DISCOVER-1, among patients receiving guselkumab 100 mg every four weeks (q4w) and every eight weeks (q8w), 59 percent and

52 percent achieved a 20 percent improvement in the primary endpoint of ACR response (ACR20), respectively, vs 22 percent on placebo (both p<0.001). In DISCOVER-2, the primary endpoint was also met; 64 percent of patients receiving guselkumab q4w or q8w achieved an ACR20 response, vs 33 percent on placebo (both p<0.0001).

- In DISCOVER-1, 37 percent of guselkumab q4w and 30 percent of guselkumab q8w patients achieved an ACR50 improvement, vs 9 percent on placebo (both p<0.0001). In DISCOVER-2, 33 percent of guselkumab q4w and 31 percent of guselkumab q8w patients achieved the same endpoint at week 24, vs 14 percent on placebo (both p<0.0001). Higher proportions of patients receiving guselkumab q4w or q8w also attained an ACR70 response at week 24, vs the placebo groups.
- In DISCOVER-2, where the impact of guselkumab on inhibition of radiographic damage progression was studied, guselkumab q4w demonstrated statistically significant inhibition of radiographic progression of joint structural damage as measured by mean improvement from baseline in van der Heijde score (p=0.011).[a] Guselkumab q8w demonstrated numerical but not statistically significant inhibition of structural damage compared to placebo at week 24 (p=0.072).

- **Skin:**
  - Among patients who had clinically relevant psoriasis at baseline in DISCOVER-1, 75 percent receiving guselkumab q4w and 57 percent receiving guselkumab q8w achieved clear or almost clear skin at week 24[b], vs 15 percent on placebo (both p<0.0001). In DISCOVER-2, 68 percent of patients receiving guselkumab q4w and 70 percent receiving guselkumab q8w achieved the same endpoint at week 24, vs 19 percent on placebo (both p<0.0001).
  - Higher Psoriasis Area and Severity Index (PASI) 75, PASI 90, PASI 100 response rates were observed in the guselkumab groups vs the placebo groups at week 24 (in DISCOVER-1, all unadjusted p<0.0001 with PASI 100 being p=0.0005 and in DISCOVER-2, all unadjusted p<0.0001).

- **Soft tissue inflammation and composite measures of disease activity:**
    - Based on analysis of pooled data from DISCOVER-1 and -2, among patients who had enthesitis (pain where the bone, tendon and ligament meet) at baseline, enthesitis resolved in 45 percent of guselkumab q4w and 50 percent of guselkumab q8w patients, vs 29 percent on placebo (both p=0.0301).[c]
    - Based on analysis of pooled data from DISCOVER-1 and -2, among patients who had dactylitis (severe inflammation of the finger and toe joints) at baseline, dactylitis resolved in 64 percent of guselkumab q4w patients and 59 percent of q8w patients, vs 42 percent on placebo (p=0.011 and p=0.0301, respectively).[d]
    - In DISCOVER-1, 30 percent of guselkumab q4w and 23 percent of guselkumab q8w patients were considered to have achieved minimal disease activity, vs 11 percent on placebo (p=0.0002 and p=0.012, respectively). In DISCOVER-2, 19 percent of guselkumab q4w patients and 25 percent of guselkumab q8w patients achieved the same endpoint, vs 6 percent on placebo (both p<0.0001).[e]
- **Patient-reported outcome measures assessing physical function and health-related quality of life:**
    - Guselkumab patients reported clinically meaningful mean improvements in Health Assessment Questionnaire Disability Index (HAQ-DI)[f] (all p<0.0001) and the 36-Item Short-Form Health Survey (SF-36)[g] Physical Component Summary score (PCS)[h], which measures patient-reported functional health and well-being from baseline (in DISCOVER-1, both p<0.0001 and in DISCOVER-2, both p=0.011). Improvements from baseline that did not reach statistical significance versus placebo (all p>0.05) were reported in SF-36 Mental Component Summary score (MCS), which measures patient-reported mental well-being.
- **Safety:**
    - In DISCOVER-1 and -2, serious adverse events up to week 24 in q4w (0 and 3 percent) and q8w (3 and 1 percent) were similar to those in the placebo (4 and 3 percent).

- Observed adverse events (AEs) were generally consistent with previous studies of guselkumab and current prescribing information. In DISCOVER-1, 55 percent of patients receiving guselkumab q4w, 54 percent of patients receiving guselkumab q8w, and 60 percent of patients receiving placebo reported AEs up to week 24. In DISCOVER-2, AEs were reported by 46 percent of patients receiving guselkumab q4w, 46 percent of patients receiving guselkumab q8w, and 41 percent of patients in the placebo groups.
- No opportunistic infections and cases of new inflammatory bowel disease were observed in patients treated with guselkumab.
- No new safety signals were reported.

"The IL-23 immune pathway is associated with a number of immune-mediated inflammatory diseases, including psoriasis and psoriatic arthritis," said Alyssa Johnsen, M.D., Ph.D., Vice President, Rheumatology Disease Area Leader, Janssen Research & Development, LLC. "We're excited to share the DISCOVER-1 and -2 data in psoriatic arthritis, a disease that is a concern for so many who are also grappling with psoriasis, where guselkumab has already made an impact."

Guselkumab was first approved by the European Commission on 23 November 2017 for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.[7] It is currently approved in 72 countries for this indication.

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Key definitions

[a] The van der Heijde modified Sharpscore (modified for use in psoriatic arthritis) is a method used to assess and rate erosions and joint space narrowing in radiographs of hands and feet.[8]

[b] Investigator Global Assessment score of 0 or 1, and a $\geq$2 grade reduction in body surface area affected.[9]

[c] Resolution of enthesitis was defined as complete absence of enthesitis in any location measured by Leeds Enthesitis Index.[9]

[d] Resolution of dactylitis was defined as complete absence of dactylitis in 20 sites (10 fingers, 10 toes) as measured by Dactylitis Severity Scale.[9]

[e] Patients were considered to have achieved minimal disease activity if fulfilling at least five of the following seven criteria: tender joint count 1 or less, swollen joint count 1 or less, PASI score 1 or less, patient pain VAS score 15 or less, patient global disease activity VAS score 20 or less, HAQ-DI score 0.5 or less, and tender entheseal points 1 or less.[3]

[f] Health Assessment Questionnaire Disability Index is a patient questionnaire that assesses physical function and disability across rheumatic diseases.[9]

[g] SF-36 is a patient-reported measure of functional health and wellbeing.[9]

[h] PCS is composed of four scales assessing physical function, role limitations caused by physical problems, bodily pain, and general health.[9]

About DISCOVER-1 (NCT03162796)[9]

DISCOVER-1 was a randomised, double-blind, multicentre Phase 3 study evaluating the efficacy and safety of guselkumab administered by subcutaneous (SC) injection in participants with active PsA, including those previously treated with anti-TNF therapies. DISCOVER-1 evaluated 381 participants and ended after approximately one year.

The study consisted of: a screening phase of up to six weeks, a blinded treatment phase of 52 weeks that included a placebo-controlled period from week 0 to week 24 and an active treatment period from week 24 to week 52, and a safety follow-up phase of eight weeks after week 52 (week 52 to 60; 12 weeks from the last administration of study agent [at week 48] through to the final visit in the safety follow-up phase). Efficacy, safety, pharmacokinetic, immunogenicity and biomarker evaluations were performed in the study on a defined schedule.

About DISCOVER-2 (NCT03158285)[10]

DISCOVER-2 is a randomised, double-blind, multicentre Phase 3 study evaluating the efficacy and safety of guselkumab administered by SC injection in biologic-naïve

participants with active PsA. DISCOVER-2 is evaluating 739 participants and continuing through approximately two years.

The study consists of: a screening phase of up to six weeks, a blinded treatment phase (approximately 100 weeks) that includes a placebo-controlled period from week 0 to week 24 and an active treatment period from week 24 to week 100, and a safety follow-up phase of 12 weeks after the last administration of study agent. Efficacy, health economics, safety, pharmacokinetics, immunogenicity, biomarker and pharmacogenomics evaluations are being performed in the study on a defined schedule.

About PsA

PsA is a chronic, immune-mediated inflammatory disease characterised by peripheral joint inflammation, enthesitis, dactylitis, axial disease, and the skin lesions associated with psoriasis.[11] Studies show that up to 30 percent of people with psoriasis also develop PsA.[1] The disease causes pain, stiffness and swelling in and around the joints; it commonly appears between the ages of 30–50, but can develop at any time.[12] Though the exact cause of PsA is unknown, genes, the immune system and environmental factors are all believed to play a role in the onset of the disease.[12]

About TREMFYA® (guselkumab)[7]

Developed by Janssen, guselkumab is the first marketed monoclonal antibody that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. It is approved as a prescription medicine in the EU, U.S., Canada, Japan and a number of other countries worldwide for the treatment of adult patients with moderate to severe plaque psoriasis who may benefit from injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet [UV] light). IL-23 is an important driver of the pathogenesis of inflammatory diseases such as psoriasis and PsA.[5] In psoriasis, guselkumab is administered as a 100 mg SC injection once every 8 weeks, after starter doses at weeks 0 and 4.

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

Important Safety Information

Very common (>10%) and common AEs (>1%) in controlled periods of clinical studies with guselkumab were upper respiratory infections, gastroenteritis, herpes simplex infections, tinea infections, headache, diarrhoea, urticaria, arthralgia and injection site erythema. Most were considered to be mild and did not necessitate discontinuation of study treatment.

Please refer to the Summary of Product Characteristics for full prescribing information for guselkumab for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy:
https://www.medicines.org.uk/emc/medicine/34321

▼ Adverse events should be reported. This medicinal product is subject to additional monitoring and it is, therefore, important to report any suspected adverse events related to this medicinal product. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Janssen-Cilag Ltd on 01494 567447.

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

[i]Dr. Philip J. Mease is a paid consultant for Janssen. He has not been compensated for any media work.

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