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News Release

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A Newly Published Network Meta-Analysis (NMA) Found TREMFYA®▼ (guselkumab) Ranked Highest for Overall Level of Skin Clearance and Provided Positive Joint Efficacy Among Active Psoriatic Arthritis (PsA) Therapies

The NMA indirectly compared all published Phase 3 data for treatments that are approved or under investigation in the EU for adults with active PsA

Guselkumab ranked highest among 23 active PsA treatment regimens on skin clearance (PASI 90 response) and showed positive joint efficacy (ACR20), including inhibition of structural damage (vdH-S)

BEERSE, BELGIUM, 24 January, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced a Network Meta-Analysis (NMA) comparing first-in-class interleukin (IL)-23 inhibitor TREMFYA®▼ (guselkumab) to all advanced therapies[a] approved or under investigation for active psoriatic arthritis (PsA) using data from 33 Phase 3 randomised clinical trials (RCTs).[1] The NMA concluded guselkumab ranked highest[b] for skin clearance based on Psoriasis Area Severity Index (PASI)[c] 90 response among 23 treatment regimens (15 unique treatments including IL-23 inhibitors like guselkumab and risankizumab, subcutaneous [SC]

tumour necrosis factor inhibitors [TNFi], and Janus kinase inhibitors [JAKi]).[1] In terms of joint inflammation improvement, both guselkumab dosing regimens (100 mg every four weeks [q4w] and every eight weeks [q8w])[d] were comparable[b] to most other treatments for the modified van der Heijde-Sharp (vdH-S)[e] score, and guselkumab was generally comparable[b] to TNFi and most IL-17Ai for American College of Rheumatology (ACR) 20 response.[1,f] The analysis also confirmed the established safety profile of guselkumab in active PsA.[1] The NMA is being presented at the Maui Dermatology 2022 Meeting taking place 24-28 January, 2022. Guselkumab is approved for q8w dosing; in the EU, for PsA patients at high risk for joint damage according to clinical judgement, q4w dosing may be considered.[2,d]

"This comprehensive analytical approach helps to provide a useful comparative picture of available psoriatic arthritis medicines," said Philip J. Mease,[g] M.D., Swedish Medical Center/Providence St. Joseph Health and University of Washington in Seattle, Washington. "In my experience, thorough NMAs such as this one can help equip physicians to discuss treatment choices and therapeutic outcomes with their patients in daily practice."

NMA is a structured, protocol-driven analytical process widely accepted and utilised by regulatory agencies, health technology assessment agencies and medical guideline committees to comparatively evaluate treatment options where head-to-head data are limited or unavailable.[3-5] NMA is the most cited and the most comprehensive method available to compare studies indirectly; however, NMAs cannot replace and should not be considered the same as head-to-head clinical trials. In this NMA, the timing of primary endpoint assessment varied across RCTs, and placebo was used as the reference treatment throughout with the exception of two head-to-head studies.[1] Baseline risk adjustment was used to account for heterogeneity across study populations. The NMA builds on previous analyses, including a 2021 publication in *Rheumatology*, and now incorporates all recent clinical data updates, including the COSMOS study of guselkumab in PsA patients who had

an inadequate response to TNFi, as well as data for two new comparators, the IL-23i risankizumab and the JAKi upadacitinib.[1,6,7]

NMA results showed:[1]

- **Skin Clearance:** guselkumab ranked first and second[b] in PASI 90 response for q4w and q8w dosing,[d] respectively.
- **Joint Inflammation Improvement:** guselkumab was comparable to SC TNFi and most IL-17Ai, as measured by ACR20 response. While dosing frequency impacted modified vdH-S score,[e] both guselkumab dosing regimens achieved improvements that were comparable to most treatments and both doses of guselkumab ranked more highly on vdH-S score than risankizumab and upadacitinib.[b]
- **Low Numbers of Serious Adverse Events (SAEs):** guselkumab showed low rates of SAEs, with both dosing regimens ranking favourably among the 23 treatments for low rates of events. The number of SAEs for guselkumab were consistent with the established guselkumab safety profile.[1]

"Psoriatic arthritis is a complex disease, and physicians must consider many factors when making treatment decisions, including the relative efficacy of therapies in treating both skin and joints, as well as established safety," said Terence Rooney, M.D., Vice President, Rheumatology and Maternal-Fetal Immunology Disease Area Leader, Janssen Research & Development, LLC. "NMAs are a comprehensive, well-established approach, and can provide physicians with useful information on available therapies."

Guselkumab, alone or in combination with methotrexate (MTX), is approved in the EU for the treatment of active PsA in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug therapy.[2] The PsA approval was based on results from DISCOVER-1 and DISCOVER-2, which showed guselkumab achieved the studies' primary endpoint of ACR20 response at 24 weeks.[8,9] A comprehensive analysis of DISCOVER-2 data was

recently published in *Arthritis & Rheumatology*, representing the final results of the first-ever two-year clinical trial with an open-label extension investigating a selective IL-23 inhibitor therapy in active PsA.[10]

Janssen will present five additional posters at the Maui Dermatology Meeting, including the study design of APEX (NCT04882098),[11] investigating the effect of guselkumab on radiographic progression;[h] the design of the SOLSTICE trial (NCT04936308),[12] which further evaluates guselkumab efficacy for PsA patients with intolerance or inadequate response to TNF therapy; evidence of molecular and genetic distinctions between patients with axial PsA (axPsA) and ankylosing spondylitis and the significant pharmacodynamic effects of guselkumab in axPsA patients; and real-world evidence for PsA patients initiating guselkumab treatment in the CorEvitas Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry.

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Editor's Note:

a. Advanced therapies were defined as any targeted or biologic therapies for the treatment of PsA including: TNFi, JAKi, IL-17Ai, IL-12/23i, IL-23i, PDE4i, CTLA-4i, biologic biosimilar agents, and placebo/no treatment.[1]
b. Results are summarised by ranking treatments according to findings derived from NMAs. Conclusions (i.e., comparable) are based on an overlap of pairwise 95 percent credible intervals.[1]
c. PASI 90 is defined as at least 90 percent improvement from baseline in the PASI score. The PASI score grades the amount of surface area on each body region that is covered by Pso plaques and the severity of plaques for their redness, thickness, and scaliness.[13] PASI 90 was not a controlled endpoint in DISCOVER-1 or -2.[8,9]
d. In the EU, the recommended dose of guselkumab for patients with Pso or PsA is 100 mg by subcutaneous injection at weeks zero and four, followed by a maintenance dose every eight weeks. For PsA patients at high risk for joint

damage according to clinical judgement, a dose of 100 mg every four weeks may be considered.[2]

e. The PsA-modified vdH-S score combines erosion and joint space narrowing scores derived from radiographs of joints in body regions impacted by PsA.[14]
f. ACR20 response is defined as both at least 20 percent improvement from baseline in the number of tender and number of swollen joints, and a 20 percent improvement from baseline in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure, visual analogue pain scale, and erythrocyte sedimentation rate or C-reactive protein.[15]
g. Dr Mease is a paid consultant for Janssen. He has not been compensated for any media work.
h. Radiographic progression is a key indicator of structural damage, which includes erosion and joint space narrowing.

About the Network Meta-Analysis[1]

A systematic literature review was conducted to identify randomised controlled trials up to February 2021. A hand search identified newer agents up to July 2021. These searches identified 33 Phase 3 RCTs studying 15 targeted therapies for PsA approved or under review by the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA) in patients who were TNFi-naïve, TNFi-experienced, had an inadequate response (IR), or mixed populations for inclusion in this NMA, through July 2021. Bayesian NMAs were performed to compare therapies on ACR20 response, PASI response, modified vdH-S score and SAEs. Analyses used random effects models wherever possible, and fixed effects models when not. Wherever possible, analyses included meta-regression on baseline risk (placebo response) in order to reduce bias. Multinomial models were used for ACR and PASI. Several NMAs have compared the efficacy of treatments available for PsA, but none of these analyses have included the latest Phase 3 data for guselkumab in the TNFi-IR population or the latest comparators risankizumab and upadacitinib.[16-19] The objective of this study was to update the prior NMAs to

include these new data to determine the relative skin and joint efficacy and safety for therapies available for PsA through NMA.

This NMA adheres to all governing standards and requirements as demanded by global health technology assessment agencies, journal review committees and regulatory authorities. The NMA was funded by Janssen Research & Development, LLC.

About COSMOS (NCT03796858)[7]

COSMOS was a Phase 3b, multicenter, randomised, double-blind, placebo-controlled study to evaluate the safety and efficacy of guselkumab in 285 patients with active PsA and IR to TNFi therapy. The primary endpoint was ACR20 response at week 24. Participants were randomised (2:1) to receive guselkumab 100 mg at weeks 0, 4 and q8w thereafter, or placebo. The study included two periods: a 24-week double-blind, placebo-controlled period for the primary analysis of the efficacy and safety of guselkumab compared with placebo and a 32-week active-treatment and safety follow-up period for additional analysis of the efficacy and safety of guselkumab. Through week 48, non-responder imputation (NRI) rules were used for missing data (after the application of treatment failure rules [TFR]). Safety was monitored throughout the study to week 56.

About DISCOVER-1 (NCT03162796)[8]

DISCOVER-1 was a randomised, double-blind, multicentre Phase 3 study evaluating the efficacy and safety of guselkumab administered by SC injection in participants with active PsA, including those previously treated with one or two TNF inhibitors. DISCOVER-1 evaluated 381 participants who were treated and followed through approximately one year. The primary endpoint was response of ACR20 at week 24 and primary endpoint data were previously presented at scientific congresses and published in *The Lancet*. In addition to ACR20, multiple other clinical outcomes were assessed, including ACR50/70, resolution of soft tissue inflammation, enthesitis and dactylitis, improvement in physical function, skin clearance (IGA), and general health

outcomes (36-Item Short-Form Health Survey [SF-36] Physical Component Summary [PCS] and Mental Component Summary [MCS]).

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 a blinded active treatment period from week 24 to week 52. It also included a safety follow-up phase through week 60 (i.e., approximately 12 weeks from the last administration of study agent at week 48). Efficacy, safety, pharmacokinetic, immunogenicity and biomarker evaluations were performed in the study on a defined schedule.

About DISCOVER-2 (NCT03158285)[9]

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 patients with active PsA. DISCOVER-2 evaluated 739 participants who were treated and followed through approximately two years. The primary endpoint was response of ACR20 at week 24 and primary endpoint data were previously presented at scientific congresses and published in *The Lancet*. In addition to ACR20, multiple other clinical outcomes were assessed, including ACR50/70; resolution of soft tissue inflammation, enthesitis and dactylitis; improvement in physical function; skin clearance (IGA); and general health outcomes (SF-36 PCS and MCS). DISCOVER-2 also assessed changes in structural damage as a key secondary endpoint (PsA-modified vdH-S score).

The study consisted of a screening phase of up to six weeks, a blinded treatment phase of 100 weeks that included a placebo-controlled period from week 0 to week 24 and a blinded active treatment period from week 24 to week 100. It also included a safety follow-up phase through week 112 (i.e., approximately 12 weeks after the last administration of study agent at week 100). Clinical efficacy, radiographic efficacy, health economics, safety, pharmacokinetics, immunogenicity, biomarker,

and pharmacogenomics evaluations were performed in the study on a defined schedule.

About Psoriatic Arthritis (PsA)

PsA is a chronic, immune-mediated inflammatory disease characterised by peripheral joint inflammation, enthesitis (pain where the bone, tendon and ligament meet), dactylitis (severe inflammation of the fingers and toes), axial disease, and the skin lesions associated with plaque Pso.[20-22] In addition, in patients with PsA, comorbidities, such as obesity, cardiovascular diseases, anxiety and depression are often present.[23] Studies show up to 30 percent of people with plaque Pso also develop PsA.[24] The disease causes pain, stiffness and swelling in and around the joints; it commonly appears between the ages of 30 and 50, but can develop at any age.[24] Nearly half of patients with PsA experience moderate fatigue and about 30 percent suffer from severe fatigue as measured by the modified fatigue severity scale.[25] Although the exact cause of PsA is unknown, genes, the immune system and environmental factors are all believed to play a role in disease onset.[26]

About TREMFYA® (guselkumab)[2]

Developed by Janssen, guselkumab is the first approved fully human monoclonal antibody that selectively binds to the p19 subunit of 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 moderate to severe plaque Pso and active PsA.[27] Guselkumab is approved in the EU for the treatment of moderate to severe plaque Pso in adults who are candidates for systemic therapy and for the treatment of active PsA in adult patients who have had an inadequate efficacy or who have been intolerant to a prior disease-modifying antirheumatic drug therapy. In the EU, the recommended dose of guselkumab for patients with Pso or PsA is 100 mg by subcutaneous injection at weeks 0 and 4, followed by a maintenance dose every 8 weeks. For PsA patients at high risk for joint damage according to clinical judgement, a dose of 100 mg every 4 weeks may be considered. It is also approved in the U.S., Canada, Japan, and a number of other countries worldwide for the treatment of adults

with moderate to severe plaque Pso who are candidates for systemic therapy or phototherapy, and for the treatment of adult patients with active PsA.

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

GUSELKUMAB IMPORTANT SAFETY INFORMATION

In controlled periods of clinical studies with guselkumab, adverse drug reactions (ADRs) that consisted of respiratory tract infections were very common (≥10 percent); increased transaminases, headache, diarrhoea, arthralgia, and injection site reactions were common (≥1 to <10 percent); and herpes simplex infections, tinea infections, gastroenteritis, decreased neutrophil count, hypersensitivity, anaphylaxis, urticaria and rash were uncommon ADRs (≥0.1 percent to <1 percent).[2]

Please refer to the Summary of Product Characteristics for full prescribing information for guselkumab: https://www.ema.europa.eu/en/documents/product-information/tremfya-epar-product-information_en.pdf

ADRs should be reported▼. This medicinal product is subject to additional monitoring and it is therefore important to report any suspected ADRs related to this medicinal product.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

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Janssen Research & Development, LLC and Janssen-Cilag International NV, the marketing authorisation holder for TREMFYA® in the EU, are each 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 TREMFYA® (guselkumab) product development. 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 materialize, 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 behavior 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 January 3, 2021, 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.

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