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News Release

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**New Data Show TREMFYA®▼ (guselkumab) Binds to Both
Inflammatory Cells and Interleukin (IL)-23, Supporting a Hypothesis
for a Differentiated Mechanism from Risankizumab**

*In vitro studies suggest guselkumab neutralises IL-23 where it is produced,
enhancing the ability of guselkumab to prevent local activation of cells that drive
inflammation*

*Guselkumab is the first fully human IL-23 inhibitor indicated for adults with
moderate to severe plaque psoriasis and adults with active psoriatic arthritis*

BEERSE, BELGIUM, 18 May, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the first results of the in vitro MODIF-Y studies, supporting a hypothesis that may differentiate the mechanism of first-in-class

TREMFYA®▼ (guselkumab) from risankizumab due to guselkumab having the ability to bind to CD64 positive (CD64⁺) cells in addition to interleukin (IL)-23 – both of which are key components of the immune system involved in triggering inflammatory responses.^{1,2} These findings are being presented at the Society for Investigative Dermatology (SID) annual meeting, taking place May 18-21, 2022 in Portland, Oregon, demonstrate guselkumab binds simultaneously to CD64 via its native fragment crystallizable (Fc) region and to IL-23 via its antigen-binding region, suggesting the potential to neutralise IL-23 right at the site where it is secreted.¹ Further studies will be conducted in vitro and in vivo to generate additional evidence supporting this hypothesis.

IL-23, a cytokine secreted by activated monocyte/macrophage and dendritic cells, is known to be a driver of inflammatory diseases, including plaque psoriasis (Pso), psoriatic arthritis (PsA), and inflammatory bowel disease (IBD).^{3,a} CD64 is a receptor that binds the Fc region of immunoglobulin G⁴ and is highly expressed on the surface of certain immune cells that are major producers of IL-23.⁴⁻⁷

“The initial results of these studies show the potential differentiating mechanism of guselkumab,” said presenting study author James G. Krueger, M.D., Ph.D., D. Martin Carter Professor in Clinical Investigation and Co-director, Center for Clinical and Translational Science, The Rockefeller University in New York.^b “Its ability to bind to CD64⁺ cells may physically place guselkumab right on the surface of these major IL-23-producing immune cells, which are key drivers of inflammation in diseases such as psoriasis and psoriatic arthritis. This potentially allows guselkumab to neutralise IL-23 where it is being produced and prevent IL-23 from acting in the local tissue microenvironment.”

The MODIF-Y studies explored mechanisms potentially underpinning therapeutic profile differences between guselkumab, a fully human monoclonal antibody specific for the p19 subunit of IL-23 with a native Fc region, and risankizumab, a humanised anti-IL-23 monoclonal antibody with a mutated Fc region.

Differentiated, Local Neutralisation of IL-23 at its Source

- The results from these studies show that guselkumab is differentiated from risankizumab by the capacity of guselkumab to bind via its native Fc region to CD64, which is expressed on IL-23-producing cells.¹ This raises the possibility that guselkumab may bind to IL-23 while also being localised to IL-23-producing cells through its binding to CD64, thus neutralising IL-23 at its cellular source.¹ Risankizumab shows negligible binding to CD64 due to its mutated Fc region.^{1,8}
- CD64⁺ mononuclear phagocytes represent the predominant IL-23 source in psoriatic skin and IBD, and increased frequency of CD64⁺ monocytes correlates with markers of joint disease activity in active PsA.⁵⁻⁷
- These studies also showed that guselkumab and risankizumab display comparable affinity for binding IL-23 and potency for inhibiting IL-23-mediated signaling.¹

Potential for Enrichment in Inflamed Tissues

- Binding to CD64 raises the hypothesis that the presence of guselkumab may be enriched at the intercellular interface between IL-23-producing and -responsive cells within the inflamed tissue. This may in turn enhance the ability of guselkumab to neutralise IL-23 where it is produced in inflammatory diseases.¹

The results of these molecular investigations follow previous publications of Phase 3 clinical trials demonstrating the durable, long-term efficacy and safety profile of guselkumab based on five years of data in plaque Psoriasis and two years of data in PsA.⁹⁻

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“This ability of TREMFYA to capture IL-23 right where it is produced, preventing permanent activation of IL-23-responsive cells, may help explain its durable clinical efficacy in psoriatic disease,” said Dan Cua, Ph.D., Vice President, IL-23 Pathway Leader, Janssen Research & Development, LLC. “These molecular studies also inform current and future research that fuel our critical understanding of IL-23 pathway mechanisms, biodistribution patterns, and clinical outcomes, as we seek to provide

patients with more efficacious and lasting treatments across a number of inflammatory diseases.”

Further in vivo research is being conducted on guselkumab’s biodistribution and its correlation to efficacy in the treatment of patients with PsA and IBD, which includes ongoing Phase 3 trials in Crohn’s disease and ulcerative colitis.¹²⁻¹⁴ Janssen is dedicated to continuing to investigate the pathways underlying immune-mediated diseases, focusing on improving the regulation of the immune system to create novel treatments that can effectively address the root cause of disease.

Editor’s Notes:

- a. Guselkumab is not approved to treat IBD.
- b. Dr Krueger is a paid consultant for Janssen. He has not been compensated for any media work.

About the MODIF-Y Programme¹

The studies were designed to explore potential mechanisms underpinning differences in therapeutic profiles between guselkumab, a fully human monoclonal immunoglobulin G1 lambda (IgG1 λ) antibody specific for IL-23p19 with a native fragment crystallizable (Fc) region, and risankizumab, a humanised anti-IL-23 IgG1 with a mutated Fc region, in inflammatory diseases. Functional characteristics of the antigen-binding and Fc regions of the two antibodies were compared.

About Plaque Psoriasis (Pso)

Plaque Pso is an immune-mediated disease resulting in an overproduction of skin cells, which causes inflamed, scaly plaques that may be itchy or painful.¹⁵ It is estimated that more than 125 million people worldwide live with the disease.¹⁶ Nearly one-quarter of all people with plaque Pso have cases that are considered moderate to severe.¹⁶ Living with plaque Pso can be a challenge and impact life beyond a person’s physical health, including emotional health, relationships, and handling the stressors of life.¹⁷

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.¹⁸⁻²⁰ In addition, in patients with PsA, comorbidities such as obesity, cardiovascular diseases, anxiety and depression are often present.²¹ Studies show up to 30 percent of people with plaque Pso also develop PsA.²² 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.²² 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.²³ 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.²⁴

About TREMFYA® (guselkumab)²⁵

Developed by Janssen, guselkumab is the first approved fully human monoclonal antibody that selectively binds to the p19 subunit of interleukin (IL)-23 and inhibits its interaction with the IL-23 receptor.²⁵ Guselkumab is approved in the EU for the treatment of moderate to severe plaque psoriasis (Pso) in adults who are candidates for systemic therapy, and alone or in combination with methotrexate (MTX) for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug therapy.²⁵ 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 may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light), and for the treatment of adult patients with active PsA.²⁵ Guselkumab is being investigated in Phase 3 clinical trials in both adults with moderately to severely active Crohn's disease (EudraCT 2017-002195-13)²⁶ and adults with moderately to severely active ulcerative colitis (EudraCT 2018-004002-25).²⁷

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).²⁵

Please refer to the Summary of Product Characteristics for full prescribing information for guselkumab in Pso and PsA: 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 AEs related to this medicinal product.

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 TREMFYA® in the EU, and Janssen Research & Development, LLC 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 materialise, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, 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 January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other 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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