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News Release

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TREMFYA® (guselkumab) Demonstrates a Differentiated Binding Mechanism from Risankizumab in *In Vitro* Studies

Studies suggest a mechanistic benefit of guselkumab by binding to cells that drive inflammation in the colon

BEERSE, BELGIUM, 3 March, 2023 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced additional results from *in vitro* MODIF-Y studies, which continue to support a hypothesis that not all IL-23 inhibitors are the same by demonstrating a differentiated binding mechanism for TREMFYA® (guselkumab) from risankizumab. Findings show that guselkumab is able to dose-dependently bind to CD64+[a] myeloid cells,[1] the predominant source of IL-23-driven inflammation in the gut.[2,b] Data comprise one of Janssen's 22 oral and poster

presentations at the 18th Congress of the European Crohn's and Colitis Organisation (ECCO), taking place in Copenhagen, Denmark, 1-4 March.

"These data provide new insights into the mechanism of action of guselkumab and can help in the development of treatments for conditions like inflammatory bowel disease," said study author Raja Atreya, M.D., Senior Physician and Head of the Inflammatory Bowel Disease Unit, Outpatient Clinic, and Clinical Study Centre at the Erlangen University Hospital, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany.[c] "Importantly, these data show that guselkumab has the unique ability to bind to key cells involved in inflammation, neutralizing IL-23 where it is being produced in the local tissue microenvironment, suggesting mechanistic benefit."

MODIF-Y *in vitro* outcomes (Poster P504):[1]

Results from a study comparing functional binding characteristics of guselkumab and IL-23 inhibitor risankizumab show:

- The capacity of Guselkumab for dual binding enables simultaneous binding to CD64 and neutralization of IL23 at its cellular source, differentiating guselkumab within the IL-23p19 inhibitor class[1]
- Comparatively, risankizumab showed negligible binding to transfected cell lines expressing Fcγ receptors (FcγRs) including CD64[1]
- Both therapies displayed comparable binding affinity[d] for IL-23 and equivalent potency in the inhibition of IL-23[1]

"The findings from our study demonstrate Janssen's commitment to foundational molecular science and reinforce our commitment to developing therapies that may help address unmet patient need," said Dan Cua, Ph.D., Vice President, IL-23 Distinguished Fellow, Immunology, Janssen Research & Development, LLC. "We continue to investigate the underlying science of guselkumab to further understand mechanistic differences from other IL-23 inhibitors, as well as the growing immune-mediated disease complexities such as inflammatory bowel disease, so that healthcare professionals have an array of treatment options to consider."

Further research is currently being conducted on guselkumab to investigate treatment of patients with inflammatory bowel disease, which includes ongoing Phase 3 trials in Crohn's disease (2017-002195-13) and ulcerative colitis (2018-004002-25).[3,4]

Guselkumab is not currently approved for the treatment of adults with inflammatory bowel disease in the European Union (EU).[5]

Editor's Notes:

a. CD64+ is a receptor that binds to the Fc region of antibodies and is expressed on immune cells that are major producers of IL-23.[2]

b. Frequencies of CD64+ IL-23–producing myeloid cells are increased in the inflamed colon in inflammatory bowel disease and correlated with endoscopic disease severity.[2,6]

c. Dr. Atreya received grant support from Janssen. He has not been compensated for any media work.

d. IL-23 binding affinity and cellular potency were similar for guselkumab and risankizumab.[1]

About the MODIF-Y Programme

The *in vitro* MODIF-Y studies were designed to explore potential mechanisms underpinning potential differences in therapeutic profiles between guselkumab, a fully human monoclonal immunoglobulin G1 lambda (IgG1λ) antibody specific for IL-23p19 with a native Fc region, and risankizumab, a humanised anti-IL-23p19 IgG1λ with a mutated Fc region, in inflammatory diseases.[7] Functional characteristics of the antigen-binding and Fc regions of the two antibodies were compared.[7]

About Inflammatory Bowel Disease

Inflammatory Bowel Disease (IBD) is an umbrella term for two conditions – Crohn's disease (CD) and ulcerative colitis (UC) – that cause chronic inflammation of the

gastrointestinal (GI) tract.[8] Prolonged inflammation results in damage to the GI tract.[8] The exact cause of IBD is unknown, but may be the result of the immune system's response to environmental triggers or genetic predisposition. Symptoms may vary, but may include persistent diarrhoea, abdominal pain, rectal bleeding, bloody stool, weight loss, and fatigue.[8]

About TREMFYA® (guselkumab)

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.[5] 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.[5] 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.[9,10,11]

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).[5]

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. 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. ADRs should also be reported to Janssen-Cilag Ltd on +44 (0) 1494 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 & Retina, 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 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 product development of TREMFYA® (guselkumab). 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 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 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 1, 2023, 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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