



## News Release

### Media Contact:

Bridget Kimmel  
Mobile: (215) 688-6033  
Email: bkimmel@its.jnj.com

### Investor Contact:

Raychel Kruper  
Office: (732) 524-6164  
Email: rkruper@its.jnj.com

## **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 TREMFYA neutralizes IL-23 where it is produced, enhancing the ability of TREMFYA to prevent local activation of cells that drive inflammation*

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

**SPRING HOUSE, PENNSYLVANIA, May 18, 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 the ability of TREMFYA to bind to CD64 positive (CD64<sup>+</sup>) cells in addition to interleukin (IL)-23 — both of which are key components of the immune system.<sup>1,2</sup> These findings, which are being presented at the Society for Investigative Dermatology (SID) annual

meeting May 18-21, 2022 in Portland, Oregon, demonstrate TREMFYA binds simultaneously to CD64 via its native fragment crystallizable (Fc) region and to IL-23 via its antigen-binding region, suggesting the potential to neutralize IL-23 right at the site where it is secreted.<sup>1</sup> 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).<sup>3,a</sup> CD64 is a receptor that binds the Fc region of immunoglobulin G<sup>4</sup> and is highly expressed on the surface of certain immune cells that are major producers of IL-23.<sup>4-7</sup>

“The initial results of these studies show the potential differentiating mechanism of TREMFYA,” 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.<sup>b</sup> “Its ability to bind to CD64<sup>+</sup> cells may physically place TREMFYA 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 TREMFYA to neutralize 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 TREMFYA, a fully human monoclonal antibody specific for the p19 subunit of IL-23 with a native Fc region, and risankizumab, a humanized anti-IL-23 monoclonal antibody with a mutated Fc region.

### **Differentiated, Local Neutralization of IL-23 at its Source**

- The results from these studies show that TREMFYA is differentiated from risankizumab by the capacity of TREMFYA to bind via its native Fc region to CD64, which is expressed on IL-23-producing cells.<sup>1</sup> This raises the possibility that TREMFYA may bind to IL-23 while also being localized to IL-

IL-23-producing cells through its binding to CD64, thus neutralizing IL-23 at its cellular source.<sup>1</sup> Risankizumab shows negligible binding to CD64 due to its mutated Fc region.<sup>1,8</sup>

- CD64<sup>+</sup> mononuclear phagocytes represent the predominant IL-23 source in psoriatic skin and IBD, and increased frequency of CD64<sup>+</sup> monocytes correlates with markers of joint disease activity in active PsA.<sup>5-7</sup>
- These studies also showed that TREMFYA and risankizumab display comparable affinity for binding IL-23 and potency for inhibiting IL-23-mediated signaling.<sup>1</sup>

### **Potential for Enrichment in Inflamed Tissues**

- Binding to CD64 raises the hypothesis that the presence of TREMFYA 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 TREMFYA to neutralize IL-23 where it is produced in inflammatory diseases.<sup>1</sup>

The results of these molecular investigations follow previous publications of Phase 3 clinical trials demonstrating the durable, long-term efficacy and safety profile of TREMFYA based on five years of data in plaque PsO and two years of data in PsA.<sup>9-</sup>

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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 the biodistribution of TREMFYA and its correlation to efficacy in the treatment of patients with PsA ([NCT05083078](https://clinicaltrials.gov/ct2/show/study/NCT05083078)) and

IBD, which includes ongoing Phase 3 trials in Crohn's disease ([NCT03466411](#)) and ulcerative colitis ([NCT04033445](#)).<sup>12-14</sup> 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. TREMFYA 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 Program<sup>1</sup>**

The in vitro MODIF-Y studies were designed to explore potential mechanisms underpinning differences in therapeutic profiles between TREMFYA (guselkumab), a fully human monoclonal immunoglobulin G1 lambda (IgG1 $\lambda$ ) antibody specific for IL-23p19 with a native Fc region, and risankizumab, a humanized 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.<sup>15</sup> It is estimated that eight million Americans and more than 125 million people worldwide live with the disease.<sup>16</sup> Nearly one-quarter of all people with plaque PsO have cases that are considered moderate to severe.<sup>16</sup> 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.<sup>17</sup>

**About Psoriatic Arthritis (PsA)**

PsA is a chronic, immune-mediated inflammatory disease characterized 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.<sup>18-20</sup> In addition, in patients with PsA, comorbidities such as obesity, cardiovascular diseases, anxiety and depression are often present.<sup>21</sup> Studies show up to 30 percent of people with plaque PsO also develop PsA.<sup>22</sup> 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.<sup>22</sup> 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.<sup>23</sup> 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.<sup>24</sup>

### **About TREMFYA® (guselkumab)<sup>25</sup>**

Developed by Janssen, TREMFYA 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. TREMFYA is 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 injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light), and for the treatment of adult patients with active PsA. It is also 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 response or who have been intolerant to a prior disease-modifying antirheumatic drug therapy. TREMFYA is being investigated in Phase 3 clinical trials in both adults with moderately to severely active Crohn's disease ([NCT03466411](#)) and adults with moderately to severely active ulcerative colitis ([NCT04033445](#)).

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

### **IMPORTANT SAFETY INFORMATION**

**What is the most important information I should know about TREMFYA®? TREMFYA® is a prescription medicine that may cause serious side effects, including:**

- **Serious Allergic Reactions.** Stop using TREMFYA® and get emergency medical help right away if you develop any of the following symptoms of a serious allergic reaction:
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - swelling of your face, eyelids, lips, mouth, tongue or throat
  - trouble breathing or throat tightness
  - chest tightness
  - skin rash, hives
  - itching
- **Infections.** TREMFYA® may lower the ability of your immune system to fight infections and may increase your risk of infections. Your healthcare provider should check you for infections and tuberculosis (TB) before starting treatment with TREMFYA® and may treat you for TB before you begin treatment with TREMFYA® if you have a history of TB or have active TB. Your healthcare provider should watch you closely for signs and symptoms of TB during and after treatment with TREMFYA®.

Tell your healthcare provider right away if you have an infection or have symptoms of an infection, including:

- fever, sweats, or chills
- muscle aches
- weight loss
- cough
- warm, red, or painful skin or sores on your body different from your psoriasis
- diarrhea or stomach pain
- shortness of breath
- blood in your phlegm (mucus)
- burning when you urinate or urinating more often than normal

**Do not take TREMFYA®** if you have had a serious allergic reaction to guselkumab or any of the ingredients in TREMFYA®.

**Before using TREMFYA®, tell your healthcare provider about all of your medical conditions, including if you:**

- have any of the conditions or symptoms listed in the section **“What is the most important information I should know about TREMFYA®?”**
- have an infection that does not go away or that keeps coming back.
- have TB or have been in close contact with someone with TB.
- have recently received or are scheduled to receive an immunization (vaccine). You should avoid receiving live vaccines during treatment with TREMFYA®.
- are pregnant or plan to become pregnant. It is not known if TREMFYA® can harm your unborn baby.

- are breastfeeding or plan to breastfeed. It is not known if TREMFYA<sup>®</sup> passes into your breast milk.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

**What are the possible side effects of TREMFYA<sup>®</sup>?**

**TREMFYA<sup>®</sup> may cause serious side effects. See “What is the most important information I should know about TREMFYA<sup>®</sup>?”**

**The most common side effects of TREMFYA<sup>®</sup> include:** upper respiratory infections, headache, injection site reactions, joint pain (arthralgia), diarrhea, stomach flu (gastroenteritis), fungal skin infections, herpes simplex infections, and bronchitis.

These are not all the possible side effects of TREMFYA<sup>®</sup>. Call your doctor for medical advice about side effects.

Use TREMFYA<sup>®</sup> exactly as your healthcare provider tells you to use it.

**Please read the full [Prescribing Information](#), including [Medication Guide](#) for TREMFYA<sup>®</sup>, and discuss any questions that you have with your doctor.**

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.**  
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**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](http://www.janssen.com). Follow us at [www.twitter.com/JanssenGlobal](https://www.twitter.com/JanssenGlobal).

Janssen Research & Development, LLC is a 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 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 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](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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