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For immediate release

Johnson & Johnson submits application to U.S. FDA seeking approval of TREMFYA® (guselkumab) for the treatment of moderately to severely active Crohn's disease

Submission is supported by 48-week results from the Phase 3 GALAXI and GRAVITI programs

TREMFYA® is the only IL-23 inhibitor to demonstrate strong endoscopic outcomes with subcutaneous (SC) induction, consistent with intravenous (IV) induction, and has the potential to be the first in its class to offer the option of both SC and IV induction therapy in Crohn's disease

GALAXI includes data demonstrating superior outcomes for TREMFYA® versus STELARA® (ustekinumab) in Crohn's disease

SPRING HOUSE, Pa. (June 21, 2024) /PR Newswire/ – Johnson & Johnson (NYSE: JNJ) today announced the submission of a supplemental Biologics License Application (sBLA) to the U.S. Food and Drug Administration (FDA) seeking approval of TREMFYA® (guselkumab) for the treatment of adults with moderately to severely active Crohn's disease. This marks the second submission to the FDA for TREMFYA® in inflammatory bowel disease this year following an application in March for moderately to severely active ulcerative colitis.[a]

The latest submission includes results from the Phase 3 GALAXI program,[1] which was featured as a late-breaking oral presentation at Digestive Disease Week (DDW) 2024 last month.[2] The GALAXI 2 and GALAXI 3 studies were the first-ever double-blind registrational head-to-head trials to demonstrate superiority versus ustekinumab in Crohn's disease.[2] TREMFYA® successfully met the co-primary endpoints for both SC maintenance doses (200 mg every 4 weeks [q4w] and 100 mg every 8 weeks [q8w]) compared to placebo in each individual study and demonstrated superiority to ustekinumab in multiplicity-controlled endoscopic endpoints based on data pooled from both studies.[2]

The submission also includes results from the Phase 3 GRAVITI investigational study of TREMFYA® SC induction therapy in adult patients with moderately to severely active Crohn's disease,[3] which met the co-primary endpoints, achieving statistically significant and clinically meaningful outcomes for clinical remission at Week 12 as well as endoscopic response at Week 12. In addition, all multiplicity-controlled endpoints were met compared to placebo at Week 12, Week 24 and Week 48.[4] The results from GALAXI and GRAVITI show that TREMFYA® has the potential to become the only IL-23 inhibitor to offer both subcutaneous or intravenous induction options for the treatment of Crohn's disease, and, if approved, will offer choice and versatility for patients and providers.[2,4]

"Building upon nearly three decades of leadership and innovation in immunology, we are committed to addressing the needs of people living with Crohn's disease through deep, scientific expertise and through our continued pioneering advances in the IL-23 pathway," said David Lee, M.D., Ph.D., Global Therapeutic Area Head Immunology, Johnson & Johnson Innovative Medicine. "TREMFYA has the potential to be a differentiated treatment option for patients who seek symptom relief and sustained remission. We look forward to working with the Agency in their review of the data supporting the application as we continue to innovate for people living with inflammatory bowel disease."

TREMFYA® is the first approved fully-human, dual-acting monoclonal antibody that blocks IL-23 while also binding to CD64, a receptor on cells that produce IL-23.[5] IL-23 is a cytokine secreted by activated monocyte/macrophages and dendritic cells that is known to be a driver of immune-mediated diseases including Crohn's disease.[6] TREMFYA®, the first-in-class IL-23

inhibitor, received U.S. FDA approval in July 2017 for the treatment of adult patients with moderate-to-severe plaque psoriasis and was subsequently approved for adults with active psoriatic arthritis in July 2020.[5]

Janssen-Cilag International NV, a Johnson & Johnson company, previously announced the submission of applications to the European Medicines Agency (EMA) seeking to expand the Marketing Authorization Application for TREMFYA® to include the treatment of adult patients with moderately to severely active ulcerative colitis and moderately to severely active Crohn's disease.

Editor's Notes:

a. TREMFYA® is not approved to treat ulcerative colitis or Crohn's disease.

ABOUT THE GALAXI PROGRAM (NCT03466411)

GALAXI is a randomized, double-blind, placebo-controlled, active-controlled (ustekinumab), global, multicenter Phase 2/3 program designed to evaluate the efficacy and safety of guselkumab in participants with moderately to severely active Crohn's disease with inadequate response/intolerance to conventional therapies (corticosteroids or immunomodulators) and/or biologics (TNF antagonists or vedolizumab).[1] GALAXI includes a Phase 2 dose-ranging study (GALAXI 1) and two independent, identically designed confirmatory Phase 3 studies (GALAXI 2 and 3).[1] Each GALAXI study employed a treat-through design in which participants remained on the treatment to which they were initially randomized and includes a long-term extension study that will assess clinical, endoscopic, and safety outcomes with guselkumab through a total of five years. Participants randomized to placebo were able to receive ustekinumab if clinical response was not met at Week 12. [1]

ABOUT THE GRAVITI PROGRAM (NCT05197049)

GRAVITI is a randomized, double-blind, placebo-controlled Phase 3 study to evaluate guselkumab SC induction therapy (400 mg at Weeks 0, 4, and 8) in patients with moderately to severely active Crohn's disease who experienced an inadequate response or failed to tolerate conventional therapy (i.e., corticosteroids or immunomodulators) or biologic therapy (TNF antagonists or vedolizumab).[3] The maintenance doses in GRAVITI are the same as those evaluated in GALAXI (200 mg SC q4w and 100 mg SC q8w).[3] The study employed a treat-through design, in which patients are randomized to guselkumab at Week 0 and remain on that regimen throughout the study, regardless of clinical response status at the end of induction.[3] Participants randomized to placebo were able to receive guselkumab (400 mg SC q4w x3 ➔ 100 mg SC q8w) if rescue criteria were met at Week 16.[3]

ABOUT CROHN'S DISEASE

Crohn's disease is one of the two main forms of inflammatory bowel disease, which affects an estimated three million Americans and an estimated four million people across Europe.[7,8] Crohn's disease is a chronic inflammatory condition of the gastrointestinal tract with no known cause, but the disease is associated with abnormalities of the immune system that could be triggered by a genetic predisposition, diet, or other environmental factors.[9] Symptoms of Crohn's disease can vary, but often include abdominal pain and tenderness, frequent diarrhea, rectal bleeding, weight loss, and fever. Currently no cure is available for Crohn's disease.[10]

ABOUT TREMFYA® (guselkumab)

Developed by Johnson & Johnson, TREMFYA® is the first approved fully-human, dual-acting monoclonal antibody that blocks IL-23 by binding to the p19 subunit of IL-23 and binding to CD64, a receptor on cells that produce IL-23.[3] IL-23 is an important driver of the pathogenesis of inflammatory diseases.[5] Findings for dual-acting are limited to in vitro studies that demonstrate guselkumab binds to CD64, which is expressed on the surface of IL-23 producing cells in an inflammatory monocyte model. The clinical significance of this finding is not known.[11,12,13,14]

TREMFYA® is approved in the U.S.,[5] Canada,[15] Japan[16] and a number of other countries for the treatment of adults with moderate-to-severe plaque psoriasis (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 psoriatic arthritis (PsA).[17] 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.[17]

Johnson & Johnson maintains exclusive worldwide marketing rights to TREMFYA®.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about TREMFYA® (guselkumab)?

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 use 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® 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®?

TREMFYA® may cause serious side effects. See "What is the most important information I should know about TREMFYA®?"

The most common side effects of TREMFYA® 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®. Call your doctor for medical advice about side effects.

Use TREMFYA® exactly as your healthcare provider tells you to use it.

Please read the full Prescribing Information, including Medication Guide for TREMFYA®, 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 or call 1-800-FDA-1088.

ABOUT STELARA® (ustekinumab)
STELARA® (ustekinumab), a human interleukin (IL)-12 and IL-23 antagonist, is approved in the United States for the treatment of: 1) adults and children six years and older with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy; 2) adults and children six years and older with active psoriatic arthritis; 3) adult patients (18 years and older) with moderately to severely active Crohn's disease; 4) adult patients (18 years and older) with moderately to severely active ulcerative colitis.[18]

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

IMPORTANT SAFETY INFORMATION

STELARA® is a prescription medicine that affects your immune system. STELARA® can increase your chance of having serious side effects including:

Serious Infections

STELARA® may lower your ability to fight infections and may increase your risk of infections. While taking STELARA®, some people have serious infections, which may require hospitalization, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses.

- Your doctor should check you for TB before starting STELARA® and watch you closely for signs and symptoms of TB during treatment with STELARA®.

- If your doctor feels that you are at risk for TB, you may be treated for TB before and during treatment with STELARA®.

You should not start taking STELARA® if you have any kind of infection unless your doctor says it is okay.

Before starting STELARA®, tell your doctor if you:

- think you have an infection or have symptoms of an infection such as:
  - fever, sweats, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in phlegm
  - weight loss
  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal
  - feel very tired
- are being treated for an infection or have any open cuts.
- get a lot of infections or have infections that keep coming back.
- have TB, or have been in close contact with someone with TB.

After starting STELARA®, call your doctor right away if you have any symptoms of an infection (see above). These may be signs of infections such as chest infections, or skin infections or shingles that could have serious complications. STELARA® can make you more likely to get infections or make an infection that you have worse. People who have a genetic problem where the body does not make any of the proteins interleukin 12 (IL-12) and interleukin 23 (IL-23) are at a higher risk for certain serious infections that can spread throughout the body and cause death. People who take STELARA® may also be more likely to get these infections.

Cancers

STELARA® may decrease the activity of your immune system and increase your risk for certain types of cancer. Tell your doctor if you have ever had any type of cancer. Some people who had risk factors for skin cancer developed certain types of skin cancers while receiving STELARA®. Tell your doctor if you have any new skin growths.

Posterior Reversible Encephalopathy Syndrome (PRES)

PRES is a rare condition that affects the brain and can cause death. The cause of PRES is not known. If PRES is found early and treated, most people recover. Tell your doctor right away if you have any new or worsening medical problems including: headache, seizures, confusion, and vision problems.

Serious Allergic Reactions

Serious allergic reactions can occur. Stop using STELARA® and get medical help right away if you have any symptoms of a serious allergic reaction such as: feeling faint, swelling of your face, eyelids, tongue, or throat, chest tightness, or skin rash.

Lung Inflammation

Cases of lung inflammation have happened in some people who receive STELARA® and may be serious. These lung problems may need to be treated in a hospital. Tell your doctor right away if you develop shortness of breath or a cough that doesn't go away during treatment with STELARA®.

Before receiving STELARA®, tell your doctor about all of your medical conditions, including if you:

- have any of the conditions or symptoms listed above for serious infections, cancers, or PRES.
- ever had an allergic reaction to STELARA® or any of its ingredients. Ask your doctor if you are not sure.
- are allergic to latex. The needle cover on the prefilled syringe contains latex.
- have recently received or are scheduled to receive an immunization (vaccine). People who take STELARA® should not receive live vaccines. Tell your doctor if anyone in your house needs a live vaccine. The viruses used in some types of live vaccines can spread to people with a weakened immune system, and can cause serious problems. **You should not receive the BCG vaccine during the one year before receiving STELARA® or one year after you stop receiving STELARA®.**
- have any new or changing lesions within psoriasis areas or on normal skin.
- are receiving or have received allergy shots, especially for serious allergic reactions.
- receive or have received phototherapy for your psoriasis.
- are pregnant or plan to become pregnant. It is not known if STELARA® can harm your unborn baby. You and your doctor should decide if you will receive STELARA® if you are breastfeeding or plan to breastfeed. It is thought that STELARA® passes into your breast milk.
- talk to your doctor about the best way to feed your baby if you receive STELARA®.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

When prescribed STELARA®:

- Use STELARA® exactly as your doctor tells you to.

- STELARA® is intended for use under the guidance and supervision of your doctor. In children 6 years and older, it is recommended that STELARA® be administered by a healthcare provider. If your doctor decides that you or a caregiver may give your injections of STELARA® at home, you should receive training on the right way to prepare and inject STELARA®. Your doctor will determine the right dose of STELARA® for you, the amount for each injection, and how often you should receive it. Do not try to inject STELARA® yourself until you or your caregiver have been shown how to inject STELARA® by your doctor or nurse.

Common side effects of STELARA® include: nasal congestion, sore throat, and runny nose, upper respiratory infections, fever, headache, tiredness, itching, nausea and vomiting, redness at the injection site, vaginal yeast infections, urinary tract infections, sinus infection, bronchitis, diarrhea, stomach pain, and joint pain. These are not all of the possible side effects with STELARA®. Tell your doctor about any side effect that you experience. Ask your doctor or pharmacist for more information.

Please click to read the full Prescribing Information and Medication Guide for STELARA® and discuss any questions you have with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

ABOUT JOHNSON & JOHNSON

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at https://www.jnj.com/ or at www.janssen.com/johnson-johnson-innovative-medicine. Follow us at @JNJInnovMed. Janssen Research & Development, LLC, Janssen Biotech, Inc. and Janssen-Cilag International NV are Johnson & Johnson companies.

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®. 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, Janssen Biotech, Inc., Janssen-Cilag International NV 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 December 31, 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 Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen-Cilag International NV nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

Source: Johnson & Johnson

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1. National Institutes of Health: Clinicaltrials.gov. A study of the efficacy and safety of guselkumab in participants with moderately to severely active Crohn's disease (GALAXI). Identifier: NCT03466411. Available at: https://clinicaltrials.gov/study/NCT03466411. Accessed June 2024.
2. Panaccione, R et al. Efficacy and safety of guselkumab therapy in patients with moderately to severely active Crohn's disease: results of the GALAXI 2 & 3 Phase 3 studies. Oral presentation (Abstract #1057b) at Digestive Disease Week (DDW) 2024. May 2024.
3. National Institutes of Health: Clinicaltrials.gov. A study of guselkumab subcutaneous therapy in participants with moderately to severely active Crohn's disease (GRAVITI). Identifier: NCT05197049. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT05197049. Accessed June 2024.
4. Data on file. Guselkumab. Clinical study report CNTO1959CRD3004 (GRAVITI).
5. US Food and Drug Administration. TREMFYA® prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761061s007lbl.pdf. Accessed June 2024.
6. Schinocca, C. et al. Role of the IL-23/IL-17 pathway in rheumatic diseases: an overview. Frontiers in immunology. 2021 Feb 22;12:321. Available at: https://doi.org/10.3389/fimmu.2021.637829. Accessed June 2024.
7. Crohn's & Colitis Foundation. Overview of Crohn's disease. Available at: https://www.crohnscolitisfoundation.org/what-is-crohns-disease/overview. Accessed June 2024.
8. Ng SC, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. The Lancet. 2017;390:2769-78.
9. Crohn's & Colitis Foundation. What is Crohn's disease? Available at: https://www.crohnscolitisfoundation.org/what-is-crohns-disease/causes. Accessed June 2024.
10. Crohn's & Colitis Foundation. Signs and symptoms of Crohn's disease. Available at: https://www.crohnscolitisfoundation.org/what-is-crohns-disease/symptoms. Accessed June 2024.
11. Mehta H, et al. Differential changes in inflammatory mononuclear phagocyte and T-Cell profiles within psoriatic skin during treatment with guselkumab vs. secukinumab. J Invest Dermatol 2021;141(7):1707-1718. Available at: https://pubmed.ncbi.nlm.nih.gov/33524368/. Accessed June 2024.
12. Wang Y, et al. Monocytes/Macrophages play a pathogenic role in IL-23 mediated psoriasis-like skin inflammation. Sci Rep. 2019;9(1):5310. Available at: https://pubmed.ncbi.nlm.nih.gov/30926837/. Accessed June 2024.
13. Matt P, et al. Up-regulation of CD64-expressing monocytes with impaired FcγR function reflects disease activity in polyarticular psoriatic arthritis. Scand J Rheumatol 2015; 44(6):464-473. Available at: https://pubmed.ncbi.nlm.nih.gov/26084203/. Accessed June 2024.

14. McGonagle D, et al. Guselkumab, an IL-23p19 subunit–specific monoclonal antibody, binds CD64+ myeloid cells and potently neutralises IL-23 produced from the same cells. Presented at EULAR 2023, May 31-June 3.
15. The Canadian Agency for Drugs & Technologies in Health. TREMFYA® prescribing information. Available at: https://www.cadth.ca/guselkumab-0. Accessed June 2024.
16. Japan Pharmaceuticals and Medical Devices Agency. Tremfya report on the deliberation results. Available at: https://www.pmda.go.jp/files/000234741.pdf. Accessed June 2024.
17. European Commission: Tremfya (guselkumab). Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/tremfya. Accessed June 2024.
18. US Food and Drug Administration. STELARA® prescribing information. Available at: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/STELARA-pi.pdf. Accessed June 2024.