TREMFYA® (guselkumab) molecular differentiation overview

TREMFYA® is an IL-23i indicated for the treatment of adults with[1a]: Moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy; Active psoriatic arthritis

Inflammatory conditions have similarities at the cellular and clinical levels

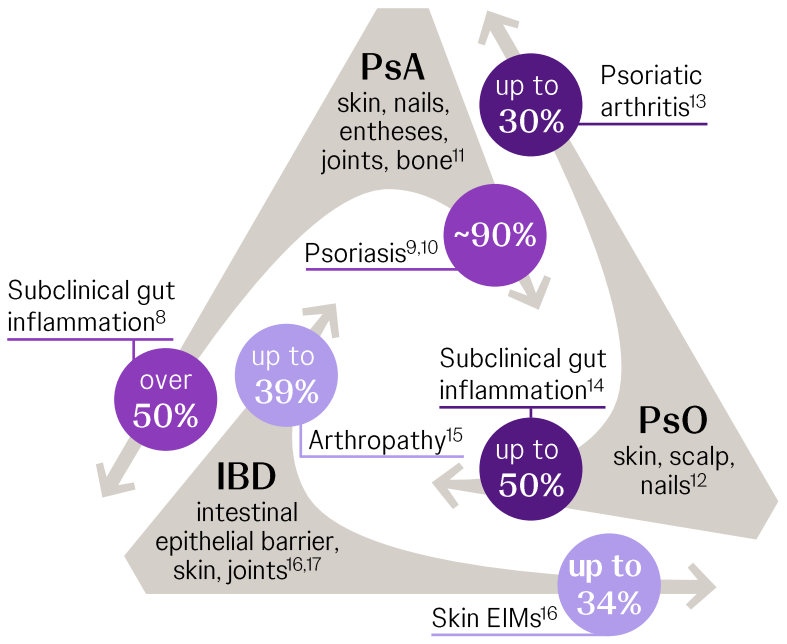
CD64+ myeloid cells are enriched in inflamed tissue across IL-23 mediated inflammatory conditions

PsO[2,3] PsA[4] IBD[5-7]

Individuals with IBD are more likely than the general population to have or develop:

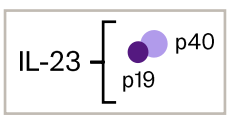
- Rheumatoid Arthritis[18]
- Multiple Sclerosis[19]
- Ankylosing Spondylitis[15]
- Others[15]

Inflammatory conditions are complex and may present with extra-intestinal, extra-articular, and extra-cutaneous manifestations



Guselkumab is the only fully human dual-acting, selective IL-23 inhibitor designed to neutralize inflammation at its cellular source[20-25b,c]

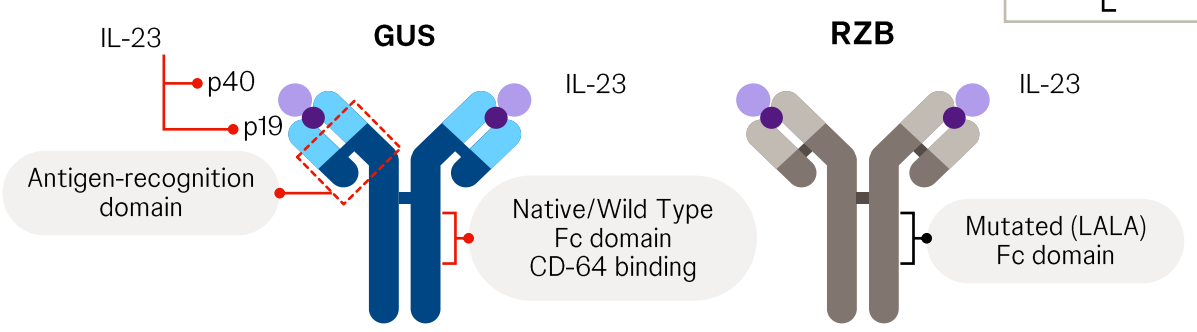
IL-23-producing CD64+ myeloid cells are increased in inflamed tissues in patients with IL-23-mediated inflammatory diseases[26-29]



Unique molecular attributes

GUS and RZB are mAbs directed against the p19 subunit of IL-23.[24, 30-33]

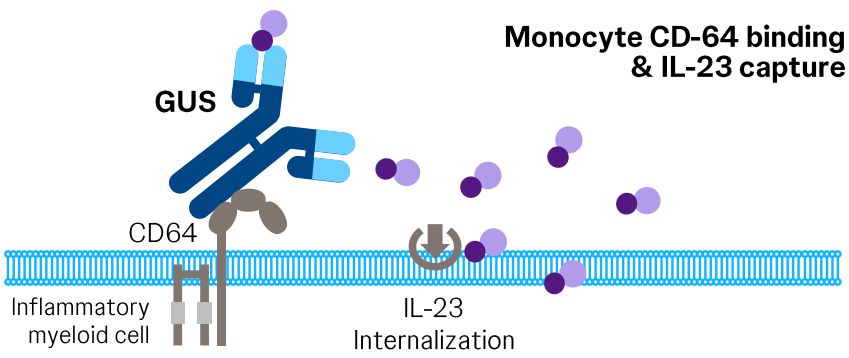
GUS is a fully human IgG 1 mAB with a native Fc region, and RZB is a humanized IgG1 mAB with a modified Fc domain[33]



CD64 binding and IL-23 capture

GUS binds to CD64 on inflammatory monocytes, while RZB does not, because of its modified Fc domain with LALA mutations.[24, 30-32]

GUS binds IL-23 with high affinity, neutralizes IL-23 with high potency, and exhibits capture of IL-23 when bound to CD64[34]



Figures adapted from Eyerich K, et al EADV 2023 annual meeting presentation.

By binding to CD64, GUS may be enriched in inflamed tissue, which may help explain the maintenance of clinical response and therapeutic differences within the IL-23i class. Further studies are needed to support this hypothesis.[24]

Target tissue enrichment

Binds at the source of inflammation (in vitro)

GUS is the only fully human dual-acting, selective IL-23i that both blocks IL-23 with high affinity and potency and binds CD64, thereby neutralizing IL-23 locally at the source of inflammation.[27]

Future considerations for TREMFYA®: patient populations in select ongoing phase 3 and 4 trials

PsO

VISIBLE:
Adults with skin of color, moderate-to-severe plaque PsO, and/or scalp PsO[35]

SPECTREM:
Adults with bio-naïve, low BSA moderate plaque PsO and special site involvement[36]

Active PsA

APEX:
Adults who are bio-naïve with active PsA and inhibiting radiographic progression[37]

STAR:
Adults who are bio-naïve with active PsA axial disease[38]

SOLSTICE:
Adult patients with active PsA and inadequate response or intolerance to a prior anti-TNFα[39]

Moderately to severely active IBD

GALAXI and GRAVITI:
Adults with CD[30,41]

QUASAR and ASTRO:
Adult patients with UC[42,43]

The safety and efficacy of the investigational uses of this product have not been determined. There is no guarantee that the investigational uses listed will be filed with and/or approved for marketing by the FDA.

For more information on ongoing trials, go to ClinicalTrials.gov. For additional information, please see TREMFYA® Prescribing Information here.

[a]TREMFYA® Dosing: 100 mg SC Weeks 0, 4, and q8w thereafter. [b]**The clinical significance of these findings is not known.** [c]Based on approved IL-23 inhibitors for moderate to severe plaque PsO, active PsA or moderately to severely active CD or UC as of March 2024.

BSA, body surface area; CD, Crohn's Disease; CD64, cluster of differentiation 64; EADV, European Academy of Dermatology and Venereology; EIM, extraintestinal manifestations; Fc, fragment crystallizable region; GUS, guselkumab; IBD, inflammatory bowel disease; IL-23, interleukin-23; IL-23i, interleukin-23 inhibitor; LALA, Leu234Ala and Leu235Ala mutations; mAb, monoclonal antibody; PsA, psoriatic arthritis; PsO, psoriasis; RZB, Risankizumab; TNF, tumor necrosis factor; TNFα, tumor necrosis factor alpha; UC, ulcerative colitis.

1. TREMFYA® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 2. Mehta H, et al. *J Invest Dermatol.* 2021;141(7):1707-1718.e9. 3. Wang Y, et al. *Sci Rep.* 2019;9(1):5310. 4. Matt P, et al. *Scand J Rheumatol.* 2015;44(6):464-473. 5. Chapuy L, et al. *Mucosal Immunol.* 2019;12(3):703-719. 6. Chapuy L, et al. *J Crohns Colitis.* 2020;14(1):79-95. 7. Kamada N, et al. *J Clin Invest.* 2008;118(6):2269-80. 8. Scher J, *J Rheum Suppl.* 2018;94:32-35. 9. Ciocon D, Kimball A. *Br J Dermatol.* 2007;157(5):850-860. 10. Pennington SR, et al. *Front Med (Lausanne).* 2021;8:723944. 11. Suzuki E, et al. *Autoimmunity Rev.* 2014;13:496-502. 12. Lowes M, et al. *Annu Rev Immunol.* 2014;32:227-255. 13. Mease P, et al. *J Am Acad Dermatol.* 2013;69(5):729-735. 14. Sanchez I, et al. *Curr Dermatol Rep.* 2018;7(1):59-74. 15. Arvikar S, et al. *Curr Rev Musculoskel Med.* 2011;4(3):123-131. 17. Levine J, et al. *Gastroenterol Hepatol.* 2011;7:235-241. 18. Matricon J, et al. *Self/NonSelf.* 2010;1:299-309. 19. Chen Y, et al. *BMC Gastroenterol.* 2020;20(1):192. 20. Wang X, et al. *Ann Clin Transl Neurol.* 2022;9(2):132-140. 21. Wojtal K, et al. *PLoS One.* 2012;7(8):e43361. 22. Vos AC, et al. *Gastroenterology.* 2011;140(1):221-230. 23. Louis E, et al. *Aliment Pharmacol Ther.* 2004;19(5):511-519. 24. Abreu M, et al. DDW 2023. Oral Presentation #3856970. 25. Krueger J, et al. ISID 2023. Poster #1591. 26. Bsat M, et al. *Eur J Immunol.* 2020;50(11):1676-1690. 27. Mehta H, et al. *J Invest Dermatol.* 2021;141(7):1707-1718.e9. 28. Chapuy L, et al. *Mucosal Immunol.* 2019;12(3):703-719. 29. Chapuy L, et al. *J Crohns Colitis.* 2020;14(1):79-95. 30. Kamada N, et al. *J Clin Invest.* 2008;118(6):2269-80. 31. Krueger J, et al. Poster #LB989 Presented at SID 2022; Portland, OR; May 18-21, 2022. 32. Atreya R, et al. ECCO 2023. Poster #P504. 33. Eyerich K, et al. AAD 2023. Poster #43272. 34. Eyerich K, et al. EADV 2023. Poster #0713. 35. VISIBLE NCT05272150. 36. SPECTREM NCT06039189. 37. APEX NCT04882098. 38. STAR NCT04929210. 39. SOLSTICE NCT04936308. 40. GALAXI NCT03466411. 41. GRAVITI NCT05197049. 42. QUASAR NCT04033445. 43. ASTRO NCT05528510.

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US-SFM-6124 04/24