Inhibition of Structural Damage Progression With Guselkumab, a Selective IL-23i, in Participants With Active PsA:

Results Through Week 24 of the Phase 3b, Randomized, Double-Blind, Placebo-Controlled APEX Study

Philip J Mease[1,2], Christopher T Ritchlin[3], Laura C Coates[4], Alexa P Kollmeier[5], Bei Zhou[6], Yusang Jiang[6], Karen Bensley[6], Koeun Im[7], Rattandeep Batra[8], Soumya D Chakravarty[9,10], Proton Rahman[11], Désirée van der Heijde[12]

[1]Rheumatology Research, Providence Swedish Medical Center, Seattle, WA, USA; [2]University of Washington School of Medicine, Seattle, WA, USA [3]Department of Medicine, Allergy/Immunology and Rheumatology, University of Rochester Medical Center, Rochester, NY, USA; [4]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre, Oxford, UK; [5]Johnson & Johnson, LLC, San Diego, CA, USA; [6]Johnson & Johnson, LLC, Spring House, PA, USA; [7]Johnson & Johnson, LLC, Cambridge, MA, USA; [8]Johnson & Johnson, Inc., Toronto, Canada; [9]Johnson & Johnson, Horsham, PA, USA; [10]Drexel University College of Medicine, Philadelphia, PA, USA; [11]Craig L Dobbin Genetics Research Centre, Faculty of Medicine, Division of Rheumatology, Memorial University of Newfoundland, St. Johns, NL, Canada; [12]Leiden University Medical Center, Leiden, The Netherlands.

Background

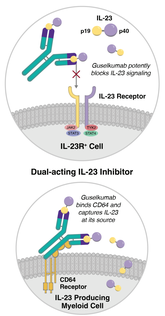
Psoriatic arthritis (PsA), a chronic, heterogeneous, inflammatory disease affecting joints and skin, can substantially impact health-related quality of life[1,2]

- Structural damage resulting from chronic inflammation leads to poorer outcomes[3]

Guselkumab (GUS) is a fully human, dual-acting, monoclonal antibody that selectively inhibits the interleukin (IL)-23p19 subunit[4]

- Indicated to treat moderate-to-severe plaque psoriasis (PsO), active PsA, and moderately-to-severely active Crohn's disease and ulcerative colitis[5]

In DISCOVER-2, biologic-naïve participants (pts) with active PsA receiving GUS every 4 weeks (Q4W) exhibited significantly less radiographic progression vs placebo (PBO); the lower rate of radiographic progression seen with GUS every 8 weeks (Q8W) vs PBO did not reach statistical significance[6]



Objectives

Report findings through W24 of the ongoing Phase 3b, randomized, double-blind, placebo-controlled APEX study (NCT04882098), intended to further evaluate GUS effects on clinical and radiographic progression outcomes in pts with active PsA

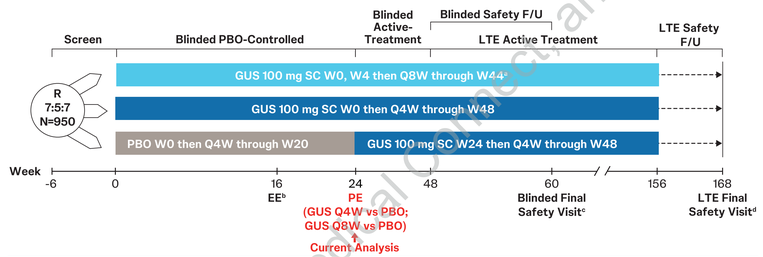
APEX Study Design

Inclusion Criteria

- ✓ Biologic-naive
- ✓ Age ≥18 years
- ✓ Active PsA ≥6 months (despite prior csDMARD, apremilast, NSAID); CASPAR criteria met
- ✓ ≥3 SJC; ≥3 TJC; CRP ≥0.3 mg/dL
- ✓ **≥2 erosive joints on hand/foot radiographs**
- ✓ Active plaque PsO (≥1 PsO plaque ≥2 cm and/or nail PsO)

Multiplicity-Controlled Endpoints

- **Primary:** ACR20 response at W24
- **Major Secondary:** Mean change in total PsA-modified vdH-S score at W24



- **Modified full analysis set (mFAS):** All randomized pts excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions; employed as the main efficacy analysis set (N=1020)
- **Safety analysis set:** All pts who received ≥1 administration of any study intervention (N=1054)

[a]*PBO SC W8 then Q8W through W48 administered to maintain blinding.* [b]*EE if <20% improvement from BL in both TJC and SJC at W16. EE pts may initiate/increase dose permitted medication up to the maximum dose, at the investigator's discretion.* [c]*Final safety visit for those who do not enter LTE.* [d]*Final safety visit for those who entered LTE.* ***ACR****=American College of Rheumatology,* ***BL****=baseline,* ***CASPAR****=CASsification criteria for Psoriatic ARthritis,* ***CRP****=C-reactive protein,* ***csDMARD****=conventional synthetic disease modifying antirheumatic drug,* ***EE****=early escape,* ***F/U****=follow-up,* ***LTE****=long-term extension,* ***NSAID****=nonsteroidal anti-inflammatory drug,* ***PE****=primary endpoint,* ***R****=randomization,* ***SC****=subcutaneous,* ***SJC****=swollen joint count,* ***TJC****=tender joint count,* ***vdH-S****=van der Heijde-Sharp.*

Key Takeaways

- ✓ **At W24 of the ongoing Phase 3b APEX study of GUS, a dual-acting selective IL-23i for PsA, the Q4W & Q8W regimens demonstrated:**
  - ✓ **Significantly higher ACR20 response rates vs PBO**
  - ✓ **Significantly lower rates of radiographic progression (Δ GUS vs PBO = -0.80)**
  - ✓ **Consistent effects on erosion & JSN scores**
  - ✓ **Higher proportion of pts with no progression of structural damage vs PBO**
  - ✓ **Higher rates of ACR50, ACR70, PASI 90 & greater improvement in physical function vs PBO; Similar AE profile for GUS and PBO; No new GUS safety signal**
- ✓ **GUS is the only selective IL-23i to demonstrate significant inhibition of structural damage progression**

Results

Characteristics of APEX pts with active and erosive PsA were comparable across groups

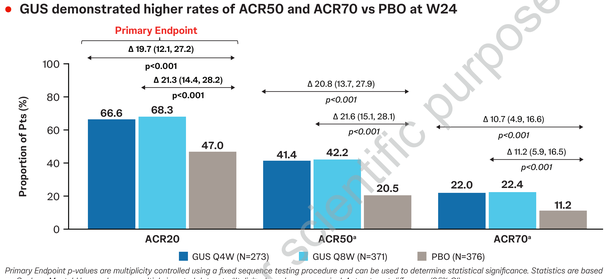
- **Background PsA medication use and treatment completion through W24 (96-97%) were consistent across treatment groups**

	GUS Q4W (N=273)	GUS Q8W (N=371)	PBO (N=376)	Total (N=1020)
Baseline Demographics				
Age, years	52.2 (13.2)	53.2 (12.9)	53.5 (13.0)	53.0 (13.0)
Male	55%	54%	57%	55%
Weight, kg	85.6 (20.1)	83.2 (17.4)	83.1 (18.2)	83.8 (18.5)
BMI, kg/m^2	29.4 (6.0)	29.0 (5.6)	28.9 (5.7)	29.1 (5.7)
PsA Characteristics				
PsA disease duration, years	7.5 (7.1)	7.2 (7.6)	7.2 (6.9)	7.3 (7.2)
SJC [0-66][a]	9.0 (6.0; 14.0)	10.0 (6.0; 14.0)	9.0 (6.0; 15.0)	9.0 (6.0; 14.0)
TJC [0-68][a]	16.0 (10.0; 27.0)	17.0 (11.0; 26.0)	16.6 (10.0; 25.5)	16.1 (10.0; 26.0)
HAQ-DI [0-3]	1.2 (0.7)	1.2 (0.6)	1.2 (0.6)	1.2 (0.7)
CRP, mg/dL[a]	0.7 (0.4; 1.5)	0.8 (0.4; 1.6)	0.8 (0.4; 1.8)	0.8 (0.4; 1.6)
Enthesitis / Dactylitis	58% / 44%	59% / 39%	59% / 45%	58% / 43%
Mean LEI [1-6] / DSS [1-60]	3.2 / 10.8	3.0 / 11.0	3.0 / 10.2	3.1 / 10.6
PsO Characteristics				
% BSA	15.0 (19.2)	16.5 (21.9)	16.3 (21.5)	16.0 (21.0)
PASI [0-72]	7.6 (8.3)	8.3 (10.1)	8.2 (9.5)	8.1 (9.4)
Radiographic Characteristics				
PsA-modified vdH-S score [0-528]	27.7 (47.6)	26.7 (43.4)	26.8 (42.2)	27.0 (44.1)
Erosion score [0-320]	13.7 (24.3)	13.4 (21.9)	13.4 (20.7)	13.5 (22.1)
JSN score [0-208]	14.0 (24.2)	13.3 (22.8)	13.4 (22.4)	13.5 (23.0)

Values are reported as mean (SD) unless otherwise noted. [a]*Values are median (IQR).* ***BMI****=Body Mass Index,* ***BSA****=body surface area,* ***DSS****=Dactylitis Severity Score,* ***HAQ-DI****=Health Assessment Questionnaire-Disability Index,* ***IQR****=interquartile range,* ***JSN****=joint space narrowing,* ***LEI****=Leeds Enthesitis Index,* ***PASI****=Psoriasis Area and Severity Index,* ***SD****=standard deviation.*

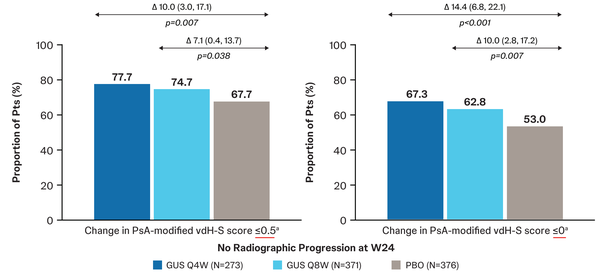
GUS demonstrated significantly higher ACR20 response rates vs PBO at W24

- **GUS demonstrated higher rates of ACR50 and ACR70 vs PBO at W24**



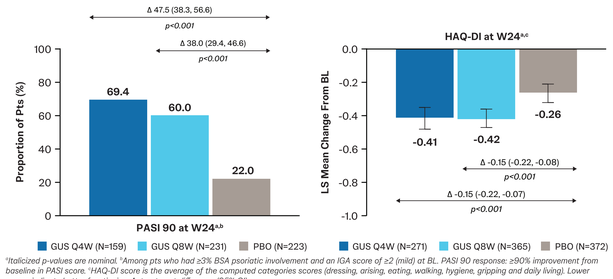
Primary Endpoint p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on Cochran-Mantel-Haenszel across multiply imputed datasets. [a]*Italicized p-values are nominal. Δ=treatment difference (95% CI).*

Higher proportions of GUS vs PBO-treated pts showed no radiographic progression



[a]*Italicized p-values are nominal. Δ=treatment difference (95% CI).*

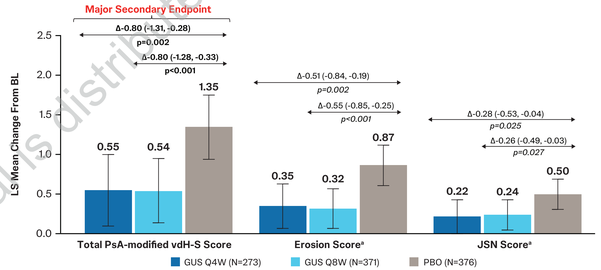
Higher skin clearance rates and greater improvement in physical function with GUS vs PBO



[a]*Italicized p-values are nominal.* [b]*Among pts who had ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at BL. PASI 90 response: ≥90% improvement from baseline in PASI score.* [c]*HAQ-DI score is the average of the computed categories scores (dressing, arising, eating, walking, hygiene, gripping and daily living). Lower scores indicate better functioning. Δ=treatment difference (95% CI).*

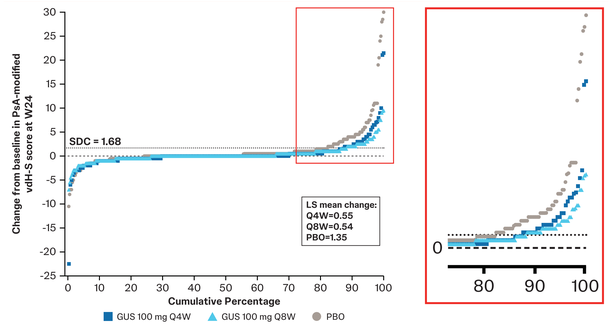
GUS exhibited significantly lower rates of radiographic progression vs PBO at W24

- **GUS exhibited consistent treatment effects for both erosion and JSN scores**



Major secondary endpoint (PsA-modified vdH-S score) p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on analysis of covariance across multiply imputed datasets. [a]*Italicized p-values are nominal. Δ=treatment difference (95% CI).* ***LS****=least squares.*

Pt-level data also showed clear separation between GUS and PBO



GUS AE profile through W24 was similar to PBO

Safety Through W24	GUS Q4W (N=280)	GUS Q8W (N=388)	PBO (N=386)
Mean weeks of follow up	24.0	23.9	23.8
Pts with ≥1:			
AE	107 (38.2%)	165 (42.5%)	144 (37.3%)
SAE	5 (1.8%)	12 (3.1%)	10 (2.6%)
AE leading to study agent d/c	2 (0.7%)	6 (1.5%)	1 (0.3%)
Infection	52 (18.6%)	91 (23.5%)	81 (21.0%)
Serious infection	2 (0.7%)	5 (1.3%)	1 (0.3%)
Active tuberculosis	0	0	0
Opportunistic infection	0	0	0
Venous thromboembolism event	1 (0.4%)	1 (0.3%)	1 (0.3%)
Anaphylactic or serum sickness reaction	0	0	0
Clinically important hepatic disorder[a]	0	0	0

Safety analysis set. AEs are coded using MedDRA Version 27.0. Data are n (%) unless otherwise noted. [a]*Clinically important hepatic disorders were prespecified as AE terms within the Medical Dictionary for Regulatory Activities category of Drug-Related Hepatic Disorders that met the criteria for an SAE or led to study agent d/c.* ***AE****=adverse event,* ***d/c****=discontinuation,* ***IBD****=inflammatory bowel disease,* ***MACE****=major adverse cardiovascular event,* ***SAE****=serious AE.*

- **Study remains blinded through W48**
- **2 pts with malignancy (prostate, renal); 1 MACE (myocardial infarction); 1 COVID-19 death in unvaccinated elderly pt**
- **No new-onset IBD**

REFERENCES: 1. Gladman DD, et al. *Q J Med.* 1987;62:127-41. **2.** Ritchlin CT, *J Rheumatol.* 2008;35:1434-7. **3.** van der Heijde D, et al. *Arthritis Res Ther.* 2020;22:18. **4.** Sachen KL, et al. *Front Immunol.* 2025;16:1532852. **5.** Janssen Biotech, Inc. *US FDA website.* Revised March 2025. **6.** Mease PJ, et al. *Lancet.* 2020;395:1126-36. **ACKNOWLEDGMENTS:** Medical writing support was provided by Mona Patel, PharmD, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298-1304). This study was sponsored by Johnson & Johnson. **DISCLOSURES: PJM:** Grants: AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Johnson & Johnson, Novartis, and UCB; Consultant: AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Century, Cullinan, Eli Lilly, Immagene, Johnson & Johnson, Novartis, Pfizer, Spyre, Takeda, and UCB; Speaker: AbbVie, Amgen, Eli Lilly, Johnson & Johnson, Novartis, Pfizer, and UCB. **CTR:** Grants: AbbVie, Amgen, UCB; Consultant: AbbVie, Amgen, Eli Lilly, Gilead, Johnson & Johnson, Novartis, Pfizer, and UCB. **LCD:** Grants: AbbVie, Amgen, Celgene, Eli Lilly, Johnson & Johnson, Novartis, Pfizer and UCB; Consultant: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Johnson & Johnson, Moonlake, Novartis, Pfizer, and UCB; Speaker: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Johnson & Johnson, Medac, Novartis, Pfizer, and UCB. **APK, BZ, YJ, KB, KI, RB,** and **SDC:** Employees of Johnson & Johnson; employees may own stock/stock options in Johnson & Johnson. **PR:** Consultant: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Johnson & Johnson, Merck, Novartis, Pfizer, and UCB; Grants: Johnson & Johnson and Novartis. **DvdH:** Consultant: AbbVie, Alfasigma, ArgenX, Bristol Myers Squibb, Eli Lilly, Grey-Wolf Therapeutics, Johnson & Johnson, Novartis, Pfizer, Takeda, and UCB; and is associate editor of Annals Rheumatic Diseases, editorial board member of Journal of Rheumatology, and director of Imaging Rheumatology BV.