Pharmacodynamic Biomarkers in Biologic-Naïve Participants With Active and Erosive Psoriatic Arthritis: Results Through Week 48 From the Phase 3 APEX Study

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Key Takeaways

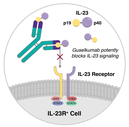
- **In the phase 3 APEX study of biologic-naïve adults with active and erosive PsA:**
  - **PsA-relevant biomarkers were elevated at baseline vs HVs**
    - **Th17 cytokine levels correlated with skin manifestations and inflammatory markers with joint disease, consistent with prior studies[6,7]**
  - **GUS demonstrated early (W4) and significant reductions in serum Th17 cytokines and inflammatory markers through W24 vs PBO**
  - **Reductions in examined biomarkers were durable with continued GUS through W48**
- **These findings provide molecular evidence supporting clinical observations of disease activity improvements with GUS across multiple PsA domains**

Background

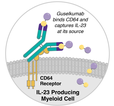
Psoriatic arthritis (PsA) is a chronic, heterogeneous, inflammatory disease affecting joints and skin, in which uncontrolled inflammation can lead to progressive structural joint damage[1]

Guselkumab (GUS)

- Fully human, dual-acting monoclonal antibody able to inhibit the interleukin (IL)-23p19 subunit and bind the CD64 receptor[2]
- Approved for adults and pediatric patients (≥6 years, ≥40 kg) with active PsA or moderate-to-severe plaque psoriasis (PsO), and adults with moderately-to-severely active Crohn's disease or ulcerative colitis[3]



Dual-acting IL-23 Inhibitor



APEX (NCT04882098)

- Ongoing phase 3b, randomized, double-blind, placebo (PBO)-controlled study assessing GUS effects on clinical outcomes and radiographic progression in biologic-naïve adults with active and erosive PsA[4]
- Met primary (≥20% improvement in American College of Rheumatology [ACR20]) and major secondary (PsA-modified van der Heijde-Sharp [vdH-S] score change from baseline) endpoints at Week (W)24 with durable responses through W48[4,5]

Objectives

Evaluate baseline relationships between clinical/radiographic characteristics and disease-relevant serum biomarkers, and assess the magnitude and durability of pharmacodynamic (PD) effects of GUS treatment in APEX participants (pts)

Methods

APEX – Study Design

- **Modified full analysis set (mFAS):** All APEX randomized pts (N=1020) excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions; employed as the main efficacy analysis set

Key Inclusion Criteria:

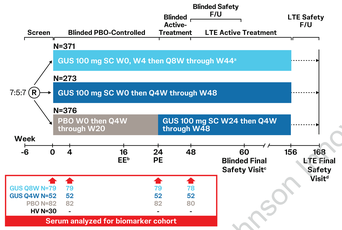
- ≥18 years, biologic-naïve
- Active PsA for ≥6 months (despite prior csDMARDs, apremilast, NSAIDs); CASPAR met
  - ≥3 SJC; ≥3 TJC; CRP ≥0.3 mg/dL
- ≥2 erosive joints on hand/foot radiographs
- Active plaque PsO
  - ≥1 PsO plaque ≥2 cm and/or nail PsO

Biomarker Cohort

- Representative of APEX mFAS, with serum collected for biomarker analyses (N=213)

HVs

- Age- and sex-matched samples (N=30) collected independently of APEX for comparative analysis use



Assessments & Analyses

Assessments	Analyses
PD effects through W48 • Serum Th17 cytokines: – Assessed using single molecule counting immunoassays: IL-17A, IL-17F and IL-22 • General inflammation markers: – Assessed using Meso-Scale Discovery immunoassays: CRP, IL-6, SAA	Non-parametric Wilcoxon rank-sum exact test for: • Log_2 serum level at baseline in pts with PsA (biomarker cohort) vs HVs • Mean log_2 change from baseline for: – GUS treatment groups through W48 – GUS vs PBO through W24
Baseline relationship between clinical/radiographic characteristics and serum biomarkers • Clinical/radiographic characteristics: – Joint disease activity: SJC, TJC, Patient Pain VAS, HAQ-DI, PhGA, DAS28, dactylitis, enthesitis – Skin disease activity: IGA score, PASI score – Structural damage progression: PsA-modified vdH-S score • Th17 cytokines: IL-17A, IL-17F, IL-22 • General inflammation markers: CRP, IL-6, SAA	Pearson correlation for: • Correlations between characteristic and baseline biomarker levels at baseline – Significance criteria: p≤0.05 and Pearson's r≥0.25

[a]PBO SC W8 then Q8W through W48 administered to maintain blinding. [b]EE if <20% improvement from baseline in both TJC and SJC at W16. EE pts may initiate/increase dose of 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 enter LTE. ***CASPAR***=CASsification criteria for Psoriatic ARthritis; ***CRP***=C-reactive protein; ***csDMARDs***=conventional synthetic disease-modifying antirheumatic drugs; ***DAS28***=Disease Activity Score 28; ***EE***=early efficacy; ***F/U***=follow-up; ***HAQ-DI***=Health Assessment Questionnaire–Disability Index; ***HV***=healthy volunteer; ***IGA***=Investigator's Global Assessment; ***LTE***=long-term extension; ***NSAID***=nonsteroidal anti-inflammatory drugs; ***PASI***=Psoriasis Area and Severity Index; ***PE***=primary endpoint; ***PhGA***=physician global assessment of arthritis and psoriasis; ***Q4W***=every 4 weeks, ***Q8W***=every 8 weeks, ***R***=randomization; ***SAA***=serum amyloid A; ***SC***=subcutaneous; ***SJC***=swollen joint count; ***Th17***=T helper 17; ***TJC***=tender joint count; ***VAS***=visual analog scale.

Results

Baseline demographics, disease characteristics, and W24 efficacy in the biomarker cohort were representative of mFAS

- Baseline pt and disease characteristics were balanced between treatment groups within the biomarker cohort

Baseline Characteristics	Biomarker Cohort GUS Q8W (N=79)	Biomarker Cohort GUS Q4W (N=52)	Biomarker Cohort PBO (N=82)	Biomarker Cohort Total (N=213)	mFAS Total (N=1020)
Demographics					
Age, years	52.3 (13.0)	53.3 (12.1)	53.2 (12.5)	52.9 (12.5)	53.0 (13.0)
Female	35%	48%	44%	42%	45%
BMI, kg/m²	29.2 (4.9)	28.9 (5.5)	29.2 (4.0)	29.1 (4.7)	29.1 (5.7)
Disease Characteristics					
SJC (0–66)	11.4 (7.0)	12.5 (11.4)	11.2 (7.5)	11.6 (8.4)	11.9 (8.9)
TJC (0–68)	20.9 (12.9)	22.9 (16.9)	18.1 (12.2)	20.3 (13.8)	20.7 (13.9)
CRP, mg/dL	15.6 (19.1)	12.0 (20.5)	15.0 (18.0)	14.5 (19.0)	16.5 (24.7)
PASI (0–72)	9.6 (12.3)	8.2 (9.2)	7.1 (7.8)	8.3 (10.0)	8.1 (9.4)
W24 Efficacy					
Change in vdH-S, GUS vs PBO[a]	0.1 (1.4)	0.2 (1.8)	1.3 (3.5)	0.6 (2.6)	p<0.001 for Q4W and Q8W
ACR20 rates, GUS vs PBO[b]	72%	69%	45%		p=0.002 for Q4W p<0.001 for Q8W

Data shown are mean (SD) unless noted otherwise. [a]*Based on Kruskal-Wallis rank sum test.* [b]*Based on Pearson's Chi-squared test.* ***ACR***=*American College of Rheumatology;* ***BMI***=*body mass index;* ***CRP***=*C-reactive protein;* ***GUS***=*guselkumab;* ***mFAS***=*modified full analysis set;* ***PASI***=*Psoriasis Area and Severity Index;* ***PBO***=*placebo;* ***Q4W***=*every 4 weeks,* ***Q8W***=*every 8 weeks,* ***SD***=*standard deviation;* ***SJC***=*swollen joint count;* ***TJC***=*tender joint count;* ***vdH-S***=*van der Heijde-Sharp;* ***W***=*week.*

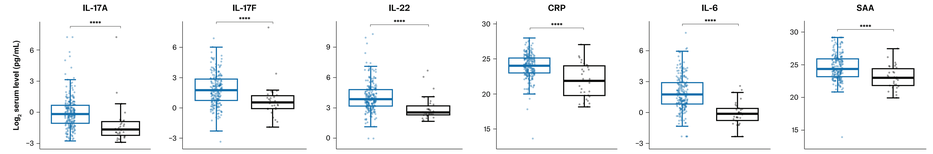
Baseline serum biomarker levels correlated with measures of joint disease activity, skin psoriasis, and structural damage

- Baseline serum Th17 cytokines and inflammatory markers were correlated with skin and joint disease activity, respectively
- Baseline IL-6 level was correlated with PsA-modified vdH-S score

		Joint disease activity								Skin disease activity		Structural damage
	BMx	SJC (0–66)	TJC (0–68)	Patient Pain (0–10)[a]	HAQ-DI (0–3)	PhGA (0–10)[a]	DAS28 (0–9.4)	Dactylitis	Enthesitis	IGA (0–4)	PASI (0–72)	vdH-S (0–528)
Baseline Th17 cytokines	IL-17A	0.12	0.15	−0.01	0.044	0.14	0.10	0.24	0.02	**0.36******	**0.46******	0.16
	IL-17F	0.11	0.19	−0.032	−0.029	0.19	0.12	0.23	−0.001	**0.42******	**0.58******	−0.009
	IL-22	0.082	0.14	0.042	0.078	0.10	0.16	0.12	−0.005	0.22	**0.35******	0.11
Baseline inflammatory markers	CRP	0.16	0.077	0.19	0.21	0.20	**0.43******	0.004	0.064	0.15	0.16	0.20
	IL-6	0.12	0.092	0.20	**0.25*****	0.20	**0.35******	0.12	4E-04	0.14	0.14	**0.33******
	SAA	0.18	0.093	**0.26*****	**0.29******	0.20	**0.42******	0.053	0.039	0.15	0.23	0.22

****p≤0.001, ****p≤0.0001 and Pearson's r≥0.25.* [a]*VAS.* ***BMx***=*biomarker;* ***CRP***=*C-reactive protein;* ***DAS28***=*Disease Activity Score 28;* ***HAQ-DI***=*Health Assessment Questionnaire–Disability Index;* ***IGA***=*Investigator's Global Assessment;* ***IL***=*interleukin;* ***PASI***=*Psoriasis Area and Severity Index;* ***PhGA***=*Physician's Global Assessment;* ***SAA***=*serum amyloid A;* ***SJC***=*swollen joint count;* ***Th17***=*T helper 17;* ***TJC***=*tender joint count;* ***VAS***=*visual analog scale,* ***vdH-S***=*van der Heijde–Sharp.*

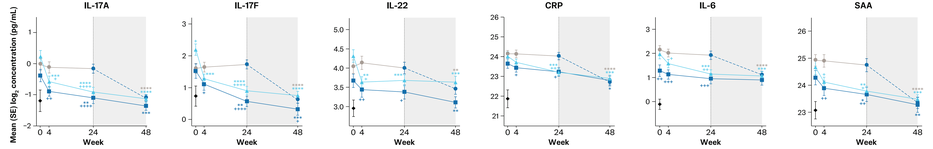
Serum levels of Th17 cytokines and inflammatory markers were elevated at baseline in pts with PsA vs HVs



*****p≤0.0001 for pts with PsA (biomarker cohort) vs HVs. Boxplots represent the median and IQR (25th–75th percentile) and 10th–90th percentiles (whiskers); dots represent individual pt data.* ***CRP***=*C-reactive protein;* ***GUS***=*guselkumab;* ***HV***=*healthy volunteer;* ***IL***=*interleukin;* ***PsA***=*psoriatic arthritis;* ***SAA***=*serum amyloid A;* ***Th17***=*T helper 17.*

GUS significantly reduced serum levels of Th17 cytokines and inflammatory markers as early as W4 and continuing through W48

- PBO-randomized pts exhibited comparable reductions in Th17 cytokines and inflammatory markers after starting GUS at W24



p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001 vs baseline within treatment group; +p≤0.05, ++p≤0.01, +++p≤0.001, ++++p≤0.0001 vs PBO. Dotted line represents time of transition of PBO to GUS Q4W. [a]N=78 at W48. [b]N=80 at W48.* ***CRP*=*C-reactive protein;* ***GUS***=*guselkumab;* ***HV***=*healthy volunteer;* ***IL***=*interleukin;* ***PBO***=*placebo;* ***Q4W***=*every 4 weeks,* ***Q8W***=*every 8 weeks,* ***SAA***=*serum amyloid A,* ***Th17***=*T helper 17,* ***W***=*week.*

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PRESENTED AT: The American College of Rheumatology (ACR) Convergence 2026; November 6–11, 2026; Orlando, FL, USA. **REFERENCES: 1.** Fitzgerald O. *Nat Rev Dis Primers.* 2021;5:3. **2.** Sachen K. *Front Immunol.* 2022;13:952822. **3.** Janssen Biotech, Inc. TREMFYA® (guselkumab) injection, for subcutaneous or intravenous use. Revised 9/2025 [prescribing information]. https://www.pjlabels.com/package-insert/product-monograph/prescribing-information/TREMFYA-pi.pdf. **4.** Mease PJ. *Ann Rheum Dis.* 2025; doi:10.1016/j.ard.2025.08.006. **5.** Fakharzadeh S. Durable Inhibition of Structural Damage Progression and Improvements in Joint Disease Activity With Guselkumab in Active and Erosive Psoriatic Arthritis: Week 48 Results From APEX. Presented at the 6th Inflammatory Skin Disease Summit (ISDS); November 12–15, 2025; New York, NY, USA. **6.** Schett G. *Arthritis Res Ther.* 2023;25:150. **7.** Siebert S. *Ther Adv Musculoskelet Dis.* 2024;16:1759720X241283536. **ACKNOWLEDGMENTS:** Medical writing support was provided by JSS Medical Research, Inc, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298–1304). Layout design and formatting for this encore presentation was provided by Ganesh Karpe of SIRO Medical Writing Pvt. Ltd., India (funded by Johnson & Johnson). This presentation was sponsored by Johnson & Johnson. **DISCLOSURES: CBM, EW, APK, KL, CC, MJL, SG, LS** and **DM:** Employees of Johnson & Johnson; may own stock/stock options in Johnson & Johnson. **PR:** Consultant: AbbVie, Amgen Inc., Bristol Myers Squibb, Celgene, Eli Lilly, Johnson & Johnson, Merck, Novartis, Pfizer, and UCB; grant/research support: Johnson & Johnson and Novartis; meeting attendance/travel support: Johnson & Johnson. **CTR:** Consultant: AbbVie, Amgen Inc., Eli Lilly, Gilead, Johnson & Johnson, Novartis, Pfizer, and UCB; grant/research support: AbbVie, Amgen Inc., and UCB. **PJMS:** Consultant: AbbVie, Amgen Inc., Bristol Myers Squibb, Century, Cullinan, Eli Lilly, Immagene, Johnson & Johnson, Merck, Moonlake, Novartis, Pfizer, Spyre, SUN Pharma, Takeda, and UCB; grant/research support: AbbVie, Amgen Inc., Bristol Myers Squibb, Eli Lilly, Johnson & Johnson, Moonlake, Novartis, Sana, Takeda, and UCB; speaker's bureau: AbbVie, Amgen Inc., Eli Lilly, Johnson & Johnson, Novartis, and UCB. **Accepted as abstract book to be published in the ARS Supplement:** European Alliance of Associations for Rheumatology (EULAR), June 3–6, 2026; London, England.