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

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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**

Background

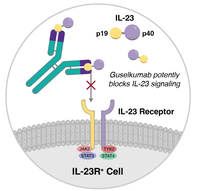
Psoriatic arthritis (PsA), a chronic, heterogeneous, inflammatory disease affecting joints and skin, can substantially impact health-related quality of life[1,2]

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

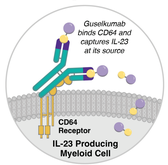
Guselkumab (GUS) is a fully human, dual-acting, monoclonal antibody that selectively inhibits the interleukin (IL)-23p19 subunit[4]

- 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]



Dual-acting IL-23 Inhibitor



Objectives

Report findings through Week (W) 24 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

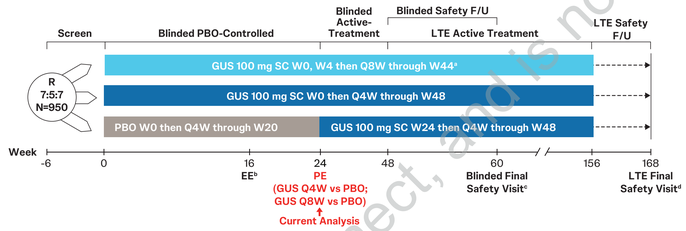
APEX Study Design

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**=CIASsification criteria for Psoriatic ARthritis, **CRP**=C-reactive protein, **csDMARD**=Conventional synthetic disease-modifying antirheumatic drug, **EE**=Early escape, **F/U**=Follow-up, **GUS**=Guselkumab, **LTE**=Long-term extension, **NSAID**=Nonsteroidal anti-inflammatory drug, **PBO**=Placebo, **PE**=Primary endpoint, **PsA**=Psoriatic arthritis, **PsO**=Plaque psoriasis, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **R**=Randomization, **SC**=Subcutaneous, **SJC**=Swollen joint count, **TJC**=Tender joint count, **vdH-S**=van der Heijde-Sharp, **W**=Week

Results

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

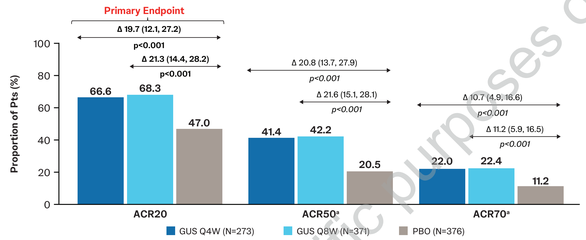
- **Background PsA medication use and treatment completion through W24 (96–97%) were consistent across treatment groups**

	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, **CRP**=C-reactive protein, **DSS**=Dactylitis Severity Score, **GUS**=Guselkumab, **HAQ-DI**=Health Assessment Questionnaire-Disability Index, **IQR**=Interquartile range, **JSN**=Joint space narrowing, **LEI**=Leeds Enthesitis Index, **PASI**=Psoriasis Area and Severity Index, **PBO**=Placebo, **PsA**=Psoriatic arthritis, **PsO**=Plaque psoriasis, **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

GUS demonstrated significantly higher ACR20 response rates vs PBO at W24

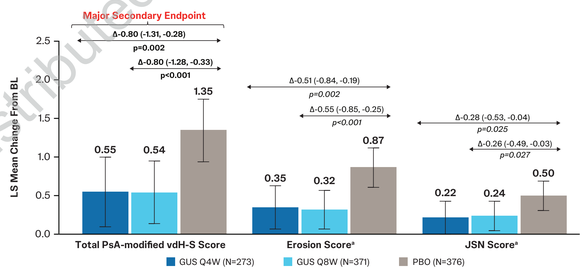
- **GUS demonstrated higher rates of ACR50 and ACR70 vs PBO at W24**



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). **ACR**=American College of Rheumatology, **CI**=Confidence interval, **GUS**=Guselkumab, **PBO**=Placebo, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks

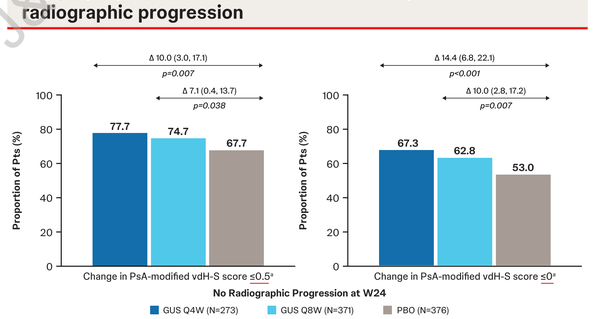
GUS exhibited significantly lower rates of radiographic progression vs PBO at W24

- **GUS exhibited consistent treatment effects for both erosion and joint space narrowing (JSN) scores**



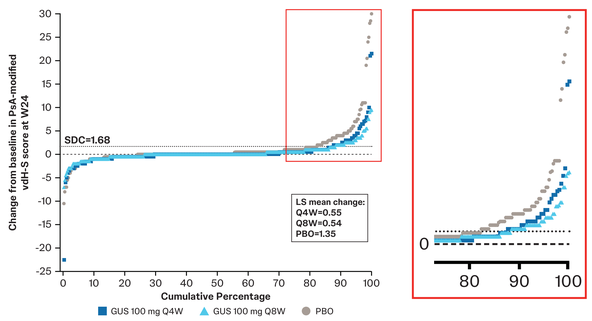
Major secondary endpoint (PsA-modified vdH-S score) p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on analysis of covariance across multiply imputed datasets. [a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **BL**=Baseline, **CI**=Confidence interval, **GUS**=Guselkumab, **JSN**=Joint space narrowing, **LS**=Least squares, **PsA**=Psoriatic arthritis, **PBO**=Placebo, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **vdH-S**=van der Heijde-Sharp

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



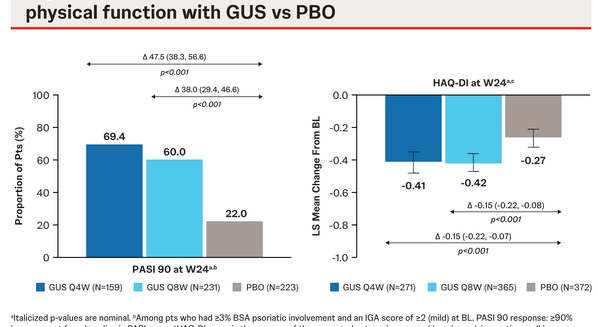
[a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **CI**=Confidence interval, **GUS**=Guselkumab, **PBO**=Placebo, **PsA**=Psoriatic arthritis, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **vdH-S**=van der Heijde-Sharp, **W**=Week

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



GUS=Guselkumab, **LS**=Least squares, **PBO**=Placebo, **PsA**=Psoriatic arthritis, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **SDC**=Smallest detectable change, **vdH-S**=van der Heijde-Sharp, **W**=Week

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). **BL**=Baseline, **BSA**=Body surface area, **CI**=Confidence interval, **GUS**=Guselkumab, **HAQ-DI**=Health Assessment Questionnaire-Disability Index, **IGA**=Investigator's Global Assessment, **LS**=Least squares, **PASI**=Psoriasis Area and Severity Index, **PBO**=Placebo, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **W**=Week

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 MedDRA 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, **GUS**=Guselkumab, **MedDRA**=Medical Dictionary for Regulatory Activities, **PBO**=Placebo, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **SAE**=Serious AE, **W**=Week

- **Study remains blinded through W48**
- **2 pts with malignancy (prostate, renal); 1 major adverse cardiovascular event (myocardial infarction); 1 COVID-19 death in unvaccinated elderly pt**
- **No new-onset inflammatory bowel disease**

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