POS1314

Icotrokinra, a First-in-Class, Targeted Oral Peptide, in Participants with Psoriatic Disease: Exploratory Assessments From a Phase 2 Psoriasis Study Informing a Phase 3 Clinical Program in Psoriatic Arthritis

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Key Takeaways

- **Exploratory assessments from the ICO PsO Phase 2 study informed the design of the ICONIC-PsA Phase 3 Program:**
  - ✓ **ICO elicited comparable PD effects between participants with PsO only and those with PsO+PsA in PsA-relevant biomarkers**
  - ✓ **ICO-treated participants with PsO+PsA reported clinically meaningful improvement in PsA-relevant domains of their HRQoL**
- **The multicenter, double-blind, PBO-controlled ICONIC-PsA 1 and ICONIC-PsA 2 studies will comprehensively evaluate ICO, a first-in-class, targeted oral peptide, in a diverse population of participants with active PsA**

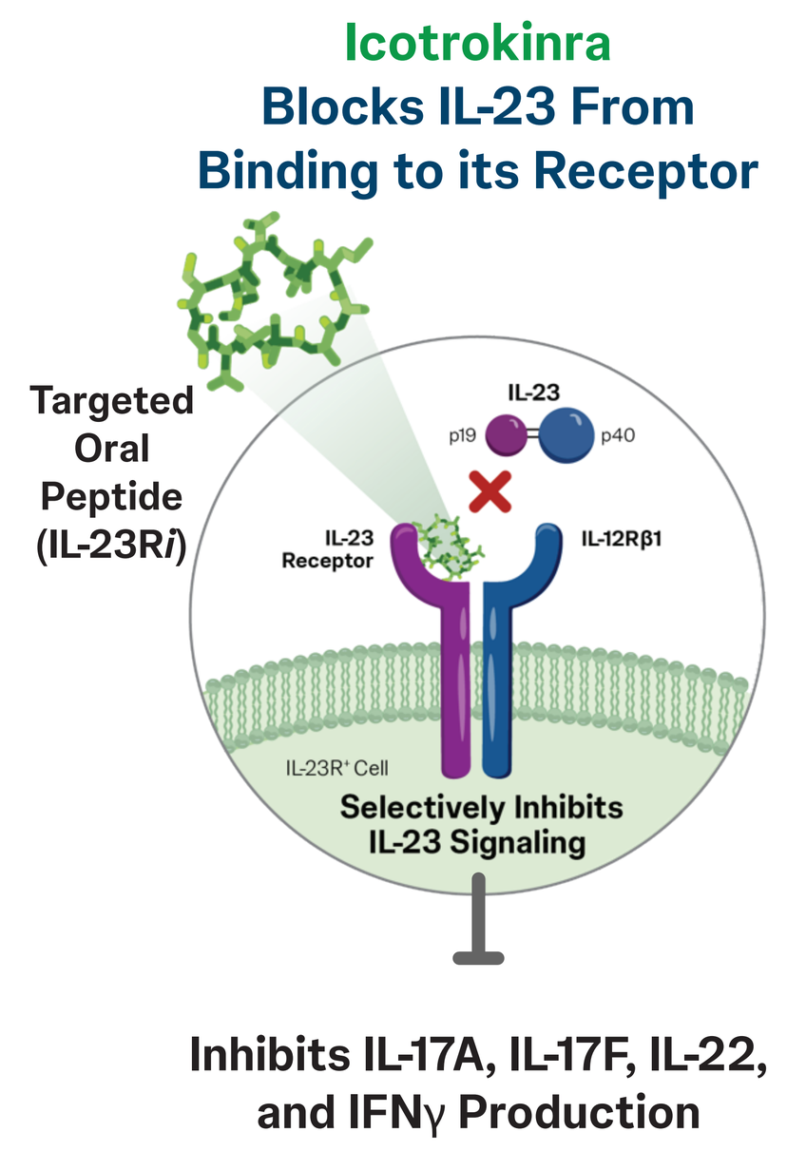
Background

Psoriatic arthritis (PsA) affects ~20-30% of patients with psoriasis (PsO)[1-3]

- PsA causes articular inflammation and damage, fatigue, pain, and impaired physical function, leading to diminished health-related quality of life (HRQoL)[4]
- Patients with active PsA are generally limited to injectable therapies to achieve high-level efficacy with a favorable safety profile
- The interleukin (IL)-23 pathway plays a pivotal role in the pathogenesis of PsO and PsA[5]

Icotrokinra (ICO) is a first-in-class, targeted oral peptide that:

- Selectively binds the IL-23 receptor and inhibits IL-23 pathway signaling[6]
- Demonstrated significant skin clearance and no safety signals through 1 year in Phase 2[7,8] and in Phase 3[9] PsO studies



Objectives

Report exploratory pharmacodynamic (PD) and clinical findings from a subset of Phase 2 FRONTIER 1 participants with PsO and history of PsA (PsO+PsA), which supported the design and development of the ICO PsA Phase 3 clinical program

Exploratory ICO PsO Phase 2 Analyses Supporting ICO PsA Phase 3 Program

ICO PsO Phase 2 (FRONTIER 1) pts with PsO and history of PsA (PsO+PsA): ICO PD effects and Impact on PROs

ICO PD effects vs pts with PsO only

- Mean log fold-change (logFC) in serum levels of β-Defensin-2 (BD-2), IL-22, IL-17A, IL-17F from baseline (BL) to Week (W) 16

PsA-relevant PROs vs PBO

- PsA-relevant domains of Patient Reported Outcome Measures Information Systems (PROMIS-29) questionnaire
  - Change from BL to W16 in Physical function, Fatigue, Pain Intensity, and Pain Interference
  - Proportion of pts achieving clinically meaningful improvement (CMI) from BL to W16 in PROMIS-29 physical/mental component summary (PCS/MCS) scores
- CMI from BL at W16
  - ≥5-points: Physical function, Fatigue, PCS/MCS scores
  - ≥2-points: Pain intensity, Pain interference

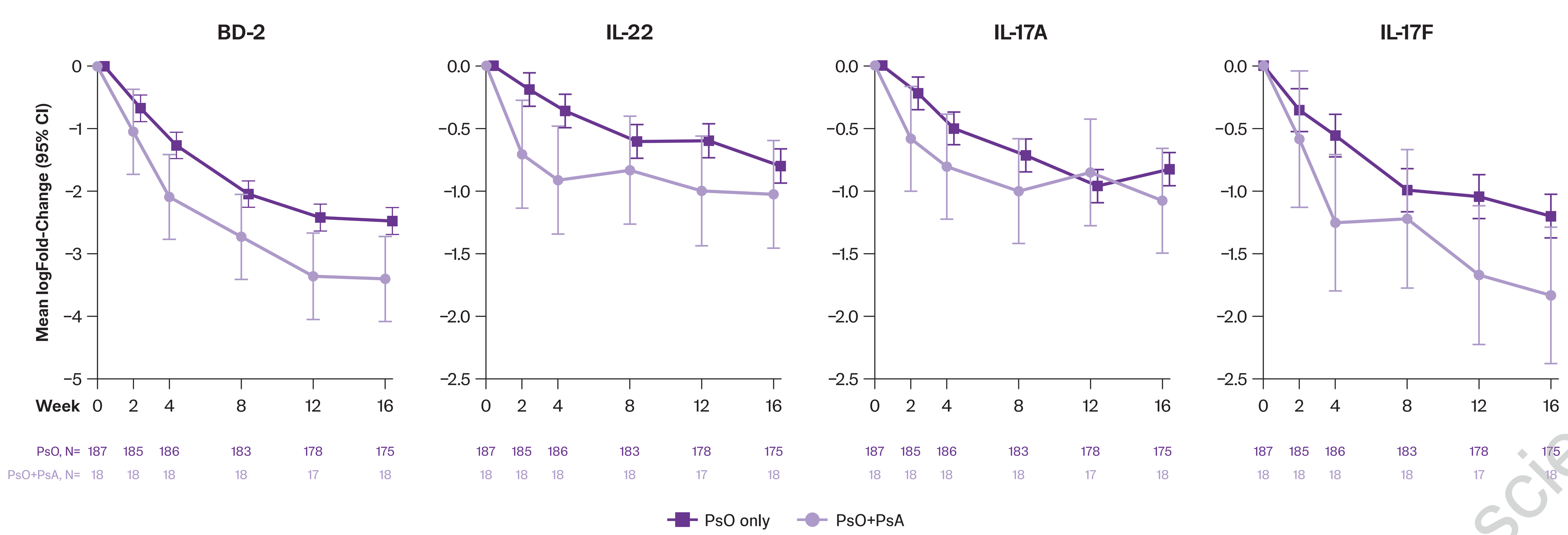
ICO PsA Phase 3 program sample sizes

ICO Phase 3 PsA sample size estimates were informed both by requisite safety data and model-based clinical response rates

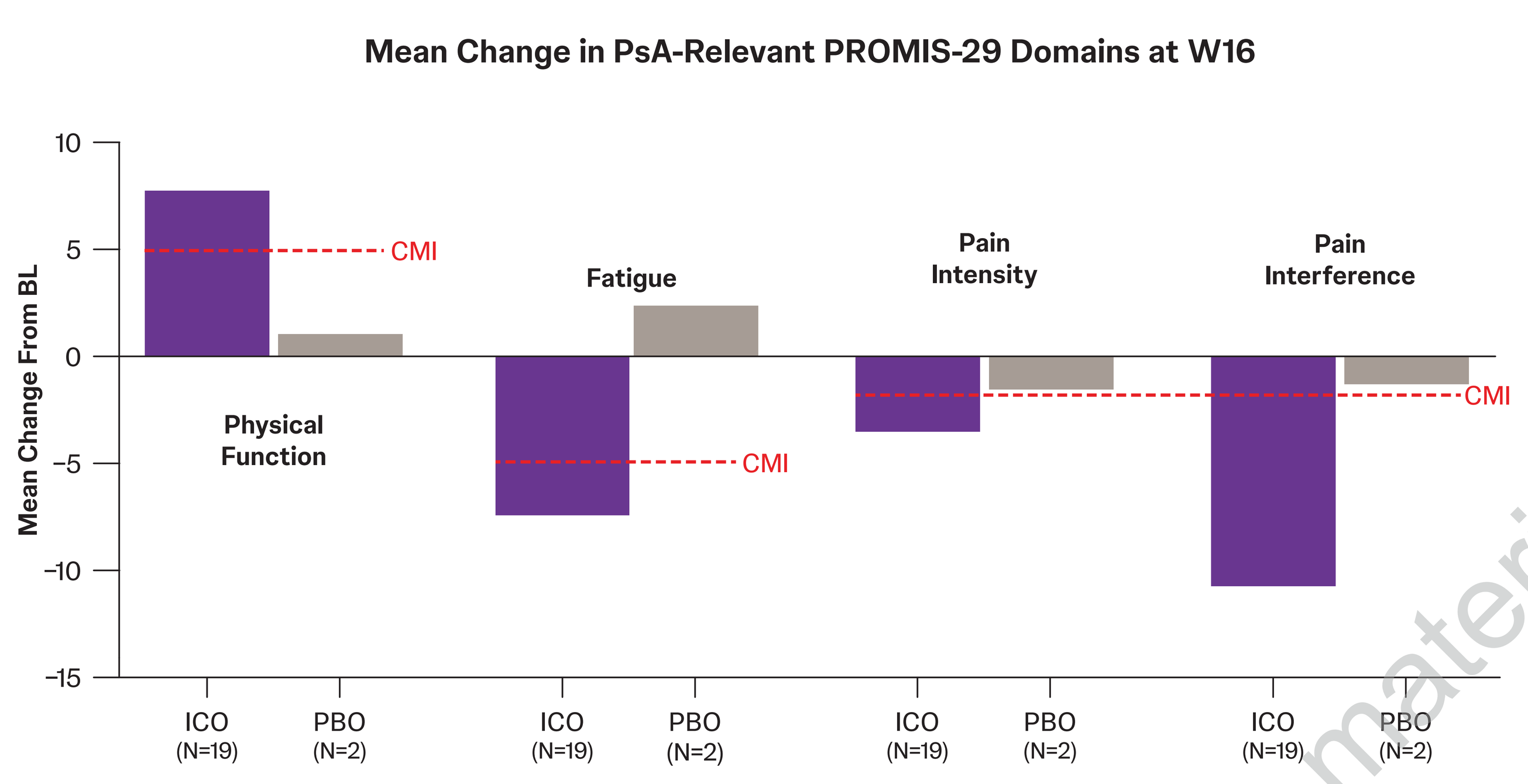
- FRONTIER 1 Meta-analysis: Psoriasis Area Severity Index (PASI) 75 response rates (Phase 2 primary endpoint) bridged to expected American College of Rheumatology (ACR) 20 response in PsA at Week (W) 16 (Phase 3 primary endpoint)
- Meta-regression modeling bridged between expected ACR20 response and other PsA clinical endpoints at W16:
  - Stringent joint disease activity (ACR50/70)
  - Change in Health Assessment Questionnaire-Disability Index (HAQ-DI) and Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue
  - Resolution of enthesitis and dactylitis
  - Multi-domain outcome measure (Minimal Disease Activity [MDA])

Exploratory ICO PsO Phase 2 Analyses

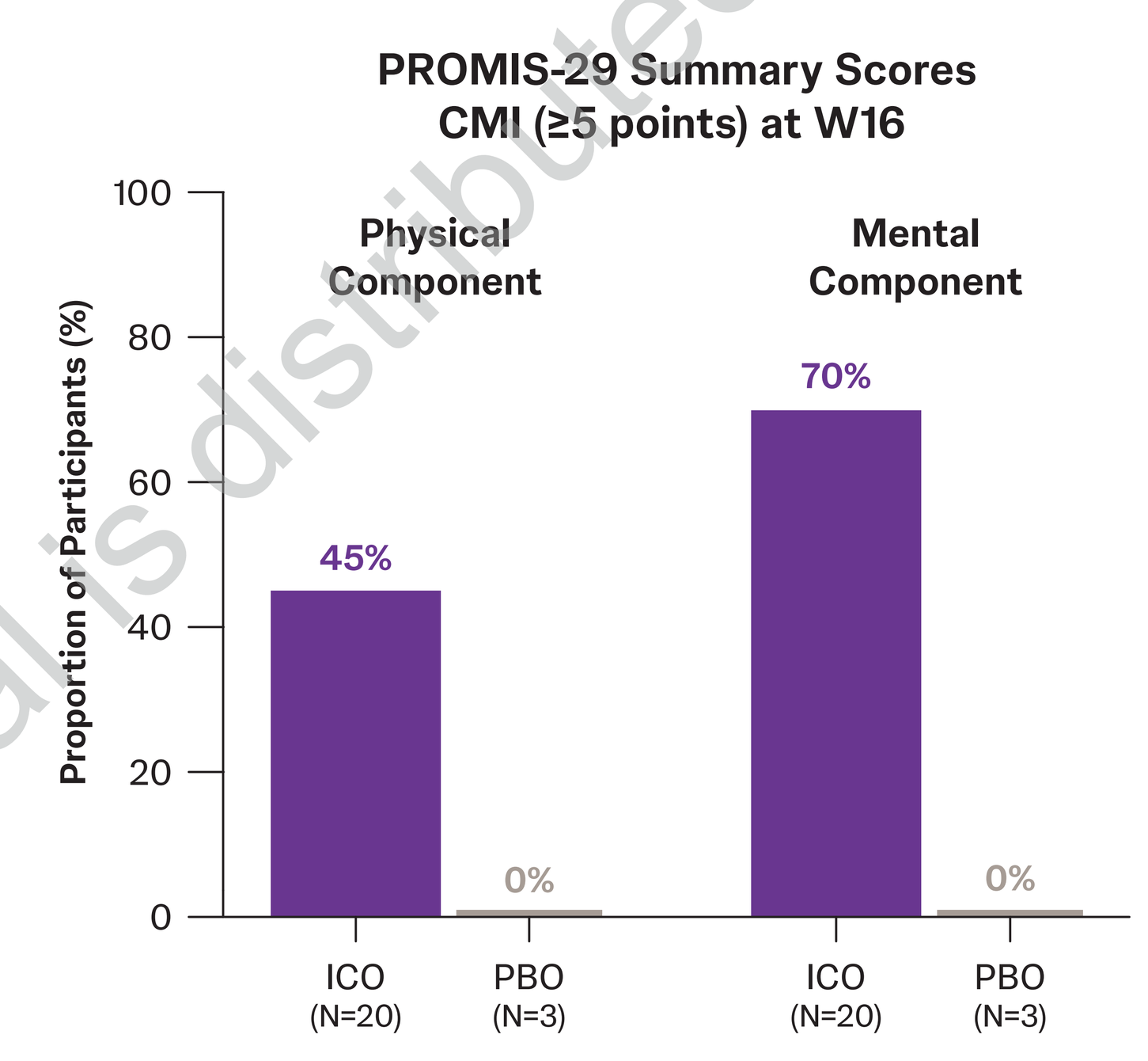
ICO elicited comparable PD effects between participants with PsO only and those with PsO+PsA, including similar decreases in serum levels of the inflammatory biomarker, BD-2, and in key PsA regulatory cytokines



ICO-treated PsO+PsA participants reported greater mean improvements across PsA-relevant domains and higher rates of clinically meaningful improvement (CMI) in physical and mental aspects of HRQoL vs PBO



Note: Red dotted lines represent ≥5-points improvement from BL or ≥2-points improvement from BL. Participants who have intercurrent events (ICE) 1-2 have zero change from BL after the event. Observed data were used for participants with ICE 3.

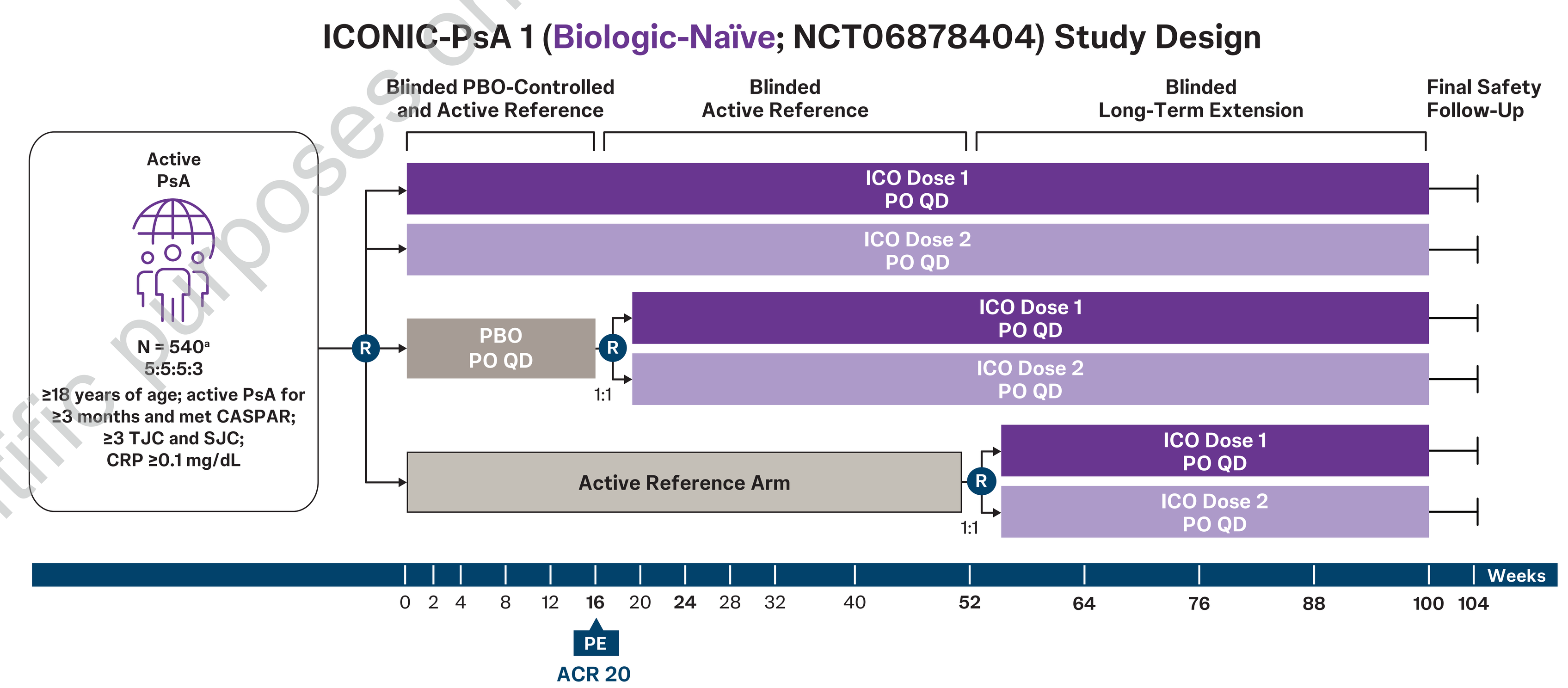


Participants with ICE 1-2 were assumed to be non-responders after the event. Observed data were used for participants with ICE 3. After accounting for the ICEs, participants with missing data were considered as non-responders.

ICONIC-PsA Phase 3 Program

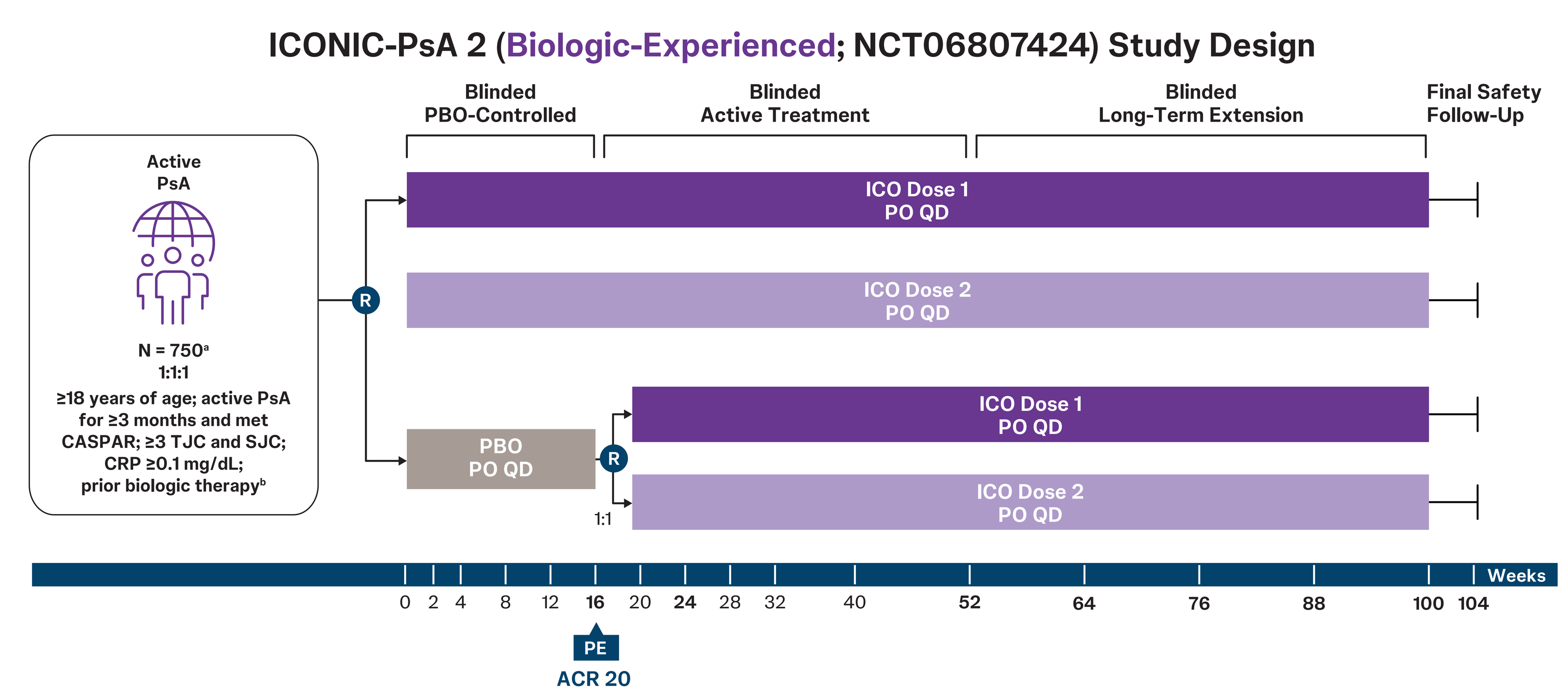
ICONIC-PsA 1 and 2 will assess the efficacy and safety of ICO vs PBO in participants with active PsA, who are biologic-naive and biologic-experienced, respectively

ICONIC-PsA 1 (Biologic-Naïve; NCT06878404) Study Design



[a]N=540 was estimated to provide ≥90% power to detect a significant difference between ICO and PBO. **CASPAR**, classification criteria for psoriatic arthritis; **CRP**, C-reactive protein; **DMARD**, disease-modifying antirheumatic drugs; **PE**, primary efficacy; **PO**, oral; **QD**, once daily; **R**, randomization; **SJC**, swollen joint count; **TJC**, tender joint count.

ICONIC-PsA 2 (Biologic-Experienced; NCT06807424) Study Design



[a]N=750 was estimated to provide ≥90% power to detect a significant difference between ICO and PBO; [b]Participants must have been previously treated with 1 biologic for PsA or PsO and the reason for discontinuation must be documented.

ICONIC-PsA 1 and ICONIC-PsA 2 endpoints

Primary Endpoint	Description
• ACR20	≥20% improvement per ACR response criteria
Secondary Endpoints	**Description**
• ACR50, ACR70	≥50% and ≥70% improvement per ACR response criteria
• PASI 75, PASI 90, and PASI 100	≥75%, ≥90%, and 100% improvement from BL in PASI score[a]
• IGA 0/1 and ≥2 grade improvement	Cleared (0), minimal (1), mild (2), moderate (3), severe (4)[a]
• Enthesitis: change from BL & resolution	LEI score range: 1-6 & Resolution: LEI=0[b]
• Dactylitis: change from BL & resolution	DSS range: 1-60 & Resolution: DSS=0[c]
• MDA	≥5 of 7 outcome measures fulfilled
• HAQ-DI score: change from BL	Range: 0-3 (0=least difficulty; 3=extreme difficulty)
• SF-36 PCS score: change from BL	Range: 0-100 (100=highest level of physical functioning)
• FACIT-Fatigue score: change from BL	Range: 0-52 (higher values indicate less fatigue)
Safety	
• AEs, clinical laboratory tests, and vital signs	

[a]Among participants with BL: BSA ≥3% and IGA score ≥2; [b]Among participants with enthesitis; [c]Among participants with dactylitis. **BSA**, body surface area; **DDS**, Dactylitis Severity Score; **IGA**, Investigator's global assessment; **LEI**, Leeds Enthesitis Index; **SF-36**, 36 Item Short Form Survey.

The ICONIC-PsA Phase 3 program plans to assess a diverse population

- Minorities are often under-recruited in PsA trials
- Representation of individuals with different racial/ethnic backgrounds sought through multiple strategies, including:
  - Targeted outreach to under-represented communities to enhance recruitment
  - Collaboration with patient advocacy groups to increase awareness and support the enrollment of a diverse PsA patient population

PRESENTED BY: Joseph F. Merola at EULAR; June 11-14, 2025; Barcelona, Spain.
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