Icotrokinra, a Novel Targeted Oral Peptide, in Patients With Psoriatic Disease: Exploratory Assessments From a Phase 2 Psoriasis Study Informing a Phase 3 Clinical Program in Psoriatic Arthritis

Joseph F. Merola[1*], Philip J. Mease[2,3], Laura C. Coates[4], Iain B. McInnes[5], Peter Nash[6], Alexis Ogdie[7], Lihi Eder[8], Mitsumasa Kishimoto[9], Anna Beutler[10], Konstantina Psachoulia[10], Shihong Sheng[11], Bei Zhou[11], Mehrdad Javidi[12], Chandni Valiathan[12], Charles Iaconangelo[11], Ya-Wen Yang[13], Arun Kannan[12], Chetan S. Karyekar[10], Tasneam Shagroni[10]

[1]Department of Dermatology and Department of Medicine, Division of Rheumatology, UT Southwestern Medical Center, Dallas, TX, USA; [2]Rheumatology Research, Providence Swedish Medical Center, Seattle, WA, USA; [3]University of Washington School of Medicine, Seattle, WA, USA; [4]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences University of Oxford Botnar Research Centre, Oxford, UK; [5]College of Medical Veterinary and Life Sciences, University of Glasgow, Glasgow, UK; [6]Griffith University and U of Queensland, Maroochydore, Queensland, Australia; [7]University of Pennsylvania School of Medicine, Philadelphia, PA, USA; [8]University of Toronto and Women's College Hospital, Toronto, ON, Canada; [9]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Mitaka, Tokyo, Japan; [10]Johnson & Johnson, Spring House, PA, USA; [11]Johnson & Johnson, Chesterbrook, PA, USA; [12]Johnson & Johnson, San Diego, CA, USA; [13]Johnson & Johnson, Horsham, PA, USA

**Presenting Author*

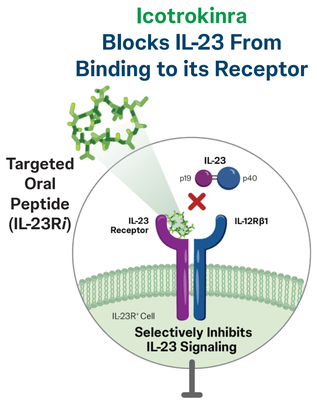
Key Takeaways

- **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) participants with PsO and history of PsA (PsO+PsA): ICO PD effects and Impact on PROs

ICO PD effects vs participants 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 patient-reported outcomes (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 participants 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

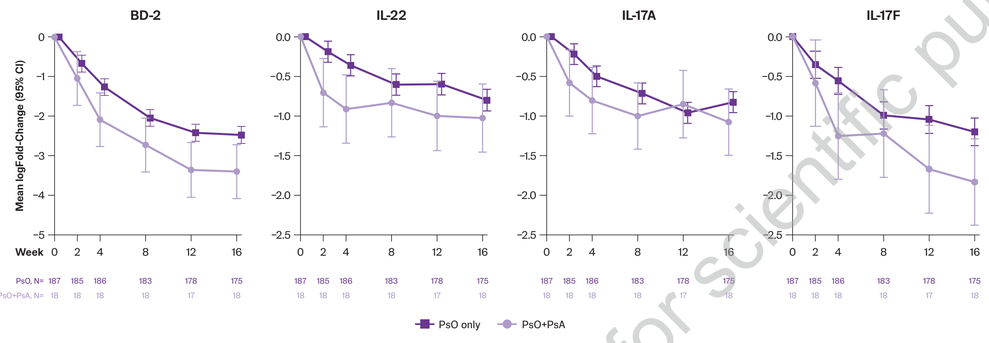
ICO PsA Phase 3 program sample sizes

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 W16 (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])

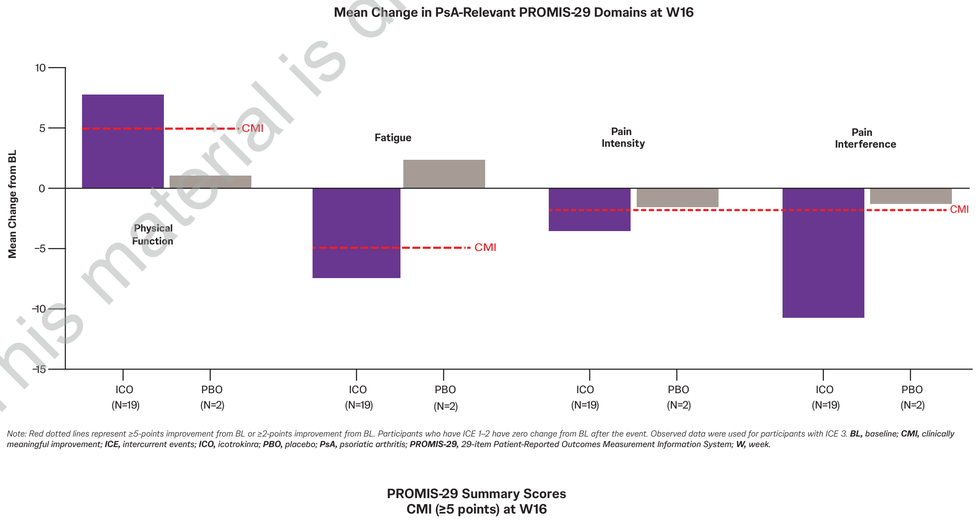
Exploratory ICO PsO Phase 2 Analyses

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

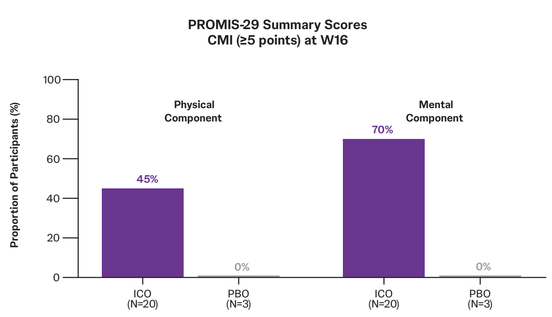


BD2, β-defensin-2; CI, confidence interval; IL, interleukin; PsA, psoriatic arthritis; PsO, psoriasis.

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 ICE 1–2 have zero change from BL after the event. Observed data were used for participants with ICE 3. **BL,** baseline; **CMI,** clinically meaningful improvement; **ICE,** intercurrent events; **ICO,** icotrokinra; **PBO,** placebo; **PsA,** psoriatic arthritis; **PROMIS-29,** 29-item Patient-Reported Outcomes Measurement Information System; **W,** week.*

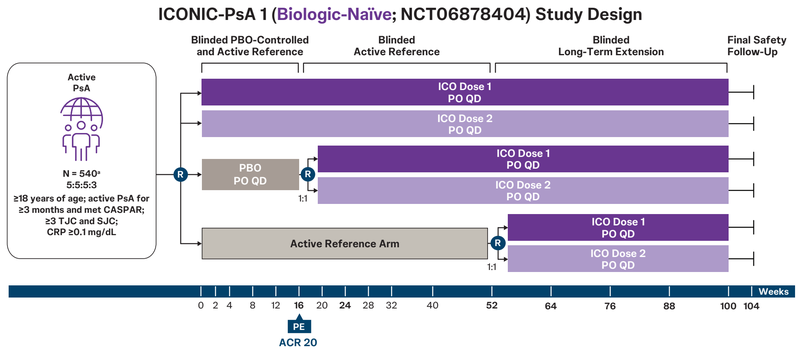


*Participants with ICE 1–2 were assumed to be non-responders after the event. Observed data were used for participants with ICE 3. After accounting for the ICEs, participants with missing data were considered as non-responders. **CMI,** clinically meaningful improvement; **ICE,** intercurrent events; **ICO,** icotrokinra; **PBO,** placebo; **PROMIS-29,** 29-item Patient-Reported Outcomes Measurement Information System; **W,** week.*

ICONIC-PsA Phase 3 Program

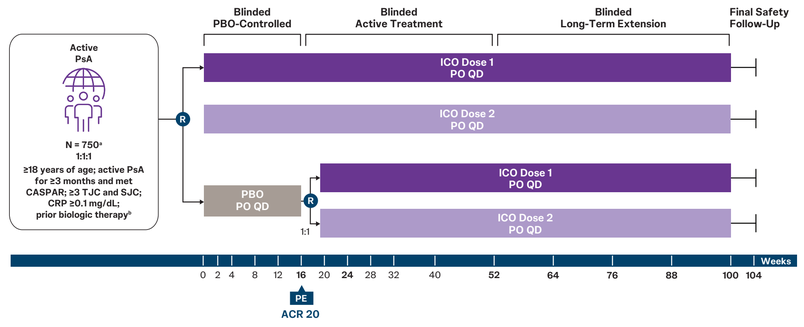
ICONIC-PsA 1 and 2 will assess the efficacy and safety of ICO vs PBO in participants with active PsA, who are biologic-naive and biologic-experienced, respectively

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



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

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



*ᵃN=750 was estimated to provide ≥90% power to detect a significant difference between ICO and PBO; ᵇParticipants must have been previously treated with 1 biologic for PsA or PsO and the reason for discontinuation must be documented. **ACR,** American College of Rheumatology; **CASPAR,** classification criteria for psoriatic arthritis; **CRP,** C-reactive protein; **ICO,** icotrokinra; **PBO,** placebo; **PE,** primary efficacy; **PO,** oral; **PsA,** psoriatic arthritis; **PsO,** psoriasis; **QD,** once daily; **R,** randomization; **SJC,** swollen joint count; **TJC,** tender joint count.*

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. **ACR,** American College of Rheumatology; **AE,** adverse event; **BL,** baseline; **BSA,** body surface area; **DDS,** Dactylitis Severity Score; **FACIT,** Functional Assessment of Chronic Illness Therapy; **HAQ-DI,** Health Assessment Questionnaire-Disability Index; **IGA,** Investigator's Global Assessment; **LEI,** Leeds Enthesitis Index; **MDA,** Minimal Disease Activity; **PASI,** Psoriasis Area Severity 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 AT: European Academy of Dermatology & Venereology (EADV) Congress 2025; Paris, France; September 17–20, 2025. **REFERENCES: 1.** Lemke S, et al. doi:10.1093/rheumatology/keae198. **2.** Ocampo D, et al. doi:10.12688/f1000research.19144.1. **3.** Merola J, et al. doi:10.1016/j.jaad.2021.09.019. **4.** Gladman D, et al. doi:10.1136/rmdopen-2019-000928. **5.** Qin-Yi S, et al. doi:10.1080/14712598.2024.2401148. **6.** Fourie AM, et al. *Sci Rep.* 2024;14:17515. **7.** Bissonnette R, et al. *N Engl J Med.* 2024;390:510–21. **8.** Ferris LK, et al. *J Am Acad Dermatol.* Published online November 14, 2024. doi:10.1016/j.jaad.2024.10.076. **9.** Bissonnette R, et al. Abstract presented at: American Academy of Dermatology (AAD) Annual Meeting; March 7–11, 2025; Orlando, FL, USA. **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. Layout design and reformatting was done by Sandeep Chavan of SIRO Medical Writing Pvt Ltd, Thane, India (funded by Johnson & Johnson). **DISCLOSURES: JFM:** Consultant and/or Investigator: AbbVie, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte, Janssen, Leo Pharma, Moonlake, Novartis, Pfizer, Sanofi-Regeneron, Sun Pharma, and UCB. **PJM:** Grants: AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, and UCB; Consultant: AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Immagene, Janssen, Novartis, Pfizer, UCB, and Ventyx; Speaker: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB. **LCC:** Grant/Research support: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB; Consultant: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Moonlake, Novartis, Pfizer, and UCB; Speaker: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Medac, Novartis, Pfizer, and UCB. **IBM:** Consultant: AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Cabaletta, Compugen, Eli Lilly, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, Sanofi, and UCB; Grant/Research support: Amgen, AstraZeneca, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Roche, and UCB; Shareholder: Causeway, and Evelo Compugen; NHS GGC Board Member; Evelo Board of Directors; and Versus Arthritis Trustee. **PN:** Grant/Research support and Consultant/Advisory Boards: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sun Pharma, UCB. **AO:** Consultant/Advisory Boards: AbbVie, Amgen, Bristol Myers Squibb, Celgene, CorEvitas, Gilead, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Pfizer, UCB; Grants: AbbVie to Penn, Pfizer to Penn, Novartis to Penn, Amgen to Forward/NDB; Other Funding: NIAMS, Rheumatology Research Foundation, National Psoriasis Foundation, University of Pennsylvania. **LE:** Consultant: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Moonlake, Novartis, Pfizer, and UCB; Grant/Research support: AbbVie, Eli Lilly, Fresenius Kabi, Janssen, Novartis, Pfizer, Sandoz, and UCB. **MK:** Consultant and/or Speaker: AbbVie, Amgen, Asahi-Kasei Pharma, Astellas, Ayumi, Bristol Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Tanabe-Mitsubishi, and UCB. **AB, KP, SS, BZ, MJ, CV, CI, Y-WY, AK, CSK,** and **TS**: Shareholder and employee of Johnson & Johnson. **PREVIOUSLY PRESENTED AT:** EULAR 2025; Barcelona, Spain; June 11–14 2025.