Icotrokinra 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 University 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, 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

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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**

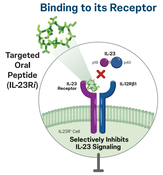
Background

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



IFNγ=interferon gamma, IL-12Rβ1=interleukin-12 receptor beta 1, IL-23R=interleukin-23 receptor, IL-23R=interleukin-23 receptor inhibitor

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 patient reported outcomes (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 PROs vs placebo (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

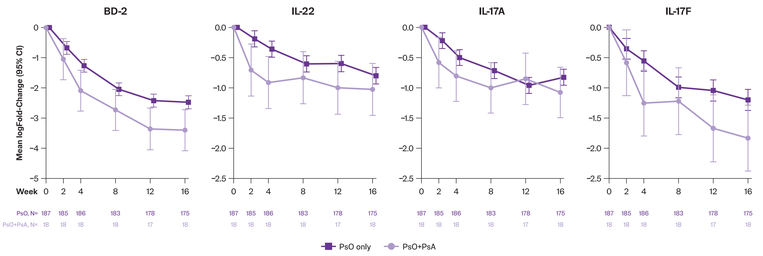
ICO PsA Phase 3 program sample sizes

ICO PsA 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])

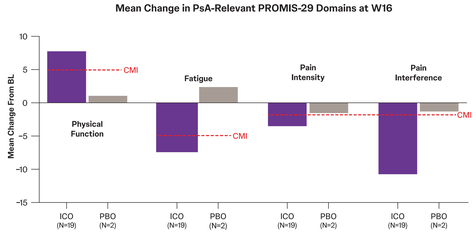
Exploratory ICO PsO Phase 2 Analyses

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

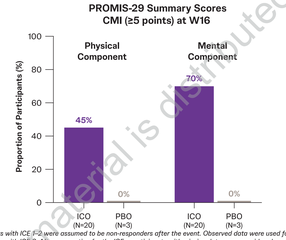


BD-2=β-Defensin-2, CI=confidence interval, IL=interleukin, PD=pharmacodynamic, PsA=psoriatic arthritis, PsO=psoriasis

ICO-treated PsO+PsA participants reported greater mean improvements across PsA-relevant domains and higher rates of 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. BL=baseline, CMI=clinically meaningful improvement, ICO=icotrokinra, PBO=placebo, PROMIS-29=Patient Reported Outcome Measures Information Systems – 29 item questionnaire, PsA=psoriatic arthritis, W=week

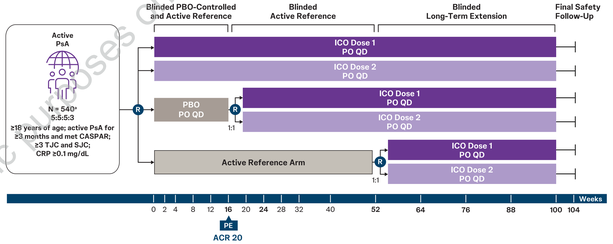


Participants with ICE 1–2 were assumed to be non-responders after the event. Observed data were used for participants with ICE 3. After accounting for the ICEs, participants with missing data were considered as non-responders. CMI=clinically meaningful improvement, ICE=intercurrent events, ICO=icotrokinra,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

ICONIC-PsA Phase 3 Program

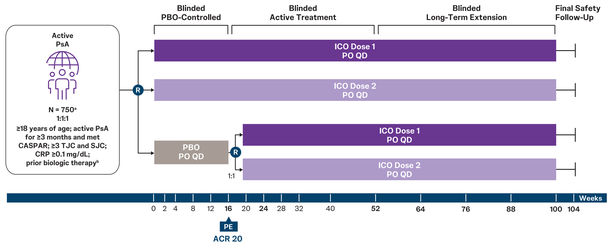
ICONIC-PsA 1 and 2 will assess the efficacy and safety of ICO vs PBO in participants with active PsA, who are biologic-naïve and biologic-experienced, respectively

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



**N=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, 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



**N=750 was estimated to provide ≥90% power to detect a significant difference between ICO and PBO; †Participants 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, 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, PCS=physical component summary, 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: Congress of Clinical Rheumatology – West; Huntington Beach, CA, USA; September 18–21, 2025. **REFERENCES:** 1. Lemke S, et al. *Rheumatology (Oxford).* 2024;63(12):3211–20. 2. Ocampo D, et al. *F1000Res.* 2019;8:F1000Research:1944.1. 3. Merola J, et al. *J Am Acad Dermatol.* 2022;86(4):746–57. 4. Gladman D, et al. *RMD Open.* 2020;6(1):e000928. 5. Shi-Yi S, et al. *Expert Opin Biol Ther.* 2024;24(10):1119–32. 6. Fourie AM, et al. *Sci Rep.* 2024;4417555. 7. Bissonnette R, et al. *N Engl J Med.* 2024;390:510–21. 8. Ferris LK, et al. *J Am Acad Dermatol.* 2025;92(3):495–502. 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). Layout, design and formatting for this encore presentation were provided by Ganesh Karpe (SIRO Medical Writing Pvt. Ltd., India), with funding from Johnson & Johnson. This study was sponsored by Johnson & Johnson. **DISCLOSURES: JFM:** Consultant and/or Investigator: AbbVie, Amgen, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Incyte, Johnson & Johnson, LEO Pharma, MoonLake Immunotherapeutics, Novartis, Pfizer, Sanofi-Regeneron, Sun Pharma, and UCB. **PJM:** Grants: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, and UCB. Consultant: AbbVie, Aclaris, Amgen, Bristol Myers Squibb, Eli Lilly, Immagene, Janssen, Novartis, Ventyx, and UCB. 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, Aclaris, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, MoonLake Immunotherapeutics, Novartis, Pfizer, and UCB. Speaker: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Medac, Novartis, Pfizer, and UCB. **CM:** Consultant: AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Calaceta Bio, 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 Therapeutics, Exelo Biosciences, Compugen, Other Roles: NIHR GIDC Board Member; Board of Directors, Exelo Biosciences, Trustee, Versus Arthritis. **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, and UCB. **AO:** Consultant/Advisory Boards: AbbVie, Amgen, Bristol Myers Squibb, Celgene, CorEvitas, Eli Lilly, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, and UCB; Grants: AbbVie (to Penn), Amgen (to Forward NDD), Novartis (to Penn), Pfizer (to Penn); Other Funding: NIAMS Rheumatology Research Foundation, National Psoriasis Foundation, University of Pennsylvania. **LE:** Consultant: AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, MoonLake Immunotherapeutics, 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 Pharmaceutical, Bristol Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, Mitsubishi Tanabe Pharma, and UCB. **AB, KP, SS, BZ, MJ, CV, CI, Y-WY, AK, CSK** and **TS:** Shareholder: Johnson & Johnson; Employee: Johnson & Johnson. Previously presented at EULAR 2025; Barcelona, Spain; June 11–14, 2025.