U.PORTO

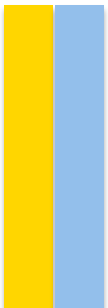
MESTRADO INTEGRADO EM MEDICINA

# Oral IL-23 inhibitors in the treatment of Psoriasis

Inês Alves Gomes

M

2025



INSTITUTO DE **CIÊNCIAS BIOMÉDICAS ABEL SALAZAR**

**Oral IL-23 inhibitors in the treatment of Psoriasis**

Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

**Estudante:**

Inês Alves Gomes

Aluna do 6º ano profissionalizante do Mestrado Integrado em Medicina

Afiliação: Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto

Correio eletrónico: up201906122@edu.icbas.up.pt

**Orientador:**

Professor Doutor Tiago da Costa Ferreira Torres

Assistente de Dermatologia e Venereologia do Centro Hospitalar Universitário do Porto

Professor auxiliar convidado de Dermatologia do Mestrado Integrado de Medicina do Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

**Coorientador:**

Doutor Martim Mondim Ferreira Caires da Luz

Universidade e Unidade Orgânica: Universidade do Porto

Dermatologia, Centro Hospitalar Universitário de Santo António - Unidade local de saúde Santo António

Junho 2025

Assinatura do estudante:

Assinatura do orientador:

Assinatura do coorientador:

**Agradecimentos**

Ao Professor Doutor Tiago Torres, pela orientação, partilha de conhecimento e apoio ao longo deste trabalho.

Ao Doutor Miguel Luz, pelo contributo e suporte ao longo do percurso.

Ao Manuel Afonso Dias e à Sara Gomes, pela leitura atenta.

A todos os que, de alguma forma, contribuíram para esta tese, o meu sincero agradecimento.

**Resumo**

A psoríase é uma doença crónica mediada pelo sistema imune, que afeta cerca de 1% a 3% da população mundial e compromete significativamente a qualidade de vida dos pacientes. A sua patogénese está associada à desregulação do eixo IL-23/IL-17, que resulta numa ativação persistente do sistema imune, na hiperproliferação dos queratinócitos e na remodelação epidérmica. Os fármacos biológicos dirigidos a este mecanismo revolucionaram o tratamento da psoríase, especialmente na psoríase moderada a grave. Dentro dos biológicos destacam-se os inibidores da IL-23 injetáveis, que oferecem elevada eficácia e respostas duradouras. No entanto, a necessidade de administração subcutânea dos mesmo dificultam a sua adesão reforçando a importância de alternativas orais eficazes.

Icotrokinra, também conhecida como JNJ-77242113, é um antagonista oral do recetor da IL-23, sendo o primeiro da sua classe, foi desenvolvido para inibir seletivamente a sinalização da IL-23 e, assim, suprimir a cascata inflamatória responsável pela progressão da psoríase. Estudos pré-clínicos demonstraram a sua capacidade de reduzir a produção de citocinas inflamatórias, melhorar a hiperplasia epidérmica e controlar a infiltração de células inflamatórias. Ensaios de Fase I definiram o seu perfil farmacocinético, evidenciando uma absorção rápida, exposição sistémica proporcional à dose e um perfil de segurança favorável. No ensaio de Fase II FRONTIER 1, icotrokinra mostrou resultados promissores, com até 79% dos pacientes a atingirem um PASI de 75 às 16 semanas no grupo de dose mais elevada. Estes achados foram reforçados pelo estudo de longo prazo FRONTIER 2, onde 76% dos pacientes mantiveram PASI 75 às 52 semanas, mantendo um perfil de segurança satisfatório.

Esta revisão avalia os dados clínicos emergentes sobre icotrokinra e explora o papel do eixo IL-23/IL-17 na psoríase. De facto, o icotrokinra pode ser uma alternativa oral conveniente aos biológicos injetáveis, este fármaco tem o potencial de melhorar a acessibilidade ao tratamento e a adesão dos doentes com psoríase moderada a grave. Contudo, são necessários mais dados provenientes de ensaios de fase III para confirmar a sua eficácia a longo prazo, segurança e aplicabilidade na prática clínica. Além disso, fatores como a variabilidade interindividual na resposta, potenciais preocupações de segurança a longo prazo e a relação custo-eficácia devem ser cuidadosamente avaliados antes da sua adoção generalizada.

A metodologia baseou-se numa pesquisa bibliográfica realizada nas bases de dados PubMed, ScienceDirect e Scopus. Foram incluídos estudos publicados entre 2022 e 2025, selecionados com base na leitura de títulos, resumos e, posteriormente, dos textos completos. Informações sobre ensaios clínicos decorridos ou a decorrer foram obtidas através da plataforma ClinicalTrials.gov e publicações oficiais até maio de 2025.

Palavras-chave: Keywords: “icotrokinra”, “JNJ-77242113”, “IL-23”, “oral IL-23 inhibitors”, “plaque psoriasis”, and “psoriasis treatment”.

## Abstract

Psoriasis is a chronic immune-mediated skin disease affecting approximately 1% to 3% of the global population, significantly impacting patients' quality of life. The pathogenesis of psoriasis is driven by the dysregulation of the interleukin-23/interleukin-17 (IL-23/IL-17) axis, leading to sustained immune activation, keratinocyte hyperproliferation, and epidermal remodelling. Biologic therapies targeting this pathway have revolutionized the treatment of moderate-to-severe psoriasis, particularly IL-23 inhibitors, offering high efficacy and durable responses. However, the need for subcutaneous administration and potential adherence issues highlights the necessity for effective oral alternatives.

Icotrokinra, also known as JNJ-77242113, is a novel, first-in-class oral IL-23 receptor antagonist peptide designed to selectively inhibit IL-23 signalling, thereby suppressing the inflammatory cascade responsible for psoriasis progression. Preclinical studies demonstrated its ability to reduce inflammatory cytokine production and improve epidermal hyperplasia and modulated immune cell infiltration. Phase I trials established its pharmacokinetic profile, showing rapid absorption, dose-proportional systemic exposure, and a favourable safety profile. In the Phase IIb FRONTIER 1 trial, icotrokinra showed promising efficacy, with up to 79% of patients achieving a psoriasis area severity index (PASI) of 75 at week 16 in the highest-dose group. These findings were reinforced by the long-term FRONTIER 2 study, where 76% of patients maintained PASI 75 at week 52, alongside a reassuring safety profile.

This review explores the role of the IL-23/IL-17 axis in psoriasis and evaluates the emerging clinical data on icotrokinra. As a convenient oral alternative to injectable biologics, it holds the potential to improve treatment accessibility and adherence for patients with moderate-to-severe psoriasis. However, further research, particularly from ongoing Phase III trials, is needed to establish its long-term benefits, safety, and place in clinical practice. Additionally, factors such as interindividual variability in response, potential long-term safety concerns, and cost-effectiveness must be carefully assessed before widespread clinical adoption.

The methodology was based on a literature search conducted in the PubMed, ScienceDirect, and Scopus databases. Studies published between 2022 and 2025 were included, selected through the screening of titles, abstracts, and subsequently, full-text articles. Information on completed or ongoing clinical trials was also obtained through the ClinicalTrials.gov platform and official publications up to May 2025.

Keywords: “icotrokinra”, “JNJ-77242113”, “IL-23”, “oral IL-23 inhibitors”, “IL-23 inhibitors”, “plaque psoriasis”, and “psoriasis treatment”.

## List of abreviativos

ACR - American College of Rheumatology
AEs- Adverse Events
BSA -Body Surface Area
CDLQI – Children's Dermatology Life Quality Index
CGI – Clinical Global Impression
CXCLs – C-X-C motif chemokine ligands
CYP - cytochrome
DLQI - Dermatology Life Quality Index
EP- Erythrodermic Psoriasis
f-PGA – Facial Physician's Global Assessment
GPP- Generalized Pustular Psoriasis
hf-PGA – Hand and Foot Physician's Global Assessment
IFN - type I interferons
IGA -Investigator's Global Assessment
IL -interleukin
IL-23R - IL-23 receptor
JAK2- Janus kinase 2
JDA- Japanese Dermatological Association
mg - milligram
NAPSI – Modified Nail Psoriasis Severity Index
nº- number
PASI -Psoriasis Area Severity Index
PD- Pharmacodynamics
PK - pharmacokinetics
PROMIS-29-Patient-reported Outcomes Measurement Information System
PsA -psoriatic arthritis
PSSD - Psoriasis Symptoms and Signs Diary
RORγt - retinoic acid-related orphan receptor gamma t
SAEs - Serious Adverse Events
sPGA-G – Static Physician's Global Assessment of Genital Psoriasis
ss-IGA – Scalp-Specific Investigator's Global Assessment
STATs - signal transducer and activator of transcription
TEAEs - treatment-emergent adverse events
Th - T helper cell
TNF-α - tumor necrosis factor alpha
TYK2- tyrosine kinase 2 inhibitor

## Index

## Table list

## 1 | Introduction

Psoriasis is a chronic inflammatory skin condition driven by immune system dysregulation, affecting approximately 1% to 3% of the global population. It typically follows a bimodal distribution and has a substantial impact on patients' quality of life. [1, 2]

The primary forms of psoriasis include chronic plaque psoriasis—the most common, accounting for 85% to 90% of cases—along with guttate, pustular, and erythrodermic variants. Although skin manifestations are the most obvious expression of psoriasis, it's a multisystem disease, capable of compromising multiple organs and often associated with various comorbidities. [1, 2, 3]

Due to the complexity of this condition, diagnosing psoriasis necessitates a detailed and comprehensive evaluation. The diagnosis is primarily clinical, relying on the visual assessment of skin lesions, with physical examination playing a key role. Beyond determining the specific subtype, it is crucial to assess disease severity—classified as mild, moderate, or severe—using measures such as body surface area (BSA) and the psoriasis area and severity index (PASI) to evaluate its potential systemic impact on the patient. [4]

Given the complex nature of psoriasis pathophysiology, managing the condition poses a considerable challenge, necessitating advanced and multifaceted therapeutic strategies. Current treatment strategies aim not only to alleviate symptoms but also to enhance patients' quality of life and prevent disease progression. These strategies include topical therapies, phototherapy, systemic treatments, and biologic agents that target specific immune pathways. [5]

For mild psoriasis (BSA < 3%), initial treatment typically involves topical therapies, including high-potency corticosteroids, vitamin D analogs (such as calcipotriene and calcitriol), calcineurin inhibitors (tacrolimus, pimecrolimus), and keratolytic agents like tazarotene and salicylic acid. In cases resistant to topical therapy, narrowband ultraviolet B phototherapy may be considered. For moderate-to-severe psoriasis (BSA ≥ 3%), systemic therapies play a central role, either as standalone treatments or in combination with topical agents and phototherapy. Conventional systemic options include methotrexate, acitretin, ciclosporin, and apremilast, with selection based on disease presentation, patient characteristics, and contraindications. Biologic therapies have transformed the treatment landscape by specifically targeting immune pathways involved in psoriasis. These include tumor necrosis factor-alpha (TNF-α) inhibitors (etanercept, infliximab, adalimumab), interleukin (IL) - 12/23 inhibitors (ustekinumab), IL-17 inhibitors (secukinumab, ixekizumab, brodalumab), and IL-23 inhibitors (guselkumab, risankizumab, tildrakizumab). These agents provide superior efficacy and longer-lasting disease control, marking a significant advancement in the management of moderate-to-severe psoriasis. [5, 6, 7]

Building upon this therapeutic evolution, the treatment landscape for psoriasis has significantly evolved with the introduction of monoclonal antibodies that specifically target inflammatory cytokines or their receptors. Several of these biologic therapies—such as ustekinumab (targets IL-12/23), guselkumab, tildrakizumab, and risankizumab—focus on inhibiting IL-23, a key driver of T-cell activation in psoriasis. Despite their high efficacy and favorable long-term safety profiles, subcutaneous administration poses limitations for some patients in terms of adherence and convenience. In contrast, oral treatments, including apremilast (a phosphodiesterase 4 inhibitor) and deucravacitinib (a tyrosine kinase 2 [TYK2] inhibitor), offer an alternative, but their efficacy remains moderate, and long-term safety data on TYK2 inhibitors are still limited. These limitations underscore the need for novel oral therapies that optimize efficacy, safety, and patient adherence in psoriasis management. [5, 7]

## 2 | Objectives

This article aims to review the role of Icotrokinra (JNJ-77242113) in the treatment of psoriasis.

## 3 | Methods

A literature search was conducted across multiple databases, including PubMed, ScienceDirect and Scopus. Information on completed or ongoing clinical trials was also obtained through the ClinicalTrials.gov platform and official publications up to May 2025. The key search terms employed consisted in combinations of the following medical terms: “icotrokinra”, “JNJ-77242113”, “IL-23”, “oral IL-23 inhibitors”, “IL-23 inhibitors”, “plaque psoriasis” and “psoriasis treatment”. The selection of articles was based on an analysis of their titles and reading of their abstracts, followed by a full reading of the articles selected. Inclusion criteria comprised articles published in English between 2022 and May 2025. This review ultimately included 14 articles, 13 clinical trials and 4 official publications.

## 4 | Discussion

### 4.1 | The role of IL-23/IL-17 axis on psoriasis

The development of psoriasis is driven by a multifactorial interplay of genetic predisposition, environmental influences, and intricate immune mechanisms, though its exact pathogenesis remains incompletely understood. Various external factors, including infections, psychological stress, tobacco use, alcohol consumption, and certain medications (such as beta-blockers and lithium), have been identified as potential triggers or exacerbating agents, particularly in individuals with an underlying genetic susceptibility. [3, 4, 5]

Upon exposure to these triggers, keratinocytes in the epidermis release endogenous nucleotides and antimicrobial peptides, initiating the local inflammatory cascade. Among these peptides, IL-37 stands out for its ability to stimulate plasmacytoid dendritic cells to produce type I interferons (IFN-α and IFN-β), which in turn activate myeloid dendritic cells. Acting as antigen-presenting cells, these myeloid dendritic cells secrete key pro-inflammatory cytokines, including TNF-α, IL-23, and IL-12.[5, 6]

IL-23 and IL-12 are crucial for T-helper cell expansion, specifically Th17 and Th1 cells, respectively. At a molecular level, the binding of IL-23 to its receptor activates TYK2 and Janus kinase 2 (JAK2), leads to the phosphorylation of signal transducer and activator of transcription 3 (STAT3). Once activated, STAT3 translocates into the nucleus, where it promotes the expression of pro-inflammatory genes, including retinoic acid-related orphan receptor gamma t (RORγt). In turn, RORγt acts as a master transcription factor that drives the differentiation of naïve T cells into Th17 cells. [5, 6, 7, 9]

Th17 cells emerge as the predominant pro-inflammatory T-cell subtype in psoriasis, producing a range of effector cytokines including IL-17A, IL-17F, IL-22, and TNF-α. These cytokines orchestrate the key histopathological features of the disease. Under stimulation by IL-17A, IL-17F, and TNF-α, keratinocytes produce C-X-C motif chemokine ligands (CXCLs), such as CXCL1 and CXCL8 (also known as interleukin-8), which play a crucial role in neutrophil recruitment and amplification of the inflammatory response. Additionally, IL-22 contributes to epidermal hyperplasia by promoting keratinocyte proliferation and inhibiting terminal differentiation, while also impairing skin barrier function. TNF-α acts synergistically with IL-17 to perpetuate inflammation through activation of both innate and adaptive immune cells. Furthermore, angiogenesis is enhanced within psoriatic plaques, largely due to cytokine-induced upregulation of vascular endothelial growth factor. [5, 9]

Recent studies have also highlighted the role of skin-resident memory T cells in disease recurrence. These long-lived CD8+ or CD4+ cells persist in previously affected skin, maintaining a local pro-inflammatory environment even after clinical resolution. Their presence helps explain the frequent relapse of psoriatic lesions in the same anatomical locations and represents a potential future therapeutic target. [3, 9]

Therefore, this process triggers a self-perpetuating inflammatory feedback loop, leading to the formation of psoriatic plaques. The persistent activation of dendritic cells in the skin results in continuous IL-23 production, sustaining the inflammatory cycle and disease progression. [3, 5, 9]

### 4.2 | IL-23 inhibitors

IL-23 inhibitors have significantly transformed the management of moderate-to-severe psoriasis. These biologic therapies selectively block either the p19 or p40 subunit of IL-23, thereby preventing the activation of the Th17 inflammatory pathway, a key driver of psoriasis pathogenesis. Both clinical trials and real-world evidence consistently highlight their strong efficacy, with high PASI 75/90/100 response rates and sustained disease control over time. Compared to traditional TNF-α inhibitors, IL-23 inhibitors demonstrate greater specificity, resulting in fewer unintended effects and an improved safety profile. [10]

Ustekinumab, the first biologic targeting the IL-12/23 pathway via the p40 subunit, marked a significant advance at the time of its approval. However, newer IL-23–selective agents — namely guselkumab, risankizumab, and tildrakizumab — which specifically target the p19 subunit, have shown superior long-term efficacy and durability. Accordingly, these agents are now strongly recommended for the treatment of moderate to severe psoriasis in several international clinical practice guidelines, including those of the American Academy of Dermatology - National Psoriasis Foundation, the European Dermatology Forum, and the UK's National Institute for Health and Care Excellence. [5, 11,12]

Despite their proven efficacy, IL-23 inhibitors present some challenges. As biologics, they require subcutaneous administration at regular intervals, which can be a barrier to adherence for some patients, particularly those seeking more convenient treatment options. While their safety profile is generally well-established, long-term immunosuppressive risks, including potential infections or malignancies, remain areas of ongoing investigation. Additionally, although these drugs provide long-lasting remission, some patients may experience secondary loss of response, necessitating treatment adjustments or combination therapies. [5, 11]

### 4.3 | Oral IL-23 inhibitors

In contrast to injectable biologics, which neutralize circulating cytokines such as IL-23 by targeting their p19 or p40 subunits, oral IL-23 inhibitors represent a novel therapeutic strategy that interferes with receptor-mediated signalling at the cellular level. These agents aim to retain the high efficacy of biologic therapies while offering the added convenience of oral administration, potentially improving long-term adherence and treatment accessibility. This innovation is particularly relevant for patients who are needle-averse or who prefer more flexible, self-managed therapeutic regimens. [5, 10, 13]

Icotrokinra is the first oral therapy of its kind developed for the treatment of psoriasis. This investigational macrocyclic peptide, resulting from a collaboration between Janssen Biotech and Protagonist Therapeutics, was engineered to selectively and potently bind to the IL-23 receptor, thereby inhibiting IL-23–mediated signalling and downstream inflammatory responses. [10, 13]

IL-23 is a pivotal cytokine in the IL-23/IL-17 axis, promoting the differentiation and maintenance of Th17 cells, which secrete IL-17, IL-22, and TNF-α, driving chronic inflammation and keratinocyte hyperproliferation in psoriasis. By blocking IL-23 receptor signalling, icotrokinra interrupts this pathogenic cascade, presenting itself as a promising targeted oral option for patients with moderate-to-severe psoriasis who may benefit from effective and convenient systemic therapy.[5, 9, 10]

Preclinical studies have shown that icotrokinra can significantly reduce the production of key inflammatory cytokines, resulting in improvements in epidermal hyperplasia and reductions in immune cell infiltration. In vitro, the compound exhibited high binding affinity to the IL-23 receptor (KD: 7.1 pM) and selectively inhibited IL-23–induced STAT3 phosphorylation in human peripheral blood mononuclear cells, while sparing IL-12–mediated STAT4 signalling. This selectivity may help preserve Th1 immune responses, potentially reducing the risk of certain infections associated with broader immunosuppression. It also suppressed IFN-γ production in whole blood from both healthy donors and psoriasis patients. [8]

In vivo, animal models of IL-23–driven inflammation—including trinitrobenzene sulfonic acid - induced colitis and IL-23–induced skin inflammation—showed significant reductions in dermal thickening and cytokine expression, including IL-17A, IL-17F, and IL-22, with therapeutic effects observed at doses as low as 0.3 milligrams per kilogram per day. [8]

Currently, several phase II and phase III trials are underway to better define its long-term clinical benefits and to assess its suitability for future regulatory approval. This revision will focus particularly on several key studies, namely: FRONTIER 1 and FRONTIER 2, ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, ICONIC-TOTAL, and ICONIC-LEAD. FRONTIER 1 and 2 are Phase 2b multicenter, randomized, placebo-controlled, dose-ranging studies designed to evaluate the efficacy and safety of JNJ-77242113 in the treatment of moderate-to-severe plaque psoriasis.[13, 14] ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 are Phase 3, multicenter, randomized, double-blind studies that are both placebo-controlled and include an active comparator arm using deucravacitinib. These trials aim to further assess the efficacy and safety of JNJ-77242113 in patients with moderate-to-severe plaque psoriasis. [15, 16] ICONIC-LEAD is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial incorporating a randomized withdrawal and retreatment component, it´s designed to evaluate the long-term efficacy and safety of JNJ-77242113 in patients with moderate-to-severe plaque psoriasis. [17] ICONIC-TOTAL is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial focusing specifically on the efficacy and safety of JNJ-77242113 in patients with plaque psoriasis involving special anatomical areas. [18]

### 4.3.1 | Pharmacodynamics and Pharmacokinetics

The pharmacokinetic (PK) profile of icotrokinra, a high-affinity oral IL-23 receptor antagonist, was first established in healthy adult volunteers through a Phase I clinical trial (NCT05703841). This study, involving 30 participants, evaluated both single and multiple ascending dose regimens. Icotrokinra demonstrated rapid absorption, with peak plasma concentrations occurring within 2 to 5 hours post-administration. Systemic exposure increased proportionally across doses ranging from 10 to 1000 milligrams (mg), and the observed terminal half-life of 9 to 16 hours supported once- or twice-daily dosing schedules. Importantly, systemic exposure was consistent across demographic subgroups, with no clinically relevant variability observed based on age, body weight, or sex, suggesting a predictable pharmacokinetic behavior and no need for dose adjustment in the studied population. [6, 8]

In the Phase IIb FRONTIER 1 study (NCT05223868), the pharmacokinetic profile of icotrokinra was further evaluated in patients with moderate-to-severe plaque psoriasis across multiple dosing regimens. The study confirmed linear pharmacokinetics, with higher doses resulting in proportionally increased systemic exposure and correlated with greater clinical response. The long-term extension study, FRONTIER 2 (NCT05364554), reinforced these findings by demonstrating sustained plasma concentrations over 52 weeks of continuous treatment. Importantly, no evidence of drug accumulation or unexpected pharmacokinetic variation was observed. These data support icotrokinra's long-term stability, dose proportionality, and predictable exposure profile in clinical use. [13, 14]

Phase III trials, the ICONIC-ADVANCE 1 (NCT06143878) and ICONIC-ADVANCE 2 (NCT06220604), further supported this profile, and ongoing studies are contributing additional data in special populations. [14, 15] Notably, the ICONIC-LEAD (NCT06095115) study provided the first pharmacokinetic and pharmacodynamics (PD) insights in adolescents aged 12 years and older, showing consistent systemic exposure with adult populations and no need for dose adjustments based on age. [17, 19]

Moreover, the ICONIC-TOTAL (NCT06095102) trial is expanding the understanding of icotrokinra's pharmacodynamic behavior in anatomically complex regions such as the scalp and genital area. These areas often pose absorption challenges, yet preliminary data suggest icotrokinra maintains therapeutic concentrations and biological activity in these regions, reinforcing its systemic bioavailability and distribution. [18, 19]

Regarding drug metabolism, icotrokinra is primarily processed in the liver via cytochrome (CYP) P450 enzymes, predominantly CYP3A4, with minimal involvement of CYP2C9 and CYP2D6, suggesting a low risk for significant drug-drug interactions. However, caution may be necessary when co-administered with strong CYP3A4 modulators, such as ketoconazole, rifampicin, or certain corticosteroids, which are commonly used in patients with comorbid conditions. [8, 11]

Overall, icotrokinra demonstrates a favorable PD and PK profile, marked by rapid absorption, predictable exposure, minimal accumulation, and broad applicability across patient populations and anatomical sites. These features support its role as a first-in-class oral IL-23 receptor antagonist with potential advantages in terms of accessibility and adherence.[8, 9, 11, 14]

### 4.3.2 | Efficacy

A phase IIb, multicenter, randomized, double-blind, placebo-controlled study (FRONTIER 1) evaluated the efficacy of icotrokinra in 255 patients with moderate-to-severe plaque psoriasis. Participants were assigned in a 1:1:1:1:1:1 ratio to receive one of five icotrokinra dosing regimens (25 mg once daily, 25 mg twice daily, 50 mg once daily, 100 mg once daily, or 100 mg twice daily) or placebo for 16 weeks. The primary endpoint was the proportion of patients achieving at least a 75% reduction in the PASI at week 16. Icotrokinra treatment demonstrated a clear dose–response relationship, with PASI 75 response rates of 37%, 51%, 58%, 65%, and 79% across increasing doses, compared to 9% in the placebo group ($p < 0.001$). Additionally, higher PASI thresholds were also met: PASI 90 was achieved in up to 60% of patients in the highest dose group (with 26%, 27%, 51%, 47% in the 25 mg once daily, 25 mg twice daily, 50 mg once daily, 100 mg once daily, respectively), and PASI 100 in up to 40% (12%, 10%, 26%, 23% in the 25 mg once daily, 25 mg twice daily, 50 mg once daily, 100 mg once daily, respectively) Finally, investigator's global assessment (IGA) scores of 0 or 1 was achieved by 64% of patients receiving 100 mg twice daily, indicating near-complete or complete skin clearance. [13]

The FRONTIER 2 long-term extension study continued to evaluate the efficacy and safety of icotrokinra over 52 weeks. Among the 255 patients from FRONTIER 1, 227 (89%) continued treatment. Those initially on icotrokinra maintained their assigned dose, while placebo patients switched to 100 mg once daily. At week 52, in the highest-dose group (100 mg twice daily), 76% of patients maintained PASI 75, 64% reached PASI 90, and 40% sustained PASI 100 responses. Additionally, 43% of patients in this group achieved complete skin clearance (IGA 0) by week 5. Beyond efficacy, patient-reported outcomes also improved significantly: at week 52, a Dermatology Life Quality Index (DLQI) score of 0 or 1 was achieved in a substantial proportion of patients, reflecting minimal impact of psoriasis on daily life. Furthermore, the Psoriasis Symptoms and Signs Diary (PSSD) revealed meaningful improvements in itch and pain, with 50% of patients achieving at least a 4-point reduction — the threshold for clinical significance. [14]

Phase III trials further validated these outcomes. The ICONIC-LEAD study included both adults and adolescents (aged 12+) with moderate-to-severe plaque psoriasis demonstrated that by week 16, 65% of patients on once-daily icotrokinra achieved IGA 0/1 and 50% reached PASI 90, compared to 8% and 4% in the placebo group, respectively ($p < 0.001$). By week 24, efficacy further improved: 74% reached IGA 0/1, 65% PASI 90, and 40% PASI 100. In very recent data, adolescents

showed particularly strong outcomes, with 75% achieving IGA 0 and 63.6% achieving PASI 100, supporting consistent efficacy across age groups and reinforcing its safety profile. [19, 20, 21]

The ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 trials demonstrated icotrokinra superiority over deucravacitinib, a TYK2 inhibitor, in patients with plaque psoriasis. Both trials met their co-primary endpoints (IGA 0/1 and PASI 90 at week 16) with icotrokinra demonstrating superiority over both placebo and deucravacitinib. In ICONIC-ADVANCE 1, 68% of patients on icotrokinra achieved PASI 90 at week 16, versus 46% on deucravacitinib and 8% on placebo. Similar results were seen in ICONIC-ADVANCE 2, with 70% achieving PASI 90 on icotrokinra compared to 44% on deucravacitinib. Updated data presented reaffirmed these advantages, with high durability of these responses through week 24. [19, 20, 21]

The ICONIC-TOTAL study is a Phase III trial evaluating icotrokinra in patients with plaque psoriasis affecting anatomically difficult areas such as the scalp, genital region, palms, and soles. Preliminary 2025 results showed that icotrokinra significantly improved local disease severity, with over 60% of patients achieving PASI 90 and approximately 45% reaching IGA 0/1 in these specific regions by week 16. These results are especially relevant, as conventional therapies often fail to achieve satisfactory outcomes in such areas. [19, 20, 21]

Overall, icotrokinra has shown robust and sustained efficacy in improving clinical outcomes and patient-reported measures, with a strong safety profile, across various populations and treatment contexts. These results position it as a promising oral therapy for moderate-to-severe plaque psoriasis. [13, 14, 19, 20, 21]

### 4.3.3 | Safety

The phase IIb FRONTIER 1 study found icotrokinra to be well tolerated, with a safety profile comparable to placebo. The most frequently observed treatment-emergent adverse events (TEAEs)—defined as medical events that newly occurred or worsened following the initiation of study treatment—included nasopharyngitis (7%), upper respiratory tract infections (5%), diarrhea (5%), headache (4%), and cough (4%). This category differs from general adverse events (AEs), which include any unwanted medical event that happens during the trial, regardless of their temporal relation to treatment or causality. TEAEs are commonly graded by severity (mild, moderate, or severe), while serious adverse events (SAEs) are defined by regulatory criteria as events that result in hospitalization, significant disability, are life-threatening, or result in death. Across the various icotrokinra dosing groups, the overall incidence of adverse events ranged from 47% to 62%, closely aligning with the 51% observed in the placebo group. [13]

FRONTIER-2 evaluated 52 weeks of treatment, followed by a 4-week safety follow-up, extending through week 56. Between weeks 16 and 56, 59% of patients reported at least one AEs, most of which were mild to moderate. The most frequent TEAEs were nasopharyngitis (18%), upper

respiratory tract infection (10%), COVID-19 (5%), musculoskeletal pain (7%), and headache (3.5%). Gastrointestinal events were reported in 6% of patients, with diarrhea being the most common. SAEs occurred in 4% of patients, but none were considered treatment related. Reported SAEs included isolated cases of coronary artery disease, cerebrovascular accident, and ventricular dysfunction. Importantly, despite being an immunomodulatory therapy, icotrokinra has not been associated with an increased incidence of opportunistic infections such as tuberculosis, herpes zoster, or invasive fungal infections. This may be partly attributed to its receptor-level selectivity, which allows for preservation of IL-12-mediated STAT4 signalling and Th1 responses. Unlike broader immunosuppressants, this selective inhibition of the IL-23 pathway may help maintain host defence against intracellular pathogens, supporting a more favorable infectious risk profile. [9, 14]

Regarding treatment discontinuation, rates were low (2%), and no safety signals were identified. Laboratory evaluations, electrocardiograms, and vital sign monitoring revealed no clinically significant abnormalities. These findings suggest that long-term exposure to icotrokinra does not result in cumulative toxicity or systemic organ impairment. [14]

Data from the phase III ICONIC-LEAD trial corroborated these findings. The incidence of TEAEs was 49% in both the treatment and placebo arms, with no emergent safety concerns. Reported adverse events mirrored those seen in earlier trials and remained mostly mild to moderate in intensity. Importantly, the safety profile in adolescents was consistent with that observed in adults, with no additional safety risks identified in this subgroup. [19, 20, 21]

Additional safety data from the ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 studies showed a similar incidence of TEAEs between the icotrokinra and deucravacitinib treatment groups. Most adverse events were of mild to moderate severity, and there was no increase in SAEs or treatment discontinuations with icotrokinra. No new safety signals emerged through week 24, further supporting the reproducibility of its safety profile in larger and diverse populations. [19, 20, 21]

The ICONIC-TOTAL also demonstrated safety outcomes consistent with previous studies. Importantly, no increase in local irritation, systemic hypersensitivity, or site-specific adverse effects was observed, supporting the tolerability of icotrokinra in regions where the skin barrier is more vulnerable. [21, 22]

Compared to injectable IL-23 inhibitors such as guselkumab and risankizumab, which have demonstrated a robust long-term safety profile, early-phase data on icotrokinra suggest a similarly favorable safety profile, with no added risk attributable to its oral administration. Across clinical trials, no clinically significant hepatic, renal, hematologic, or electrocardiographic abnormalities have been observed. While direct comparative studies are lacking, these findings support the potential suitability of icotrokinra for long-term systemic use in psoriasis management. [10, 13, 14]

Overall, icotrokinra demonstrated a favorable safety and tolerability profile over one year of continuous treatment, with most adverse events being mild to moderate and no unexpected safety concerns. [13, 14, 19, 20, 21, 22]

## 5 | Conclusions

Icotrokinra is a first-in-class oral IL-23R antagonist that selectively disrupts the IL-23/IL-17 axis by inhibiting downstream STAT3 activation and the subsequent production of key effector cytokines, including IL-17A, IL-17F, and IL-22. Unlike monoclonal antibodies targeting the IL-23 cytokine directly, it acts at the receptor level, preserving IL-12/STAT4 signalling and Th1 responses, which may help maintain host immunity while providing targeted anti-inflammatory effects. [8, 9]

Across multiple clinical trials—including FRONTIER 1 and 2, ICONIC-LEAD, ICONIC-ADVANCE 1 and 2, and ICONIC-TOTAL—icotrokinra has consistently demonstrated high levels of clinical efficacy in the treatment of moderate-to-severe plaque psoriasis. Significant improvements were observed across all key endpoints, including PASI 75/90/100 and IGA 0/1, with rapid onset of action, sustained skin clearance, and improved patient-reported outcomes. These benefits were also evident in adolescent populations and in patients with psoriasis affecting anatomically sensitive and difficult-to-treat areas, such as the scalp, genital region, palms, and soles. [13, 14, 19, 20, 21, 22]

The safety profile of icotrokinra has remained favorable throughout all phases of development. Adverse events were generally mild to moderate and comparable to placebo, with no emerging safety concerns across diverse populations. Moreover, its oral formulation did not introduce additional safety risks compared to established injectable IL-23 inhibitors, such as guselkumab or risankizumab. Rigorous safety monitoring—including laboratory testing, ECGs, and independent adjudication—reinforces the robustness of these findings. [10, 13, 14, 19, 20, 21, 22]

Emerging translational data suggest that icotrokinra may exert disease-modifying effects by modulating skin-resident memory T cells, potentially contributing to durable remission beyond treatment discontinuation—although this remains an exploratory hypothesis. Its unique combination of biologic-level efficacy, oral administration, and receptor-level selectivity offers a promising alternative for patients who prefer non-injectable therapies or face adherence challenges, thus bridging a critical therapeutic gap in systemic psoriasis care. Furthermore, ongoing clinical trials in other immune-mediated inflammatory diseases—including ulcerative colitis, generalized pustular psoriasis, and psoriatic arthritis—highlight its potential as a versatile IL-23–targeted platform therapy extending beyond dermatology. [14, 19, 20, 21, 22, 23, 24, 25, 26]

In summary, icotrokinra represents a promising oral therapeutic option for moderate-to-severe plaque psoriasis, combining strong efficacy, sustained benefit, and a well-tolerated safety profile. Continued investigation in psoriasis and other immune-mediated conditions will be key to defining its full clinical potential. [13, 14, 19, 20, 21, 22]

## 6 | References


1. Garner KK, Hoy KDS, Carpenter AM. Psoriasis: Recognition and Management Strategies. Am Fam Physician. 2023;108(6):562–573.
2. Estevinho T, Lé AM, Torres T. Deucravacitinib in the treatment of psoriasis. *J Dermatol Treat*. 2023;34(1):2154122.
3. Mrowietz U, Lauffer F, Sondermann W, Gerdes S, Sewerin P. Psoriasis as a systemic disease. *Dtsch Arztebl Int*. 2024;121:467–72.
4. Nicolescu AC, Ionescu MA, Constantin MM, et al. Psoriasis management challenges regarding difficult-to-treat areas: therapeutic decision and effectiveness. Life. 2022;12(12):2050.
5. Drakos A, Torres T, Vender R. Emerging oral therapies for the treatment of psoriasis: a review of pipeline agents. *Pharmaceutics*. 2024;16(1):111.
6. Lee HJ, Kim M. Challenges and future trends in the treatment of psoriasis. *Int J Mol Sci*. 2023;24(17):13313.
7. Carmona-Rocha E, Rusiñol L, Puig L. New and emerging oral/topical small-molecule treatments for psoriasis. *Pharmaceutics*. 2024;16:239.
8. Fourie AM, Cheng X, Chang L, Greving C, Li X, Knight B, et al. JNJ-77242113, a highly potent, selective peptide targeting the IL-23 receptor, provides robust IL-23 pathway inhibition upon oral dosing in rats and humans. Sci Rep 2024;14(17515):1–15.
9. Sieminska I, Pieniawska M, Grzywa TM. The Immunology of Psoriasis—Current Concepts in Pathogenesis. Clin Rev Allergy Immunol 2024;66(164):164–191.
10. Blauvelt A, Chiricozzi A, Ehst BD, Lebwohl MG. Safety of IL-23 p19 inhibitors for the treatment of patients with moderate-to-severe plaque psoriasis: a narrative review. Adv Ther 2023;40(3410):3410–3433.
11. Ruggiero A, Megna M, Fabbrocini G, Ocampo-Garza SS. Anti-IL23 biologic therapies in the treatment of psoriasis: real-world experience versus clinical trials data. Immunol Res 2023;71(328):328–355.
12. Armstrong AW, Gelfand JM, Yamauchi PS, et al. Biologic treatment options for moderate-to-severe psoriasis: A perspective based on efficacy, safety, and guidelines from the AAD-NPF, EDF, and NICE. Journal of the American Academy of Dermatology. 2023;88(5):1223–1238. doi:10.1016/j.jaad.2022.12.009
13. Bissonnette R, Pinter A, Ferris LK, Gerdes S, Rich P, Vender R, et al. An oral interleukin-23–receptor antagonist peptide for plaque psoriasis. N Engl J Med 2024;390(6):510–521.
14. Ferris LK, Bagel J, Huang YH, Pink AE, Tyring SK, Kokolakis G, et al. FRONTIER-2: a phase 2b, long-term extension, dose-ranging study of oral JNJ-77242113 for the treatment of moderate-to-severe plaque psoriasis. J Am Acad Dermatol 2025;92(3):495–502.
15. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 for the treatment of participants with moderate to severe plaque psoriasis; 2025 Apr 25 [cited 2025-05-13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06143878
16. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 for the treatment of participants with moderate to severe plaque psoriasis (ICONIC-ADVANCE 2); 2025 Apr 27 [cited 2025-05-13]. Available from https://clinicaltrials.gov/ct2/show/NCT06220604
17. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 in adolescent and adult participants with moderate to severe plaque psoriasis (ICONIC-LEAD); 2025 Apr 27 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06095115

18. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 for the treatment of participants with plaque psoriasis involving special areas (scalp, genital, and/or palms of the hands and the soles of the feet) (ICONIC-TOTAL); 2025 Apr 4 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06095102
19. 19. Studna A. Johnson & Johnson's Icotrokinra succeeds across multiple trials in moderate-to-severe plaque psoriasis, ulcerative colitis [Internet]. Applied Clin Trials. 2025 Mar 12 [cited 2025 May 13]. Available from: https://www.appliedclinicaltrialsonline.com/view/johnson-johnson-icotrokinra-succeeds-across-multiple-trials-moderate-severe-plaque-psoriasis-ulcerative-colitis
20. Tracy D. Johnson & Johnson's Icotrokinra demonstrates significant skin clearance in adolescents with moderate-to-severe plaque psoriasis [Internet]. Pharm Exec. 2025 Apr 11 [cited 2025 May 13]. Available from: https://www.pharmexec.com/view/johnson-johnson-icotrokinra-demonstrates-significant-skin-clearance-adolescents-moderate-severe-plaque-psoriasis
21. Johnson & Johnson. Icotrokinra results show potential to set a new standard of treatment in plaque psoriasis [Internet]. Johnson & Johnson Media Center. [date unknown] [cited 2025 May 13]. Available from: https://www.jnj.com/media-center/press-releases/icotrokinra-results-show-potential-to-set-a-new-standard-of-treatment-in-plaque-psoriasis
22. Meara K. Icotrokinra shows high rates of skin clearance in scalp, genital psoriasis [Internet]. Drug Topics. 2025 May 12 [cited 2025 May 13]. Available from: https://www.drugtopics.com/view/icotrokinra-shows-high-rates-of-skin-clearance-in-scalp-genital-psoriasis
23. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 for the treatment of participants with generalized pustular psoriasis or erythrodermic psoriasis; 2025 Apr 27 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06295692
24. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study to evaluate the efficacy and safety of JNJ-77242113 (icotrokinra) in biologic-naïve participants with active psoriatic arthritis (ICONIC-PsA 1); 2025 Apr 27 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06878404
25. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study to evaluate the efficacy and safety of icotrokinra (JNJ-77242113) in biologic-experienced participants with active psoriatic arthritis (ICONIC-PsA 2); 2025 Apr 27 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06807424
26. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 in participants with moderately to severely active ulcerative colitis (ANTHEM-UC); 2025 Apr 27 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT06049017
27. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 for the treatment of moderate-to-severe plaque psoriasis (SUMMIT); 2025 Apr 27 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT05357755
28. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 following oral administration in healthy Chinese adult participants; 2023 Jun 5 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT05703841
29. ClinicalTrials.gov (Internet). Bethesda (MD): National Library of Medicine (US). A study of JNJ-77242113 in healthy Japanese and Chinese participants; 2025 Feb 3 [cited 2025 May 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT05062200

## 7 | Appendix

**Table 1:** Clinical trials completed evolving JNJ-77242113 [13, 14, 27, 28, 29]

| Study | Design | Outcomes | Results | Safety |
|---|---|---|---|---|
| **FRONTIER 1 NCT05223868 A Phase 2b Multicenter, Randomized, Placebo Controlled, Dose-ranging Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis** | **Study type**: Interventional<br><br>**Study Phase:** phase 2<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113 - tablet will be administered orally.<br>• Drug: Placebo - tablet will be administered orally.<br><br>**Sexes:** All<br><br>**Ages:** 18 Years and older<br><br>**Enrolment (Actual)**: 255 | ***Primary outcomes:***<br>• Percentage of participants achieving PASI 75 score at week 16<br>***Secondary outcomes:***<br>• Change from Baseline in PASI Total Score at Week 16<br>• Percentage of Participants Achieving PASI 90 score at Week 16<br>• Percentage of Participants Achieving PASI 100 score at Week 16<br>• Percentage of Participants Achieving an IGA Score of Cleared (0) or Minimal (1) at Week 16<br>• Change from Baseline in BSA at Week 16<br>• Change from Baseline in PSSD Symptoms Scores at Week 16<br>• Change from Baseline in PSSD Signs Score at Week 16<br>• Percentage of Participants Achieving PSSD Symptoms Score=0 at Week 16 in Participants with a Baseline Symptoms Score >=1<br>• Percentage of Participants Achieving PSSD Sign Score=0 at Week 16 in Participants with a Baseline Sign Score >=1<br>• Percentage of Participants Achieving a DLQI of 0 or 1 at Week 16 in Participants with Baseline DLQI Score >1<br>• Change from Baseline in PROMIS-29 Domain Score at Week 16<br>• Percentage of Participants Who Achieve >= 5-Point Improvement from Baseline in PROMIS-29 Domain Score at Week 16 | A total of 255 patients underwent randomization. The mean PASI score at baseline was 19.1. The mean duration of psoriasis was 18.2 years, and 78% of the patients across all the trial groups had previously received systemic treatments. At week 16, the percentages of patients with a PASI 75 response were higher among those in the JNJ-77242113 groups (37%, 51%, 58%, 65%, and 79% in the 25-mg once-daily, 25-mg twice-daily, 50-mg once-daily, 100-mg once-daily, and 100-mg twice-daily groups, respectively) than among those in the placebo group (9%), a finding that showed a significant dose–response | The most common adverse events included coronavirus disease 2019 (in 12% of the patients in the placebo group and in 11% of those across the JNJ-77242113 dose groups) and nasopharyngitis (in 5% and 7%, respectively).<br><br>The percentages of patients who had at least one adverse event were similar in the combined JNJ-77242113 dose group (52%) and the placebo group (51%).<br><br>There was no evidence of a dose-related increase in adverse events across the JNJ-77242113 dose groups |

| | | | | |
|---|---|---|---|---|
| | | • Nº of Participants with AEs [Time Frame: Up to 24 weeks]<br>• Nº of Participants with SAEs [Time Frame: Up to 24 weeks] | relationship (P<0.001). | |
| **FRONTIER 2 NCT05364554 A Phase 2b Multicenter, Long-Term Extension, Dose-ranging Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis** | **Study type:** Interventional<br><br>**Study Phase:** phase 2<br><br>**Study Design**<br>• Allocation: Non-Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>Condition: Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113 - JNJ-77242113 tablet will be administered orally.<br><br>Sexes: All<br><br>**Ages:** 18 Years and older<br><br>**Enrolment (Actual)**: 227 | ***Primary outcomes:***<br>• Percentage of Participants Achieving PASI 75 score at Week 36<br>***Secondary outcomes:***<br>• Percentage of Participants Achieving PASI 90 score at Week 36<br>• Percentage of Participants Achieving PASI 100 score at Week 36<br>• Change From Baseline in PASI Total Score at Week 36<br>• Percentage of Participants Achieving an IGA Score of Cleared (0) or Minimal (1) at Week 36<br>• Change from Baseline in PSSD Symptoms Scores at Week 36<br>• Change from Baseline in PSSD Signs Score at Week 36<br>• Percentage of Participants Achieving PSSD Symptoms Score=0 at Week 36 Among Participants with a Baseline (in the Originating Study) Symptoms Score >=1<br>• Percentage of Participants Achieving PSSD Signs Score=0 at Week 36 Among Participants with a Baseline (in the Originating Study) Signs Score >=1<br>• Percentage of Participants Achieving PSSD Signs Score=0 at Week 36 Among Participants with a Baseline (in the Originating Study) Signs Score >=1<br>• Nº of Participants with SAEs | Most FRONTIER-1 patients (227; 89%) continued to FRONTIER-2, maintaining response rates from W16–52.<br><br>The highest response rates were seen with JNJ-77242113 100 mg BID.<br>At W52:<br>⇒ PASI 75: 76%<br>⇒ PASI 90: 64%<br>⇒PASI 100: 40%<br>⇒ IGA 0/1: 74%<br>⇒ Inves IGA 0: 43%<br>The main reason for treatment discontinuation in FRONTIER-2 was lack of efficacy, more frequent in lower-dose groups.<br>Only 2 patients (100 mg onde daily) and 1 patient (100 mg BID) discontinued for this reason. | From W16–56, 59% of JNJ-77242113-treated patients experienced ≥1 adverse event-<br>The most common AEs were nasopharyngitis (18%), upper respiratory tract infection (10%), and COVID-19 (5%). GI-related AEs occurred in 12% of PBO-treated and 11% of JNJ-77242113-treated patients, with no increase in GI AEs from W16–56 across JNJ-77242113 groups.<br>Serious AEs occurred in 4% of patients but were unrelated to treatment.<br>No dose-dependent increase in the occurrence of AEs was observed. |

| | | | | |
|---|---|---|---|---|
| **SUMMIT NCT05357755** ***A Phase 2a Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy, Safety, and Tolerability of an Oral Tablet Formulation of JNJ-77242113 for the Treatment of Moderate-to-Severe Plaque Psoriasis*** | **Study type**: Interventional<br><br>**Study Phase:** phase 2<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113<br>  • JNJ-77242113 will be administered orally as delayed release tablets.<br>  • Other Names: PN-21235, PN-235<br>• Drug: Placebo - Matching placebo will be administered orally as delayed release tablets.<br><br>**Sexes:** All<br><br>**Ages:** 18 Years to 75 Years<br><br>**Enrolment (Actual)**: 90 | ***Primary outcomes:***<br>• Percentage of Participants PASI 75 score at Week 16 [Time Frame: Week 16]<br><br>***Secondary outcomes:***<br>• Nº of Participants with AEs Time Frame: Up to Week 24]<br>• Nº of Participants with SAEs [Time Frame: Up to Week 24]<br>• Change from Baseline in PASI Total Score at Week 16 [Time Frame: Baseline and Week 16]<br>• Percentage of Participants Achieving PASI 90 score at Week 16 [Time Frame: Week 16]<br>• Percentage of Participants Achieving PASI 100 score at Week 16 [Time Frame: Week 16]<br>• Percentage of Participants Achieving an IGA Score of Cleared (0) or Minimal (1) at Week 16 [Time Frame: Week 16]<br>• Percentage of Participants Achieving an IGA Score of Cleared (0) at Week 16 [Time Frame: Week 16]<br>• Change from Baseline in BSA at Week 16 [Time Frame: Baseline and Week 16] | The study has not been publicly submitted, but its completion date was released as April 10, 2023. | |
| **NCT05703841 An Open-label, Single-dose Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of JNJ-77242113** | **Study type**: Interventional<br><br>**Study Phase:** phase 1<br><br>**Study Design:**<br>• Allocation: Randomized | ***Primary outcomes:***<br>• Area Under the Plasma Concentration versus Time Curve from Time Zero to Time of the Last Measurable Concentration (AUC[0-last]) of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>• Area Under the Plasma Concentration versus Time | The study has not been publicly submitted, but its completion date was recorded as April 12, 2023. | |

| | | | | |
|---|---|---|---|---|
| **Following Oral Administration in Healthy Chinese Adult Participants** | • Interventional Model: Parallel Assignment<br>• Masking: None (open label)<br>• Primary Purpose: Treatment<br><br>**Condition:** Healthy<br><br>**Intervention:**<br>• Drug: JNJ-77242113<br>  • JNJ-77242113 will be administered orally as an immediate release (IR) film-coated tablet.<br>  • Other Names: PN-21235, PN-235<br><br>**Sexes:** All<br><br>**Ages:** 18 Years to 55 Years (adult)<br><br>**Enrolment (Actual)**: 30 | Curve from Time Zero to Infinite Time of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>• Maximum Observed Plasma Concentration of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>• Time to Reach the Maximum Observed Plasma Concentration of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>• Apparent Elimination Half-life of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>• Apparent Total Systemic Clearance of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>• Apparent Volume of Distribution of JNJ-77242113 [Time Frame: Predose up to Day 3]<br>***Secondary outcomes:***<br>• Nº of Participants with Abnormalities in Physical Examinations [Time Frame: Up to Day 35]<br>• Nº of Participants with Abnormalities in 12-Lead ECGs [Time Frame: Up to Day 35]<br>• Nº of Participants with Abnormalities in Vital Signs [Time Frame: Up to Day 35]<br>• Nº of Participants with Abnormalities in Clinical Laboratory Tests [Time Frame: Up to Day 35]<br>• Nº of Participants with AEs [Time Frame: Up to Day 35] | | |

| | | | | |
|---|---|---|---|---|
| **NCT05062200 A Randomized, Double-blind, Placebo-controlled, Single Ascending Dose Study to Investigate Safety, Tolerability, and Pharmacokinetics of JNJ-77242113 in Healthy Japanese Participants and a Single Dose Study to Investigate Safety, Tolerability, and Pharmacokinetics of JNJ-77242113 in Healthy Chinese Participants** | **Study type**: Interventional<br>**Study Phase:** phase 1<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: sequential Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br>**Condition:** Healthy<br><br>**Intervention**<br>• Drug: JNJ-77242113 - JNJ-77242113 tablet will be administered orally.<br>• Drug: Placebo – Matching placebo tablet will be administered orally.<br>**Sexes:** All<br>**Ages:** 20 Years to 60 Years (adult)<br>**Enrolment (Actual)**: 36 | ***Primary outcomes:***<br>• Parts 1, 2 and 3: Nº of Participants with AEs as a Measure of Safety and Tolerability [Time Frame: Up to 6 weeks]<br>• Parts 1, 2 and 3: Plasma Concentration of JNJ-77242113 [Time Frame: Predose up to 48 hours post dose (Up to Day 3)]<br><br>***Secondary outcomes:***<br>• *Not provided* | The study has not been publicly submitted, but its completion date was recorded as September 28, 2022. | |

**Table 2:** Clinical trials in development evolving JNJ-77242113 [15, 16, 17, 18, 23, 24, 25, 26]

| Study | Design | Outcomes | Results |
|---|---|---|---|
| **ICONIC-LEAD NCT06095115 A Phase 3 multicenter randomized double-blind, placebo-controlled Study to Evaluate the Efficacy and Safety of JNJ77242113 for the treatment of** | **Study type:** Interventional<br><br>**Study Phase**: phase 3<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator) | ***Primary outcomes:***<br>• Percentage of participants achieving an IGA score of 0 or 1 and greater than or equal to (>= )2- grade improvement from baseline to week 16<br>• Percentage of participants achieving PASI 90 response at week 16<br><br>***Secondary outcomes:***<br>• Percentage of Participants Achieving an IGA Score of 0 at Week 16<br>• Percentage of Participants Achieving PASI 75 Response at Weeks 4 and 16<br>• Percentage of Participants Achieving PASI 90 Response at Week 8 | The study has not been publicly submitted, but the estimated completion date is April 6, 2027. |

| | | | |
|---|---|---|---|
| **participants with moderate to severe plaque psoriasis with randomized withdrawal and retreatment** | • Primary Purpose: Treatment<br><br>**Condition:** Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113 will be administered orally.<br>• Drug: Placebo will be administered orally.<br><br>**Sexes:** All<br><br>**Ages:** 12 Years and older<br><br>**Enrolment (Actual):** 684 | • Percentage of Participants Achieving PASI 100 Response at Week 16<br>• Percentage of Participants Achieving ss-IGA Score of 0 or 1 and >=2 Grade Improvement Baseline to Week 16<br>• Percentage of Participants Achieving PSSD Symptom Score of 0 at Weeks 8 and 16<br>• Percentage of Participants Achieving >=4-Point Improvement from Baseline in PSSD Itch Score to Weeks 4 and 16<br>• Time to Loss of PASI 75<br>• Time to Loss of PASI 90<br>• Nº of Participants with Treatment-emergent AEs<br>• Nº of Participants with Treatment-emergent SAEs<br>• Change from baseline in BSA at week 16<br>• Change from baseline in PASI total score at week 16<br>• Percent Improvement in PASI Score from Baseline to Week 16<br>• Percentage of Participants Achieving a sPGA-G Score of 0 or 1 and at Least a 2-grade Improvement in Genital Psoriasis from Baseline to Week 16<br>• Percentage of Participants Achieving a hf-PGA Score of 0 or 1 and at Least a 2-grade Improvement at week 16<br>• Percent Change from Baseline in Modified Nail Psoriasis Severity Index score at week 16<br>• Percent of Participants Achieving f-PGA Score of 0 or 1 at Week 16<br>• Change From Baseline in PSSD Symptom score at week 16<br>• Change From Baseline in PSSD sign score at week 16<br>• Percentage of Participants Achieving PSSD Sign Score of 0 at Week 16<br>• Percentage of Participants Achieving Genital Psoriasis Sexual Frequency Questionnaire Item 2 score of 0 or 1 at Week 16<br>• Percentage of Participants Achieving DLQI Score of 0 or 1 at Week 16<br>• Change From Baseline in total DLQI score at week 16<br>• Change from Baseline in Domain Scores of the PROMIS-29 Score at Week 16<br>• Percentage of participants achieving Children's Dermatology Life Quality Index (CDLQI) score of 0 or 1 at Week 16<br>• Change From Baseline in CDLQI at Week 16<br>• Change From Baseline in the Domain Scores of the PROMIS-25 Paediatric Score at Week 16 | |

| | | | |
|---|---|---|---|
| | | • Percentage of Participants Achieving IGA Score of 0 at Week 52<br>• Percentage of Participants Achieving PASI 100 Response at Week 52<br>• Time to Loss of IGA 0 to 1 Response<br>• Percentage of Adolescent Participants Achieving IGA Score of 0 or 1 and >=2 Improvement from Baseline to Week 52<br>• Percentage of Adolescent Participants Achieving PASI 75 Response at Week 52<br>• Percentage of Adolescent Participants Achieving PASI 90 Response at Week 52 | |
| **ICONIC-ADVANCE 1-NCT06143878 A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled and Deucravacitinib Active Comparator-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants with Moderate to Severe Plaque Psoriasis** | **Study type**: Interventional<br><br>**Study Phase**: phase 3<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113 will be administered orally.<br>• Drug: JNJ-77242113 matching placebo will be administered orally.<br>• Drug: Deucravacitinib will be administered orally<br>• Drug: Deucravacitinib matching placebo will be | ***Primary outcomes:***<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving an IGA Score of 0 or 1 and Greater Than or Equal to (>=) 2-Grade Improvement from Baseline to Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving PASI 90 Response at Week 16 [Time Frame: Baseline and Week 16<br><br>***Secondary outcomes:***<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving an IGA Score of 0 at Week 16 [Time Frame: Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving PASI 75 Response from Baseline to Weeks 4 and 16 [Time Frame: Baseline, Week 4, and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving PASI 90 Response at Week 8 [Time Frame: Baseline and Week 8]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving PASI 100 Response at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving ss-IGA Score of 0 or 1 and >=2 Grade Improvement from Baseline at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving PSSD Symptom Score of 0 at Weeks 8 and 16 [Time Frame: Weeks 8 and 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving >=4 Point Improvement from Baseline in PSSD Itch Score at Weeks 4 and 16 [Time Frame: Baseline, Week 4, and Week 16]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving an IGA Score of 0 or 1 and >=2 Grade Improvement from | The study has not been publicly submitted, but the estimated primary completion date is March 13, 2025 (final data collection for the primary outcome measure), and the estimated study completion date is June 1, 2027 |

| | | | |
|---|---|---|---|
| | administered orally.<br>**Sexes:** All<br>**Ages:** 18 Years and older<br>**Enrolment (Actual)**: 774 | Baseline at Weeks 16 and 24 [Time Frame: Baseline, Week 16, and Week 24]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving an IGA Score of 0 at Weeks 16 and 24 [Time Frame: Weeks 16 and 24]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving PASI 75 Response at Weeks 16 and 24 [Time Frame: Baseline, Week 16 and Week 24].<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving PASI 90 Response at Weeks 16 and 24 [Time Frame: Baseline, Week 16, and Week 24]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving PASI 100 Response at Weeks 16 and 24 [Time Frame: Baseline, Week 16, and Week 24]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants with PSSD Symptom Score of 0 at Week 16 [Time Frame: Week 16]<br>• Nº of Participants with AEs [Time Frame: Up to 165 weeks]<br>• Nº of Participants with SAEs [Time Frame: Up to 165 weeks]<br>• Change From Baseline in BSA at Week 16 [Time Frame: Baseline and Week 16]<br>• Change from Baseline in PASI Total Score at Week 16 [Time Frame: Baseline and Week 16]<br>• Percent Improvement in PASI Score from Baseline at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving a sPGA-G Score of 0 or 1 and at Least a 2-grade Improvement from Baseline to Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving a hf-PGA Score of 0 or 1 and at Least a 2-grade Improvement from Baseline to Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percent Change from Baseline in Modified mNAPSI Score at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percent of Participants Achieving f-PGA Score of 0 or 1 at Week 16 [Time Frame: Week 16]<br>• JNJ-77242113 and Placebo Group: Change from Baseline in PSSD Symptom Score at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants with PSSD Sign Score of 0 at Week 16 [Time Frame: Week 16] | |
| **ICONIC-ADVANCE 2-NCT06220604 A phase 3 Multicenter, Randomized, Double-blind Placebo-Controlled and Deucravacitinib Active comparator-controlled Study to Evaluate the efficacy and safety of JNJ-77242113 for the treatment of participants with moderate to severe plaque psoriasis** | **Study type**: Interventional<br><br>**Study Phase:** phase 3<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113 will be administered orally.<br>• Drug: matching placebo will be administered orally.<br>• Drug: Deucravacitinib will be administered orally<br>• Drug: Deucravacitinib matching placebo will be administered orally.<br><br>**Sexes:** All | | The study has not been publicly submitted, but the estimated primary completion date is March 13, 2025 (final data collection for the primary outcome measure), and the estimated study completion date is September 20, 2027. |

| | | | |
|---|---|---|---|
| | **Ages:** 18 Years and older<br><br>**Enrolment (Actual)**: 731 | • JNJ-77242113 and Placebo Group: Percentage of Participants with PSSD Sign Score of 0 at Week 16 [Time Frame: Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving GenPs-SFQ Item 2 score of 0 or 1 at Week 16 [Time Frame: Week 16]<br>• JNJ-77242113 and Placebo Group: Percentage of Participants Achieving DLQI Score of 0 or 1 at Week 16 [Time Frame: Week 16]<br>• JNJ-77242113 and Placebo Group: Change from Baseline in Total DLQI Score at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Placebo Group: Change from Baseline in Domain Scores of the PROMIS-29 Score at Week 16 [Time Frame: Baseline and Week 16]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving DLQI Score of 0 or 1 at Weeks 16 and 24 [Time Frame: Weeks 16 and 24]<br>• JNJ-77242113 and Deucravacitinib Group: Percentage of Participants Achieving PSSD Symptom Score of 0 at Weeks 16 and 24 [Time Frame: Weeks 16 and 24]<br>• Percentage of Participants Who Achieve PASI 75 Response After Week 24 Among PASI 75 Non-responders to Deucravacitinib at Week 24 [Time Frame: Baseline and from Week 24 through Week 156]<br>• Percentage of Participants Who Achieve PASI 90 Response After Week 24 Among PASI 90 Non-responders to Deucravacitinib at Week 24 [Time Frame: Baseline and from Week 24 through Week 156]<br>• Percentage of Participants Achieving IGA Score of 0 or 1 after Week 24, Among Participants with IGA score >=2 at Week 24 in the Deucravacitinib Group [Time Frame: From Week 24 through Week 156] | |
| **ICONIC-TOTAL NCT06095102 A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment** | **Study type**: Interventional<br><br>**Study Phase:** phase 3<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment | ***Primary outcomes:***<br>• Percentage of Participants Achieving an IGA Score of 0 or 1 and greater than or Equal to (>=) 2 Grade Improvement from Baseline at Week 16<br><br>***Secondary outcomes:***<br>• Percentage of Participants ss-IGA Score of 0 or 1 at week 16<br>• Percentage of Participants Achieving PSSI 90 at week 16<br>• Percentage of Participants Achieving a sPGA-G Score of 0 or 1 at week 16<br>• Percentage of Participants Achieving a hf-PGA Score of 0 or 1 at week 16 | The study has not been publicly submitted, but the estimated completion date is June 10, 2027. |

| | | | |
|---|---|---|---|
| **of Participants with Plaque Psoriasis Involving Special Areas** | • Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Plaque Psoriasis<br><br>**Intervention**<br>• Drug: JNJ-77242113 will be administered orally.<br>• Drug: Placebo will be administered orally.<br><br>**Sexes:** All<br><br>**Ages:** 12 Years and older<br><br>**Enrolment (Actual):** 311 | • Percentage of Participants Achieving PSSD Symptoms Score of 0 at week 16<br>• Percentage of Participants Achieving >=4 Point Improvement from baseline in PSSD Itch Score at week 16<br>• Percentage of Participants Achieving GenPs-SFQ item 2 score of 0 or 1 at week 16<br>• Percentage of Participants Achieving >=4-Point Improvement from baseline in Scalp Itch NRS Score at week 16<br>• Percentage of participants achieving >=4-Point improvement from baseline in GPSS score at week 16<br>• Nº of Participants with AEs<br>• Nº of Participants with SAEs<br>• Percentage of Participants Achieving PASI 90 Response at week 16<br>• Percentage of Participants Achieving PASI 75 Response at week 16<br>• Change from baseline in PASI total score at week 16<br>• Change From Baseline in BSA at week 16<br>• Percent Change from Baseline in mNAPSI Score at week 16<br>• Percentage of Participants Achieving f-PGA Score of 0 or 1 at Week<br>• Percentage of Participants Achieving an IGA Score of 0 at week 16<br>• Percentage of Participants Achieving PSSD Symptom Score of 0 at Week 8<br>• Change From Baseline in PSSD Symptom Score at week 16<br>• Percentage of Participants Achieving >=4-Point Improvement from Baseline in PSSD Itch Score at week 4<br>• Change from baseline in PSSD sign score at week 16<br>• Percentage of Participants Achieving PSSD Sign Score of 0 at week 16<br>• Percentage of Participants Achieving DLQI Score of 0 or 1 at week 16<br>• Percentage of Participants Achieving Children's CDLQI score of 0 or 1 at week 16<br>• Change From Baseline in Domain Scores of the PROMIS-29 Score at week 16<br>• Change From Baseline in Domain Scores of the PROMIS-25 Score at Week 16<br>• Change From Baseline in Palmoplantar Quality of Life Instrument Score at week 16<br>• Change from baseline in GPSS total score at week 16 | |

| | | | |
|---|---|---|---|
| ***NCT06295692*** **A Phase 3, Multicenter, Open-label Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Participants with Generalized Pustular Psoriasis or Erythrodermic Psoriasis** | **Study type**: Interventional<br>**Study Phase:** phase 3<br>**Study Design**<br>• Allocation: N/A<br>• Interventional Model: single group assignment<br>• Masking: non (open label)<br>• Primary Purpose: Treatment<br>**Condition:**<br>• Generalized Pustular Psoriasis (GPP)<br>• Erythrodermic Psoriasis (EP)<br>**Intervention**<br>• Drug: JNJ-77242113 will be administered orally.<br>**Sexes:** All<br>**Ages:** 12 Years and older<br>**Enrolment (Actual):** 540 | ***Primary outcomes:***<br>• Percentage of Participants with GPP who Experience Treatment Success Based on CGI Scale According to Japanese Dermatological Association (JDA) Total Score at Week 16<br>• Percentage of Participants with EP who Experience Treatment Success Based on CGI Scale at Week 16<br>***Secondary outcomes:***<br>• Percentage of Participants with GPP who Experience Treatment Success Based on clinical global impression (CGI) Scale According to JDA Total Score Over Time<br>• Percentage of Participants with EP who Experience Treatment Success Based on CGI Scale Over Time<br>• Change From Baseline in Total Score of JDA Severity Index for GPP<br>• Change From Baseline in Severity Classification of JDA Severity Index for GPP<br>• Change From BSA for EP<br>• Percentage of Participants who Achieved an IGA Score of Cleared (0) or Minimal (1)<br>• Percentage of Participants who Achieve an IGA Score of Cleared (0)<br>• Percent Improvement from Baseline in PASI<br>• Change From Baseline DLQI Score<br>• Percentage of Participants who Achieve a DLQI Score of 0 or 1<br>• Change from baseline in EuroQol-5 Dimension 5-Level.<br>• Percentage of Participants with AEs | The study has not been publicly submitted, but the estimated study completion date is October 14, 2027. |
| **ICONIC-PsA 1 NCT06878404 A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of JNJ-77242113 for the Treatment of Biologic-naïve Participants with Active Psoriatic Arthritis** | **Study type**: Interventional<br>**Study Phase:** phase 3<br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br>**Condition:** Arthritis Psoriatic | ***Primary outcomes:***<br>• Proportion of Participants who Achieved an American College of Rheumatology (ACR) 20 Response at week 16 [Time Frame: Week 16]<br>***Secondary outcomes:***<br>• Proportion of participants who achieved PASI 75 response at week 16 among participants with baseline BSA greater than equal to (>=) 3 Percent (%) and with baseline IGA score of >=2 [Time Frame: week 16]<br>• Proportion of participants who achieved PASI 90 response at week 16 among participants with Baseline BSA >=3% and with baseline IGA Score of >=2 [Time Frame: week 16]<br>• Proportion of participants who achieved PASI 100 response at week 16 among participants with Baseline BSA >=3% and with baseline IGA Score of >=2 [Time Frame: week 16]<br>• Proportion of participants with an IGA Psoriasis Score of 0 or 1 And >=2 Grade Improvement from | The study has not been publicly submitted, but the estimated primary completion date is October 2, 2026 (final data collection for the primary outcome measure), and the estimated study |

| | | | |
|---|---|---|---|
| | **Intervention**<br>• Drug: Icotrokinra will be administered.<br>• Drug: placebo will be administered.<br>• Drug: Active reference comparator drug will be administered.<br><br>**Sexes:** All<br><br>**Ages:** 18 Years and older<br><br>**Enrolment (Actual):** 540 | Baseline at week 16 Among Participants with Baseline BSA >=3% and with baseline IGA Score of >=2 [Time Frame: week 16]<br>• Proportion of participants who achieved an ACR 50 Response at Week 16 [Time Frame: week 16]<br>• Proportion of participants who achieved an ACR 70 Response at Week 16 [Time Frame: week 16]<br>• Change from baseline in Health Assessment Questionnaire-Disability Index Score at week 16 [Time Frame: From baseline up to week 16]<br>• Changes from baseline in 36 Item short form survey physical component summary score at week 16 [Time Frame: from baseline up to week 16]<br>• Proportion of participants with Resolution of Enthesitis at Week 16 Among Those with Enthesitis at Baseline [Time Frame: Week 16]<br>• Change from baseline in Enthesitis Score at Week 16 in Participants with Enthesitis at Baseline [Time Frame: Baseline and Week 16]<br>• Proportion of participants with Resolution of Dactylitis at Week 16 Among Those with Dactylitis at Baseline [Time Frame: Week 16]<br>• Change From Baseline in Dactylitis Score at Week 16 in Participants with Dactylitis at Baseline [Time Frame: From baseline up to Week 16]<br>• Proportion of participants who achieved Minimal Disease Activity at Week 16 [Time Frame: Week 16]<br>• Change from baseline in Functional Assessment of Chronic Illness Therapy - Fatigue Score at Week 16 [Time Frame: From baseline up to Week 16] | completion date is December 29, 2028. |
| **ICONIC-PsA 2 NCT06807424 A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of JNJ-77242113 for the Treatment of Biologic-experienced Participants with Active Psoriatic Arthritis** | **Study type**: Interventional<br><br>**Study Phase:** phase 3<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Arthritis Psoriatic<br><br>**Intervention**<br>• Drug: Icotrokinra will be administered.<br>• Drug: placebo will be administered.<br><br>**Sexes:** All<br>**Ages:** 18 Years and older<br>**Enrolment (Actual):** 750 | | The study has not been publicly submitted, but the estimated primary completion date is February 10, 2027 (and the estimated study completion date is October 18, 2028. |

| | | | |
|---|---|---|---|
| **ANTHEM-UC NCT06049017 A Phase 2b Multicenter, Randomized, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of JNJ-77242113 for the Treatment of Moderately to Severely Active Ulcerative Colitis** | **Study type**: Interventional<br><br>**Study Phase:** phase 2<br><br>**Study Design**<br>• Allocation: Randomized<br>• Interventional Model: Parallel Assignment<br>• Masking: Double (Participant, Investigator)<br>• Primary Purpose: Treatment<br><br>**Condition:** Colitis Ulcerative<br><br>**Intervention**<br>• Drug: JNJ-77242113 will be administered orally.<br>• Drug: Placebo will be administered orally.<br><br>**Sexes:** All<br><br>**Ages:** 18 Years to 75 years old<br><br>**Enrolment (Actual):** 252 | ***Primary outcomes:***<br>• Percentage of Participants with Clinical Response at Week 12 [Time Frame: Week 12]<br><br>***Secondary outcomes:***<br>• Percentage of Participants with Clinical Remission at Week 12 [Time Frame: Week 12]<br>• Percentage of Participants with Symptomatic Remission at Week 12 [Time Frame: Week 12]<br>• Percentage of Participants with Endoscopic Improvement at Week 12 [Time Frame: Week 12]<br>• Percentage of Participants with Histologic-endoscopic Mucosal Improvement at Week 12 [Time Frame: Week 12]<br>• Percentage of Participants with AE and SAEs [Time Frame: Up to Week 76] | The study has not been publicly submitted, but the actual primary completion date was September 26, 2024 (final data collection for the primary outcome measure), and the estimated study completion date is January 16, 2026. |

INSTITUTO DE **CIÊNCIAS BIOMÉDICAS ABEL SALAZAR**