

Takeda Announces Late-Breaking Data from Phase 2b Study of TAK-279, an Investigational, Oral, Once-Daily TYK2 Inhibitor, in Patients with Active Psoriatic Arthritis at American College of Rheumatology Convergence Annual Meeting

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- The Study Met Its Primary Endpoint with 53.3% and 54.2% of Patients Treated With TAK-279 (15 mg and 30 mg Respectively) Achieving At Least an ACR 20 Response Compared to 29.2% in the Placebo Group at Week 12(p = 0.002)¹
- TAK-279 Demonstrated Improvements in Key Secondary Endpoints and a Safety Profile Consistent with the Phase 2b Psoriasis Study¹
- Takeda Will Initiate Phase 3 Studies in Plaque Psoriasis in FY23 and Psoriatic Arthritis in FY24, While Exploring TAK-279 in Systemic Lupus Erythematosus, Inflammatory Bowel Disease and Other Indications

OSAKA, Japan & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Takeda (**TSE:4502/NYSE:TAK**) today announced that the company will present positive results from its randomized, double-blind, placebo-controlled, Phase 2b trial evaluating TAK-279, an investigational oral allosteric tyrosine kinase 2 (TYK2) inhibitor with next generation selectivity, in patients with active psoriatic arthritis. These data (**Abstract #L12**) will be presented on Tuesday, November 14 as part of the late-breaking poster session from 9:00 AM - 11:00 AM PT at the American College of Rheumatology (ACR) Convergence 2023 in San Diego, California.

The study met its primary endpoint with a statistically significant proportion of patients, 53.3% (15 mg) and 54.2% (30 mg), treated with TAK-279 achieving at least an American College of Rheumatology 20 (ACR 20) response compared to 29.2% in the placebo arm at week 12 ($p = 0.002$).¹ The safety and tolerability profile of TAK-279 in the trial was consistent with that observed in the Phase 2b psoriasis study.¹ There was no statistically significant difference in ACR 20 seen in the TAK-279 5 mg arm (35.2%) compared to the placebo arm (29.2%).¹

“There remains a critical unmet need for psoriatic arthritis treatment options that not only improve the signs and symptoms of the condition, but are well tolerated and convenient for patients,” said Alan Kivitz, MD, MACR, the study’s principal investigator. “As psoriatic arthritis is a condition with diverse presentations of inflammation and skin involvement, the improvements seen with just 12 weeks of treatment in this Phase 2b study in patients with a low mean baseline C-reactive protein level are particularly encouraging. These results support the continued evaluation, across the psoriatic arthritis disease spectrum, of TAK-279, a once-daily oral TYK2 inhibitor with next generation selectivity.”

The study also demonstrated improvements in key secondary endpoints:

- At 15 mg and 30 mg of TAK-279, 26.7% ($p=0.005$) and 26.4% ($p=0.009$) of patients achieved ACR 50 response compared to 9.7% of patients on placebo.¹
- A numerically higher proportion of patients treated with TAK-279 15 mg (14.7%) and 30 mg (13.9%) achieved ACR 70 compared to those on placebo (5.6%).¹
- In patients with a body surface area (BSA) greater than or equal to 3% at baseline, Psoriasis Area and Severity Index (PASI) 75 was achieved in a greater proportion of patients treated with TAK-279 (45.7% [30 mg], 28.3% [15 mg] and 25.6% [5 mg]; $p = 0.002, 0.101$ and 0.186 vs placebo [15.4%]).¹
- In patients with Physician Global Assessment of Psoriasis (PGA-PsO) ≥ 2 at baseline, a greater proportion of patients treated with TAK-279 30 mg achieved a PGA-PsO score of 0 (clear) or 1 (almost clear) and at least a 2-point improvement from baseline compared to placebo (32.8% [30 mg], 20.6% [15 mg], 20.4% [5 mg] vs. 15.8% [placebo]; $p = 0.034$ for 30 mg).²
- Reductions were observed in mean change from baseline in the tender joint count and swollen joint count in all groups, with higher reductions with the 15 mg and 30 mg doses compared to placebo and 5 mg TAK-279.¹
- Minimal disease activity (MDA) response rates were higher in TAK-279 15 mg and 30 mg groups than in placebo (28.0% [15 mg] and 29.2% [30 mg]; $p = 0.017$ and 0.014 vs. placebo [12.5%]).²

The most common treatment-emergent adverse events (TEAEs) in patients who received TAK-279 5 mg, 15 mg, or 30 mg versus placebo, respectively, were nasopharyngitis (8.5%, 9.3%, 9.7%, 4.2%), upper respiratory tract infections (11.3%, 4%, 9.7%, 2.8%), headache (2.8%, 8.0%, 5.6%, 4.2%) and rash (4.2%, 8%, 5.6%, 0%).¹ No opportunistic infections, major adverse cardiovascular events or differences in mean laboratory parameters of interest were observed, compared with placebo. There was no clinically significant difference in adverse event rates

between doses of TAK-279. Serious and grade 3 or higher TEAEs occurred infrequently and at a similar rate in the TAK-279 and placebo groups.¹

“Based on these promising efficacy and safety results, achieved at 12 weeks, we plan to initiate a Phase 3 study of TAK-279 in psoriatic arthritis as well as commence a Phase 3 study in plaque psoriasis,” said Andy Plump, President, Research & Development, Takeda. “We are also advancing the development of TAK-279 in Crohn’s disease, ulcerative colitis and systemic lupus erythematosus and exploring a range of other potential indications. These opportunities are being explored in parallel with the psoriasis and psoriatic arthritis programs.”

About TAK-279

TAK-279 is a highly selective, oral allosteric tyrosine kinase 2 (TYK2) inhibitor in late-stage development,³ with approximately 1.3 million-fold greater selectivity for TYK2 as compared with JAK1.⁴ TAK-279 has the potential to become an important treatment option in multiple immune-mediated inflammatory diseases. In Phase 1 studies, TAK-279 showed a good tolerability profile, a dose-dependent trend in exploratory clinical activity and a pharmacokinetic profile allowing for once-daily solid oral dosing.⁵ In a Phase 2b study in patients with moderate-to-severe psoriasis, a statistically significant greater proportion of patients receiving TAK-279 achieved Psoriasis Area and Severity Index (PASI) 75, 90 and 100 in the 5mg, 15mg and 30mg dosing arms compared to placebo at 12 weeks.³ TAK-279 is an investigational compound that has not been approved for use by any regulatory authority.

About the TAK-279 Phase 2b Study in Psoriatic Arthritis

The Phase 2b study (**NCT05153148**) is a randomized, multicenter, double-blind, placebo-controlled multiple-dosed trial designed to evaluate the efficacy, safety and tolerability of TAK-279 in patients with active psoriatic arthritis.⁶ Eligible patients were aged ≥ 18 years, with psoriatic arthritis symptoms for ≥ 6 months prior to screening, met Classification criteria for Psoriatic Arthritis (CASPAR), and had ≥ 3 tender and ≥ 3 swollen joint counts (TJC/SJC) at enrollment despite prior NSAID, DMARD or biologic treatment.⁶ In total, 290 patients were randomized and treated (1:1:1:1 ratio) to receive one of three doses of TAK-279 or placebo once daily for 12 weeks with a 4 week safety follow up period; 245 completed 12 weeks’ treatment.^{1,6} Baseline characteristics were generally comparable across groups (except for a lower mean TJC in the 30 mg group); 58.6% had BSA $\geq 3\%$ (of which mean baseline PASI score was 6.2), and 32.1% had prior biologic use (20.7% TNFis).¹ Mean baseline high-sensitivity C-reactive protein (hsCRP) was 7.0 mg/L; 45.9% had hsCRP ≥ 3 mg/L.¹ The primary endpoint was the proportion of patients achieving at least an ACR 20 response at week 12.⁶

The ACR 20, ACR 50, and ACR 75 are composite measures defined as 20%, 50% and 75% improvement, respectively, in the number of tender and number of swollen joints, and in three of the following five criteria: patient global assessment of psoriatic arthritis, physician global assessment of psoriatic arthritis, patient pain scale, disability history questionnaire and an acute phase reactant.⁶

The Psoriasis Area and Severity Index (PASI) is a scoring system to evaluate baseline and response of therapy in psoriasis. PASI 75 is a binary outcome that indicates a 75% or greater improvement in PASI from baseline.⁷

About Psoriatic Arthritis

Psoriatic arthritis is a chronic immune-mediated inflammatory disease, characterized by inflammation causing joint pain, stiffness, and swelling and occurs with the skin condition psoriasis.⁸ Psoriatic arthritis affects approximately 10 million people globally.⁹ Psoriatic arthritis is a heterogeneous condition - affecting everyone differently.¹⁰ Symptoms may be mild or severe, affect just a few or many joints, and symptoms can come and go.¹⁰ Chronic inflammation seen in psoriatic arthritis may result in irreversible joint damage if not managed appropriately.⁸ Progressive disease is associated with substantial physical disability¹¹ and significant mental health disorders, such as anxiety and depression.¹²

About Tyrosine Kinase 2 (TYK2) Inhibitors

Tyrosine kinase 2 (TYK2) is an intracellular enzyme that belongs to the Janus family of protein tyrosine kinases.¹³ TYK2 is a member of the Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway, which mediates signaling downstream of key immune cytokine receptors.¹³ Inflammatory cytokine signaling is associated with several immune-mediated inflammatory diseases, including psoriasis, psoriatic arthritis, systemic lupus erythematosus and inflammatory bowel disease.¹⁴ Selective allosteric inhibition of TYK2 may be a promising therapeutic approach to target immune-mediated inflammation while potentially decreasing the risk of JAK-related toxicity.¹⁵

About Takeda

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