Lilly's peresolimab Phase 2a rheumatoid arthritis trial published in The New England Journal of Medicine

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Peresolimab met the primary efficacy endpoint in patients with refractory rheumatoid arthritis (RA)

Study evaluated a novel approach to treating patients with autoimmune diseases

INDIANAPOLIS, May 18, 2023 /PRNewswire/ -- *The New England Journal of Medicine* today published detailed results from Eli Lilly and Company's (NYSE: LLY) phase 2a study of peresolimab in rheumatoid arthritis (RA), in which peresolimab met the primary endpoint for efficacy and had similar rates of adverse events between peresolimab and placebo arms. These data represent the first clinical evidence that stimulating the endogenous PD-1 inhibitory pathway could be an effective approach to treat rheumatologic disease. The phase 2a clinical trial (NCT04634253) evaluated the safety and efficacy of peresolimab in adult participants with moderate-to-severe RA who had an inadequate response to prior conventional, biologic or synthetic disease modifying antirheumatic drugs (DMARDs).

"In the study, peresolimab showed meaningful results in refractory RA patients," said Jay Tuttle, Ph.D, study first author and associate vice president, research and development at Lilly. "Refractory patients make up approximately 21% of the RA population[1], having tried and failed multiple treatments, and are often hesitant to try new options. While still early, these data signify an important potential new therapeutic approach for RA patients, including both refractory and biologic-naïve patients."

Peresolimab is an investigational humanized immunoglobulin G1 monoclonal antibody that stimulates human programmed cell death protein 1 (PD-1), a checkpoint inhibitory receptor, that may induce physiological immune inhibitory pathways to restore immune homeostasis. RA, a form of rheumatologic disease, is a systemic autoimmune disease characterized by inflammation and progressive destruction of joints.[2,3] While several treatment options exist, including the use of oral conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) — such as methotrexate, the current standard of care; and injectable, biological disease-modifying antirheumatic drugs (bDMARDs) — many patients do not reach or maintain their therapeutic goals.[4,5,6] There remains a crucial unmet need to provide new treatment options for better overall patient care, particularly for refractory and biologic-experienced patients.

"Lilly is proud to share these results in *The New England Journal of Medicine*, which reinforce our commitment to discoveries that may transform care for patients. Our ultimate objective in treating immunologic conditions is to achieve not only symptom reduction, but to also induce immune homeostasis and achieve longstanding resolution of disease," said Ajay Nirula, M.D., Ph.D, study senior author and senior vice president, Immunology at Lilly. "These early data for peresolimab in RA reflect our commitment to develop first-in-class therapeutic options for patients."

These data were first presented as a late-breaking abstract at the American College of Rheumatology (ACR) annual Convergence in November 2022. In this phase 2a, double-blind, randomized, placebo-controlled trial, adult patients with moderate-to-severe RA who had an inadequate response to, a loss of response to, or unacceptable side effects with conventional synthetic disease-modifying antirheumatic drugs (DMARDs) or to biologic or targeted synthetic DMARDs to receive 700 mg of peresolimab, 300 mg of peresolimab, or placebo intravenously once every 4 weeks. The primary outcome was the change from baseline to week 12 in the Disease Activity Score for 28 joints based on the C-reactive protein level (DAS28-CRP). The primary comparison was between the 700-mg group and the placebo group.

At week 12, the change from baseline in the DAS28-CRP was significantly greater in the 700-mg peresolimab group than in the placebo group (least-squares mean change [±SE], −2.09±0.18 vs. −0.99±0.26; difference in change, −1.09 [95% confidence interval, −1.73 to −0.46]; P<0.001). The results of the analyses of secondary outcomes favored the 700-mg dose over placebo with respect to the ACR20 response, but not with respect to the ACR50 and ACR70 responses — defined as improvements from baseline of 20%, 50%, and 70% or more, respectively, in the numbers of tender and swollen joints and in at least three of five important domains — at week 12.

Noted improvements were seen in the Clinical Disease Activity Index (CDAI) in participants treated with both peresolimab doses compared to placebo. In addition, low disease activity was maintained through Week 24 in most patients achieving CDAI low disease activity at Week 14.

Adverse events were similar in the peresolimab and placebo groups. Treatment emergent events were mild or moderate in severity, with the most common events being infections and infestations, in addition to skin and subcutaneous tissue disorders. A single serious adverse event (worsening of hypothyroidism, 700 mg) was reported during the treatment period, which did not result in participant discontinuation from the study. There were no deaths reported in the study, and no reports of malignancy in participants receiving peresolimab.

The results support further clinical evaluation of peresolimab in rheumatologic diseases. Future studies will continue evaluating peresolimab as treatment for RA, including the ongoing RESOLUTION-1 (NCT05516758) clinical trial, a phase 2b study of peresolimab in adult participants with moderate-to-severe RA. Additionally, Lilly is considering evaluating peresolimab in other autoimmune diseases.

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Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about *peresolimab* as a potential treatment for people with rheumatoid arthritis and the timeline for future readouts, presentations, and other milestones relating to peresolimab and its clinical trials, and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that peresolimab will prove to be a safe and effective treatment for rheumatoid arthritis or other autoimmune diseases, that peresolimab will receive regulatory approval, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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