



Horizon Therapeutics plc Announces Phase 2 Trial Evaluating Dazodalibep for the Treatment of Sjögren's Syndrome Meets Primary Endpoint

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- The Company plans to work with the FDA to design a Phase 3 program in moderate-to-high systemic disease activity patients to begin in 2023, ahead of expectations -

DUBLIN--(BUSINESS WIRE)--Sep. 12, 2022-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced that its Phase 2 trial evaluating dazodalibep for the treatment of Sjögren's syndrome met the primary endpoint in patients with moderate-to-high systemic disease activity as defined by the European Alliance of Associations for Rheumatology (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) score of ≥ 5 . At Week 24, patients treated with dazodalibep achieved a 6.3-point reduction in their ESSDAI score and patients treated with placebo achieved a 4.1-point reduction, resulting in a statistically significant least squares mean difference of 2.2 points ($p=0.017$).

"These data are compelling in that dazodalibep achieved the primary endpoint with statistical significance in patients with moderate-to-high systemic disease activity as defined by ESSDAI, which represents a significant step towards developing a treatment for Sjögren's syndrome, a disease with no FDA-approved treatments available," said Elizabeth H.Z. Thompson, Ph.D., executive vice president, research and development, Horizon. "We continue to see evidence that dazodalibep's mechanism of action is potentially effective across many autoimmune diseases and we look forward to working with regulators to further our Sjögren's clinical development program."

In addition to the primary endpoint, numerical improvements were seen in key secondary, exploratory and post-hoc analyses. These included measures of dryness, which is an important symptom for patients living with Sjögren's syndrome as it impacts chewing, swallowing and dentition. Fatigue as measured by Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) and physical functioning measured using the 36-Item Short Form Health Survey (SF-36) showed numerical improvements, as did the number of tender and swollen joints. In addition, a post-hoc responder analysis of patients achieving high levels of improvement on ESSDAI favored dazodalibep over placebo. The trial was only powered for the primary endpoint.

Dazodalibep was well tolerated in the trial. The most common adverse events were COVID-19 infection, diarrhea, dizziness, ligament sprain and upper respiratory infections.

"Sjögren's is a devastating autoimmune disease with many unmet treatment needs," said Frederick B. Vivino, M.D., M.S., former Director of the Penn Sjögren's Center and chief, division of rheumatology at Penn Presbyterian Medical Center, University of Pennsylvania Perelman School of Medicine. "It significantly impacts patient quality of life and leads to numerous serious complications. In addition to arthritis and debilitating fatigue, the internal organs are frequently affected. Dry eyes and dry mouth are not trivial symptoms and, when ignored, can lead to life-changing complications including altered vision, corneal ulcers, accelerated caries and eventual loss of the dentition."

"These positive results from the dazodalibep Phase 2 trial are good news for patients with Sjögren's syndrome," said William St. Clair, M.D., chief, division of rheumatology and immunology, Duke University Medical Center.

The topline data announced today is specific to patients with moderate-to-high systemic disease activity (as defined by ESSDAI). The Phase 2 trial is also evaluating a second, separate patient population with moderate-to-severe subjective symptoms as defined by a EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) score of ≥ 5 , which is fully enrolled and continues to progress.

The results from the Sjögren's trial follow positive results announced earlier this year from the Phase 2, randomized, double-blinded, placebo-controlled trial in rheumatoid arthritis patients. The study met its primary endpoint of change from baseline in DAS28-CRP at Day 113 in all four dazodalibep dosing arms.

Phase 2 Sjögren's Syndrome Trial Details

The Phase 2 study enrolled two Sjögren's syndrome populations: the first included a total of 74 participants with moderate-to-high systemic disease activity defined by an ESSDAI score of ≥ 5 and the second included participants with moderate-to-severe subjective symptoms defined by an ESSPRI score of ≥ 5 and residual stimulated salivary flow but with mild systemic disease activity defined by an ESSDAI score of < 5 . This study includes three periods: screening (4 weeks), treatment period (40 weeks), and follow-up period (12 weeks). In the treatment period, participants from each population were randomized at a 1:1 ratio to receive either intravenous (IV) doses of dazodalibep or placebo for 24 weeks (Stage 1). After completion of Stage 1, participants who were randomized to the dazodalibep arm in Stage 1 received placebo and participants randomized to placebo in Stage 1 received dazodalibep for the remaining 16 weeks of the treatment period (Stage 2). Participants who discontinued dazodalibep were not eligible for treatment during Stage 2. All study participants were followed for at least 12 weeks after their last dose of study drug administration. Full trial data will be presented at medical meetings and published in scientific journals once available.

About Dazodalibep

[Dazodalibep](#) is a CD40 ligand antagonist that blocks T cell interaction with CD40-expressing B cells, disrupting the overactivation of the CD40 ligand co-stimulatory pathway. Several autoimmune diseases are associated with the overactivation of this pathway. Horizon also plans to investigate dazodalibep in focal segmental glomerulosclerosis, a rare kidney disorder characterized by scarring of glomeruli.

About Sjögren's Syndrome

Sjögren's syndrome is a chronic, systemic autoimmune disease affecting exocrine glands, primarily the salivary and tear glands, with severe cases

affecting multiple organs. Like other autoimmune diseases, Sjögren's syndrome primarily affects women. The disease also has an increased risk of non-Hodgkin's B-cell lymphoma and there is an unmet medical need for patients with extraglandular disease manifestations, as currently there is no therapy that can improve or slow the course of the disease. Disease manifestations include dry mouth, dry eyes, arthritis and kidney or lung dysfunction. Between 250,000 - 350,000 people live with Sjögren's syndrome in the U.S., of which approximately 50,000 would be appropriate for novel therapies, including biologics.¹

About Horizon

Horizon is a global biotechnology company focused on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. Our pipeline is purposeful: We apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives. For more information on how we go to incredible lengths to impact lives, visit www.horizontherapeutics.com and follow us on [Twitter](#), [LinkedIn](#), [Instagram](#) and [Facebook](#).

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential benefits of dazodalibep in treating Sjögren's syndrome and other autoimmune diseases, planned regulatory meetings, timing related to clinical trials, as well as Horizon's future development plans. These forward-looking statements are based on management's expectations and assumptions as of the date of this press release and actual results may differ materially from those in these forward-looking statements as a result of various factors. These factors include, but are not limited to, risks regarding whether future data analyses or clinical trial results will be consistent with prior clinical trial or Horizon's expectations, potential delays in initiating or completing clinical trials and *those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC*. Forward-looking statements speak only as of the date of this press release and Horizon undertakes no obligation to update or revise these statements, except as may be required by law.

References

1. Maciel G, et al. Prevalence of Primary Sjögren's Syndrome in a US Population-Based Cohort. *Arthritis care & research* 2017;69(10):1612-1616

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