Presentations at the 2023 EULAR European Congress of Rheumatology Highlight New Results from Phase 2 Trial Evaluating Dazodalibep in Sjögren’s Syndrome

May 31, 2023

-- Only Sjögren’s syndrome Phase 2 trial to meet the primary endpoint in both patient population types --

-- Patients with moderate-to-severe systemic disease activity (ESSDAI score ≥5) treated with dazodalibep experienced improvement in their disease activity (6.3-point reduction) compared to those who received placebo (4.1-point reduction) --

-- Patients with moderate-to-severe symptomatology (ESSPRI score ≥5 and ESSDAI score <5) treated with dazodalibep experienced improvement in their symptoms (1.8-point reduction) compared to those treated with placebo (0.53-point reduction) --

-- Results will be featured in two separate oral presentations on June 1, 11:35-11:45 a.m. CEST and June 3, 9:35-9:45 a.m. CEST --

DUBLIN--(BUSINESS WIRE)--May 31, 2023-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced presentations of new results from the randomized, double-blind, placebo-controlled Phase 2 trial showing dazodalibep, an investigational treatment for Sjögren’s syndrome, may improve some of the most prominent effects of this chronic, systemic autoimmune condition characterized by inflammation of exocrine glands. These are the first presentations of the Phase 2 trial results and are part of expert dialogue this week at the EULAR European Congress of Rheumatology, May 31 – June 3, 2023, in Milan.

The Company’s Phase 2 trial of dazodalibep, a CD40 ligand antagonist in clinical development for Sjögren’s syndrome, evaluated two patient populations; the first group included patients with moderate-to-severe systemic disease activity, and the second group included those with moderate-to-severe symptomatology including dryness, fatigue and pain despite lacking additional organ involvement. Results from the trial indicate treatment with dazodalibep may address the unmet therapeutic needs for this challenging condition, which has no approved disease-modifying therapies to date. Dazodalibep is the only investigational medicine to achieve the primary endpoint in both patient populations in a Phase 2 trial.

“The Phase 2 trial provides encouraging evidence that those suffering from Sjögren’s could experience significant improvements of their disease with dazodalibep treatment,” said Wan-Fai Ng, Ph.D., study author and Professor of Rheumatology, Translational and Clinical Research Institute, Newcastle University, United Kingdom. “The positive results represent a significant step towards developing a treatment for these patients.”

Results in Patients with Moderate-to-Severe Systemic Disease Activity

The first population of the Phase 2 trial included patients with moderate-to-severe systemic disease activity as defined by a EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI) score of ≥5. The trial assessed changes in the ESSDAI score and other Sjögren’s measures as well as safety of dazodalibep treatment compared to placebo.

Key findings include:

- The primary endpoint was achieved, and patients treated with dazodalibep experienced a statistically significant (p-value=0.0167) and clinically meaningful improvement in their disease activity (6.3-point reduction in their ESSDAI score) versus those who received placebo (4.1-point reduction) and showed positive trends in several other assessments at Day 169.

- All ESSDAI responder analyses (pre-specified and post-hoc) favored dazodalibep over placebo, with greater numerical differences for the highest levels of response.

- Patients treated with dazodalibep experienced numerically greater improvements in ESSPRI score and fatigue compared to those who received placebo at Day 169.

- Safety profiles were similar between the groups, with the most commonly reported adverse events including COVID-19, diarrhea, dizziness, ligament sprain and upper respiratory infections.

Presentation Details:
Efficacy and Safety of Dazodalibep (VIB4920/HZN4920) in Subjects with Sjögren’s Syndrome: A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Proof of Concept Study
OP0143, June 1, 11:35-11:45 a.m. CEST, South Hall, Session Room 2

Results in Patients with Moderate-to-Severe Symptomatology

The Phase 2 trial also evaluated a second population of patients with moderate-to-severe symptomatology including dryness, fatigue and pain despite lacking additional organ involvement as defined by a EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI) score of ≥5, indicative of significant symptomatic burden; and an ESSDAI score of <5, representing limited extraglandular organ involvement.

Key findings include:

- The primary endpoint was achieved, and patients treated with dazodalibep experienced a statistically significant and clinically meaningful improvement in the key subjective symptoms of Sjögren’s syndrome (1.8-point reduction in their...
Dazodalibep (VIB4920/HZN4920) in Sjögren’s Subjects with an Unacceptable Symptom Burden: Safety and Efficacy from a Phase 2, Randomized, Double-Blind Study
LB0003, June 3, 9:35-9:45 a.m. CEST, Space 2

Results from Biomarker Analysis of Patients with Sjögren’s Syndrome

The biological mechanism of dazodalibep, focusing on specific blood biomarkers that contribute to Sjögren’s syndrome, was also studied in the Phase 2 trial. Overactivation of CD40 ligand-CD40 signaling between immune cells, including CD40 ligand on T cells and CD40 on B cells, contributes to the exaggerated immune responses that characterize Sjögren’s. Dazodalibep is a CD40 ligand antagonist designed to block this interaction and disrupts the overactivation of the CD40 ligand co-stimulatory pathway. Significant and rapid reductions in blood biomarkers associated with T and B cell co-stimulation were observed in patients who received dazodalibep as compared to placebo.

Presentation Details:
CD40L Blockade with Dazodalibep (VIB4920/HZN4920) in Subjects with Systemic Sjögren’s Syndrome
POS0815, June 1, 2:45-3:45 p.m. CEST, Poster Hall

“These presentations demonstrate our research approach at Horizon to recognize the challenges of people living with serious unmet medical needs and deliver solutions that may improve their quality of life,” said Elizabeth H.Z. Thompson, Ph.D., executive vice president, research and development, Horizon. “We look forward to continuing to develop dazodalibep and potentially transform patient care in Sjögren’s.”

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.

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-severe systemic disease activity defined by an ESSDAI score of ≥5; and the second included participants with moderate-to-severe symptomatology defined by an ESSPRI score of ≥5, and residual stimulated salivary flow but lacking additional organ involvement defined by an ESSDAI score of <5. This study included three periods: screening period (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. 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.

Forward-Looking Statements:

This press release contains forward-looking statements, including statements regarding potential benefits of dazodalibep in treating Sjögren’s syndrome and other autoimmune diseases, and 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 trials or Horizon’s expectations and potential delays in initiating or completing clinical trials. For a further description of these and other risks facing Horizon, please see the risk factors described in Horizon’s filings with the United States Securities and Exchange Commission, including those factors discussed under the caption “Risk Factors” in those filings. 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.

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