Horizon Therapeutics plc Announces Phase 2 Trial Evaluating Dazodalibep for the Treatment of Sjögren's Syndrome Meets Primary Endpoint in the Second Study Population; Only Phase 2 Trial to Meet Primary Endpoint in Both Patient Populations

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- Trial also met primary endpoint in first study population as announced September 2022 –

- The Company plans to work with the FDA to design a Phase 3 program to begin in 2023, ahead of expectations -

DUBLIN--(BUSINESS WIRE)--Jan. 18, 2023--

Horizon Therapeutics plc (Nasdaq: HZNP) today announced that the primary endpoint was met for the second population in its Phase 2 clinical trial evaluating dazodalibep for the treatment of Sjögren's syndrome. The Phase 2 trial evaluated two patient populations and positive results in the first patient population were announced in September 2022. Dazodalibep is the only medicine in development to achieve the primary endpoint in both patient populations in a Phase 2 trial.

Today, the Company announced that the second population achieved the primary endpoint. This patient population includes those with moderate-to-severe symptomatology including dryness, pain and fatigue despite lacking additional organ involvement and is defined as patients with a European Alliance of Associations for Rheumatology (EULAR) Sjögren's Syndrome Patient Reported Index (ESSPRI) score of ≥ 5, indicative of significant symptomatic burden, and a score of <5 on the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), which measures organ involvement. At Day 169, dazodalibep-treated patients achieved a 1.8-point reduction in their ESSPRI scores compared to placebo-treated patients who achieved a 0.53-point reduction, resulting in a least squares mean difference of 1.27 (p=0.0002). The ESSPRI is a composite endpoint that measures dryness, pain and fatigue severity. The previously announced positive results were in patients with moderate-to-severe systemic disease: systemic clinical manifestations in one or more organ systems in addition to the traditional Sjogren's manifestations, and an ESSDAI of ≥ 5.

"There are currently no disease-modifying FDA approved treatments for Sjögren's and the population in this trial represents a large subset of patients who have a clear unmet clinical need," 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. "Participants in this study had been excluded from other recent trials, despite their substantial disease burden. The positive results from the Phase 2 trial are very promising in addressing many debilitating symptoms of people living with Sjogren's."

In addition to the primary endpoint, statistical significance was achieved in certain secondary quality of life measures, including fatigue as measured by Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F). Dazodalibep was well tolerated with the most common adverse events through Day 169 being COVID-19 infection, nasopharyngitis and anemia.

"It is remarkable to see how these data demonstrated a significant separation in symptom intensity in patients treated with dazodalibep compared to placebo and this reinforces the potential of dazodalibep's mechanism of action for patients suffering with the disease," said Elizabeth H.Z. Thompson, Ph.D., executive vice president, research and development, Horizon. "Following these positive data, we look forward to working with regulators to continue developing dazodalibep as a potential treatment to positively impact the severe symptomatology of people living with this disease and improve their quality of life."

These data follow positive Phase 2 trial results announced in September in a separate study population. That portion of the study met its primary endpoint in patients with moderate-to-high systemic disease activity as defined by an ESSDAI score of ≥ 5. At Day 169, 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).

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 109 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

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