Horizon Therapeutics plc Announces First Patient Enrolled in Phase 2b Pivotal Trial Evaluating HZN-825 for the Treatment of Diffuse Cutaneous Systemic Sclerosis

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DUBLIN--(BUSINESS WIRE)--Nov. 9, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced the first patient has enrolled in a Phase 2b pivotal trial to evaluate its development-stage medicine HZN-825, a lysophosphatidic acid receptor 1 ($LPAR_1$) antagonist to treat people with diffuse cutaneous systemic sclerosis, a subset of systemic sclerosis (also known as scleroderma).

Systemic sclerosis is a rare, chronic, autoimmune disease marked by fibrosis, or skin thickening, caused by excess collagen production, in areas including hands, arms, legs and face. It can progress to internal organ damage including interstitial lung disease which occurs in up to 80 percent of patients.[1] There are approximately 30,000[2] people who live with diffuse cutaneous systemic sclerosis in the United States, and the disease carries one of the highest mortality rates among rheumatic diseases.[3]

“Imagine the sensation of your skin tightening and the knowledge that the disease causing that is also scarring your lungs—this is what people with diffuse cutaneous systemic sclerosis live with every day,” said Dinesh Khanna, M.D., M.Sc., professor of rheumatology and medicine at the University of Michigan and coordinating investigator for the trial. “This trial will help determine the safety, efficacy and tolerability of Horizon’s $LPAR_1$ antagonist in decreasing the decline of lung function due to fibrosis.”

Approximately 300 subjects who meet the trial eligibility criteria will be randomized in a 1:1:1 ratio to receive HZN-825 at 300 mg once daily, HZN-825 at 300 mg twice daily or placebo for 52 weeks. The primary endpoint is change in forced vital capacity (FVC) percent after 52 weeks of treatment. This is an objective endpoint that measures lung capacity and is used to assess the progression of lung disease and the effectiveness of the treatment.

“Research suggests that $LPAR_1$ inhibition is a promising approach to target fibrosis in many organ systems, including skin and lung,” said Elizabeth H.Z. Thompson, Ph.D., executive vice president, research and development, Horizon. “Current treatment provides symptomatic relief, but there are no approved therapies that slow disease progression. A more comprehensive treatment is needed to address the inflammation and fibrosis that drive this progressive disease and its high mortality rate. The enrollment of the first patient in this pivotal study marks an important milestone in assessing HZN-825 for these patients.”

Secondary endpoints include the Health Assessment Questionnaire-Disability Index, or HAQ-DI, and other patient and physician-reported outcome measures used to evaluate the efficacy of the medicine. All subjects who complete the double-blind treatment period at Week 52 will be eligible to enter a 52-week extension trial.

Results of HZN-825 Phase 2a Study in Patients with Early Diffuse Cutaneous Systemic Sclerosis

The Phase 2b pivotal trial is initiating after encouraging efficacy and safety data in a Phase 2a trial in patients with early diffuse cutaneous systemic sclerosis.[4] The placebo-controlled 8-week trial of HZN-825 in diffuse cutaneous systemic sclerosis, completed in 2018, showed a positive trend in response, with an improvement in the modified Rodnan skin score (mRSS) which is a secondary endpoint in the Phase 2b pivotal trial.

Additionally, data from the 16-week open-label extension period of the Phase 2a trial suggest that longer treatment duration may show more meaningful benefit. Seventy-nine percent of patients who received 24 weeks of treatment responded with a clinically meaningful improvement in mRSS.[4]

About HZN-825

HZN-825 is an oral selective $LPAR_1$ antagonist that has shown early signs of clinical impact in systemic sclerosis. $LPAR_1$ signaling has been implicated in fibrosis and inflammation, and preclinical and clinical evidence support the antifibrotic potential of $LPAR_1$ antagonism across organ systems, including both lung and skin.

About Horizon

Horizon is 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, please visit www.horizontherapeutics.com and follow us on Twitter, LinkedIn, Instagram and Facebook.

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to the potential benefits of HZN-825; the expected scope, endpoints and timing of Horizon’s Phase 2b clinical trial of HZN-825 and other statements that are not historical facts. These forward-looking statements are based on Horizon’s current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to clinical trials, including the fact that prior results may not predict future clinical trial outcomes; impacts of the

COVID-19 pandemic and actions taken to slow its spread, including potential delays in clinical trials; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information.

References

1. Denton CP, Khanna D. Systemic sclerosis. *The Lancet*. 2017;390(10103):1685-1699.
2. GlobalData. OpportunityAnalyzer: systemic sclerosis (scleroderma) – opportunity analysis and forecast to 2024. https://store.globaldata.com/report/gdhc044poa--opportunityanalyzer-systemic-sclerosis-scleroderma-opportunity-analysis-and-forecast-to-2024/. Published December 2015. Accessed April 2021. Report code: GDHC044POA.
3. Nikpour M, Baron M. Mortality in systemic sclerosis: lessons learned from population-based and observational cohort studies. *Curr Opin Rheumatol.* 2014;26(2):131-137.
4. Allanore Y, Distler O, Jagerschmidt A, et al. Lysophosphatidic acid receptor 1 antagonist SAR100842 for patients with diffuse cutaneous systemic sclerosis: a double-blind, randomized, eight-week placebo-controlled study followed by a sixteen-week open-label extension study. *Arthritis Rheumatol.* 2018;70(10):1634-1643.

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Tina Ventura
Senior Vice President, Investor Relations
Investor-relations@horizontherapeutics.com

Ruth Venning
Executive Director, Investor Relations
Investor-relations@horizontherapeutics.com

U.S. Media:
Geoff Curtis
Executive Vice President, Corporate Affairs & Chief Communications Officer
media@horizontherapeutics.com

Ireland Media:
Gordon MRM
Ray Gordon
ray@gordonmrm.ie

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