Horizon Pharma plc Completes Enrollment of Confirmatory Phase 3 Trial of Teprotumumab Ahead of Schedule

September 4, 2018

--Topline results expected in second quarter of 2019 --

DUBLIN--(BUSINESS WIRE)--Sep. 4, 2018-- Horizon Pharma plc (NASDAQ:HZNP) announced the early completion of enrollment for the confirmatory Phase 3 trial of teprotumumab in patients living with moderate-to-severe active thyroid eye disease (TED). The study (NCT03298867 and EudraCT 2017-002763-18) enrolled 83 patients at 13 sites across the United States, Germany and Italy. Topline results are expected in the second quarter of 2019.

"Our success in rapidly enrolling this trial speaks to the significant unmet need and the strong collaboration with Phase 3 study investigators," said Timothy P. Walbert, chairman, president and chief executive officer, Horizon Pharma plc. "There is no FDA-approved therapy for TED, which can result in bulging of the eyes, known as proptosis, and cause additional challenges for those living with the disease. Completing enrollment in our confirmatory Phase 3 trial marks a key milestone for people living with TED and Horizon Pharma. We look forward to the Phase 3 data analysis and the potential opportunity to bring this therapy to TED patients."

The *Treatment of Graves' **O**rbitopathy (Thyroid Eye Disease) to Reduce **P**roptosis with **T**eprotumumab **I**nfusions in a Randomized, Placebo-Controlled, **C**linical Study (OPTIC)* is a randomized, double-masked, placebo-controlled, parallel-group, multicenter study. OPTIC reached its target enrollment of 76 patients on Aug. 3, those remaining in screening were allowed to randomize for a final total of 83 patients. Patients will be randomized in a 1:1 ratio to receive eight infusions of teprotumumab or placebo every three weeks for 21 weeks. The primary endpoint is the responder rate of ≥ 2 mm reduction of proptosis, or bulging of the eye, in the study eye (without deterioration in the fellow eye) at week 24, in teprotumumab treated versus placebo treated patients. In addition, the secondary endpoints at week 24, include overall responder rate, percentage of participants with a Clinical Activity Score value of 0 or 1, mean change from baseline in proptosis measurement and the Graves' Ophthalmopathy Quality of Life questionnaire overall score. Safety is evaluated throughout the duration of the study. Teprotumumab is an investigational medicine and its safety and efficacy have not been established.

About Thyroid Eye Disease

Thyroid eye disease (TED) is a rare autoimmune disease in which the insulin-like growth factor receptor (IGF-1R) is overexpressed on eye tissues, resulting in local inflammation, orbital fibroblast proliferation and tissue expansion, which can in turn lead to proptosis, or bulging of the eye. In some cases the swelling and stiffness of the muscles due to fibroblast proliferation and inflammation displace the eyes so that they are no longer in line with each other, or the eyelids are unable to close. The inability for people living with TED to close their eyelids can lead to corneal ulcerations and potential blindness, and many also endure challenges with double vision, known as diplopia.

About Teprotumumab

Teprotumumab is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the insulin-like growth factor 1 receptor (IGF-1R). Teprotumumab has received Breakthrough Therapy, Orphan Drug and Fast Track designations from the U.S. Food and Drug Administration (FDA). The Phase 3 confirmatory study was launched in October 2017 after results from the randomized double-blind, placebo controlled Phase 2 study. Results from this study were published in the May 4, 2017, issue of *The New England Journal of Medicine*.

The Phase 2 study was designed to evaluate the efficacy and safety of teprotumumab in patients with recent onset, moderate-to-severe active TED. The primary endpoint was response in the study eye defined as a reduction in Clinical Activity Score of ≥ 2 points and reduction of proptosis of ≥ 2 mm at week 24. In the intent-to-treat population, 29 of 42 (69%) patients receiving teprotumumab and 9 of 45 (20%) patients receiving placebo were responders at week 24 ($p<0.001$). The most frequent adverse events reported (≥ 5 percent) were nausea, muscle spams, diarrhea, alopecia, hyperglycemia, dry skin, headache, paresthesia, hearing impairment and weight loss. Teprotumumab is an investigational medicine and its safety and efficacy have not been established.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the timing of results from the Phase 3 trial of teprotumumab in the treatment of TED and the potential for teprotumumab as a treatment for TED. Forward-looking statements speak only as of the date of this press release and Horizon Pharma does not undertake any obligation to update or revise these statements, except as may be required by law. 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 results of the Phase 3 trial will be consistent with results of prior trials, whether Horizon experiences delays in completing the Phase 3 trial, whether the results of the Phase 3 trial will be sufficient to support marketing approval of teprotumumab as a treatment for TED, and the risks associated with clinical development of drug candidates. For a further description of these and other risks facing Horizon, please see the risk factors described in Horizon Pharma'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 Pharma undertakes no obligation to update or revise these statements, except as may be required by law.

About Horizon Pharma plc

Horizon Pharma plc is focused on researching, developing and commercializing innovative medicines that address unmet treatment needs for rare

and rheumatic diseases. By fostering a growing pipeline of medicines in development and exploring all potential uses for currently marketed medicines, we strive to make a powerful difference for patients, their caregivers and physicians. For us, it's personal: by living up to our own potential, we are helping others live up to theirs. For more information, please visit www.horizonpharma.com. Follow @HZNPplc on Twitter, like us on Facebook or explore career opportunities on LinkedIn.

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