Horizon Pharma plc Announces First Patient Enrolled in Confirmatory Phase 3 Clinical Trial Evaluating Teprotumumab for the Treatment of Moderate-to-Severe Active Thyroid Eye Disease

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DUBLIN, Ireland, Oct. 25, 2017 (GLOBE NEWSWIRE) -- Horizon Pharma plc (NASDAQ:HZNP), a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs, today announced that the first patient has been enrolled in a confirmatory Phase 3 clinical trial evaluating its development-stage medicine teprotumumab for moderate-to-severe active thyroid eye disease (TED). The clinical trial, titled "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)", will enroll 76 patients across 11 centers in the United States, Germany and Italy. Teprotumumab has received Breakthrough Therapy, Orphan Drug and Fast Track designations from the U.S. Food and Drug Administration (FDA).

TED, also referred to as Graves' eye disease or Graves' orbitopathy, is an eye condition in which the eye muscles and fatty tissue behind the eye become inflamed. This can cause proptosis, where the eyes are pushed forward causing "staring" or "bulging" eyes and the eyes and eyelids become swollen and red. In some cases there is swelling and stiffness of the muscles that move the eyes so that they are no longer in line with each other, or the eyelids are unable to close.[1]

OPTIC is a confirmatory pivotal study initiated after clinically meaningful and highly statistically significant results from a Phase 2 study, published in *TheNew England Journal of Medicine* on May 4, 2017, showed that teprotumumab met its primary endpoint ($p < 0.001$) as well as its secondary endpoints. Teprotumumab was generally well tolerated with the majority of adverse events being mild. The only treatment-related adverse event was hyperglycemia in diabetic patients, which was controlled by adjusting diabetes medication.[2]

"There is a clinically significant unmet need among people living with TED, a rare disease with no FDA-approved treatment options, that affects more than 10,000 people in the United States," said Timothy P. Walbert, chairman, president and chief executive officer, Horizon Pharma plc. "The initiation of our confirmatory Phase 3 clinical trial evaluating teprotumumab is a significant step as we rapidly expand our strategy to pursue development-stage medicines for people living with rare and devastating diseases."

Those who meet OPTIC (NCT03298867) Phase 3 eligibility criteria will be randomized to receive eight infusions of teprotumumab or placebo every three weeks for 21 weeks. The primary endpoint will measure the proptosis responder rate of ? 2 mm reduction of proptosis in the study eye (without deterioration in the fellow eye) at week 24. In addition, the OPTIC trial will measure several secondary endpoints at week 24, including overall responder rate, percentage of participants with a Clinical Activity Score value of 0 or 1, mean change in proptosis measurement and mean change in the Graves' Ophthalmopathy Quality of Life questionnaire overall score. Safety will also be evaluated. More detailed information about the study, including eligibility requirements, is available at ClinicalTrials.gov.

"People living with TED experience debilitating, life-changing symptoms, including swelling of the eyelids, sensitivity to light, double vision and eye bulging," said Raymond Douglas, M.D., Ph.D., one of the study's principal investigators and director of the orbital and thyroid eye disease program, Cedars-Sinai Medical Center . "Based on positive results from the Phase 2 study evaluating teprotumumab, we are excited to participate in the OPTIC study and move closer to potentially bringing forward the first treatment option for moderate-to-severe active TED."

Teprotumumab Phase 2 Study Results
A randomized double-blind, placebo controlled Phase 2 study was conducted to evaluate the efficacy and safety of teprotumumab in patients with recent onset, moderate-to-severe TED. In the study, 88 patients were assigned to receive eight infusions of teprotumumab or placebo once every three weeks for 21 weeks. 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). Therapeutic effects were rapid with responder rates of 46% for patients treated with teprotumumab and 5% for patients treated with placebo at week six ($p<0.001$). Treatment with teprotumumab was well tolerated with the majority of adverse events being mild. The only treatment-related adverse event was hyperglycemia in diabetic patients, which was controlled by adjusting diabetes medication. Results from this study were published in the May 4, 2017, issue of *The New England Journal of Medicine.*

About Teprotumumab
Teprotumumab is a fully human monoclonal antibody (mAb) inhibitor of the insulin 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). After clinically meaningful and highly statistically significant results were reported in a Phase 2 study of teprotumumab, a Phase 3 confirmatory study was launched in October 2017. Teprotumumab is an investigational medicine and its safety and efficacy have not been established.

About Horizon Pharma plc
Horizon Pharma plc is a biopharmaceutical company focused on improving patients' lives by identifying, developing, acquiring and commercializing differentiated and accessible medicines that address unmet medical needs. The Company markets 11 medicines through its orphan, rheumatology and primary care business units. For more information, please visit www.horizonpharma.com. Follow @HZNPplc on Twitter, like us on Facebook, or view careers on our LinkedIn page.

Forward-Looking Statements
This press release contains forward-looking statements, including statements regarding the planned scope and design of 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 trials 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.

References:

1. American Thyroid Association. Graves' Eye Disease Fact Sheet. Available at https://www.thyroid.org/graves-eye-disease/. Accessed Oct. 17, 2017.
2. Teprotumumab for Thyroid-Associated Opthalmopathy. *New England Journal of Medicine*. 4 May 2017. http://www.nejm.org/doi/full/10.1056/NEJMoa1614949. Accessed Oct. 17, 2017.

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