Horizon Pharma plc Announces Presentation of Data From 48 Week Off-Therapy Follow-Up to the Phase 2 Trial of Teprotumumab

October 4, 2018

-- Data presented during an oral session at the American Thyroid Association Annual Meeting --

DUBLIN--(BUSINESS WIRE)--Oct. 4, 2018-- Horizon Pharma plc (NASDAQ:HZNP) announced new data from the Phase 2 clinical trial of teprotumumab for people living with moderate-to-severe active thyroid eye disease (TED) showing a majority of patients that had reductions in proptosis at week 24 maintained these reductions 48 weeks following the study completion, or nearly a year off therapy. The results of this investigational medicine were presented during an oral session at the American Thyroid Association (ATA) Annual Meeting, Oct. 3 – 7, 2018, in Washington, D.C.

TED is a rare autoimmune disease that is active for up to three years. During active TED the insulin-like growth factor 1 receptor (IGF-1R) is overexpressed on orbital fibroblasts, resulting in local inflammation and tissue expansion, which can in turn lead to proptosis, or bulging of the eye. This can result in stiffness of the muscles, displacement of the eyes so they are no longer in line with each other, and/or the eyelids are unable to close. The inability for people living with active TED to close their eyelids can lead to corneal ulcerations and potential blindness, and many also endure challenges with double vision, known as diplopia. Once TED is no longer active, the orbital muscles and tissues become fibrotic and, for some, changes due to local inflammation and tissue expansion can only be corrected with surgery.

“Proptosis creates numerous challenges for people living with thyroid eye disease and is the most important measure from a clinical perspective,” said George J. Kahaly, M.D., Ph.D., lead author and professor of medicine and endocrinology and metabolism, Johannes Gutenberg University Medical Center. “In addition to challenges with visual function and appearance, proptosis can lead to permanent structural changes around the eyes and is what drives the decision for surgery following active thyroid eye disease.”

The analysis of the Phase 2 data, *48-Week Follow-Up Of A Multicenter, Randomized, Double-Masked, Placebo Controlled Treatment Trial Of Teprotumumab In Thyroid-Associated Ophthalmopathy,* shows that at four weeks following the initial 24 week treatment period, proptosis response was 73.8 percent for patients receiving teprotumumab versus 13.3 percent for patients receiving placebo ($p<0.001$). In addition, 53 percent of week 24 teprotumumab proptosis responders maintained at least a 2 mm improvement relative to baseline at week 72 (48 weeks following treatment period). Teprotumumab is an investigational medicine and its safety and efficacy have not been established.

“Teprotumumab has the potential to be an impactful treatment for people living TED and the first therapy to demonstrate reduction in proptosis,” said Elizabeth Thompson, Ph.D., vice president clinical development, rare disease, Horizon Pharma plc. “We are encouraged by these data, which suggest proptosis reductions could be maintained in a majority of responders for nearly a year off therapy. Through our ongoing confirmatory Phase 3 trial and extension study, we expect to gain a deeper understanding of the effect of additional treatment for those considered non-responders as well as those who may benefit from retreatment.”

Horizon Pharma will host an investor call at 10:30 a.m. ET to discuss these data, as well as provide an overview of TED and the current treatment landscape.

Additional data from the 48 week off-therapy follow-up will be presented during an oral session on Oct. 25, 2018, at the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) and on Oct. 29, 2018, at the American Academy of Ophthalmology (AAO 2018) meeting in Chicago, IL. The presentation is titled *Diplopia Response in a Controlled Trial with Teprotumumab, an IGF-1 Receptor Antagonist Antibody for Thyroid Eye Disease.*

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). A Phase 3 confirmatory study began enrolling in October 2017 after results from the randomized double-blind, placebo controlled Phase 2 study and completed enrollment in September 2018.

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 CAS 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 spasms, diarrhea, alopecia, hyperglycemia, dry skin, dysgeusia, headache, paresthesia, hearing impairment and weight loss. Results from this study were published in the May 4, 2017, issue of *The New England Journal of Medicine*.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding 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 subsequent clinical trials will be consistent with results of prior trials, whether the results of the Phase 3 teprotumumab 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.

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 us @HZNPplc on Twitter, like us on Facebook or explore career opportunities on LinkedIn.

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