



Horizon Pharma plc Announces Presentation of Results of 48 Week Off-Therapy Follow-Up to the Phase 2 Trial of Teprotumumab at 2018 American Academy of Ophthalmology (AAO) Annual Meeting

October 29, 2018

DUBLIN--(BUSINESS WIRE)--Oct. 29, 2018-- Horizon Pharma plc (NASDAQ:HZNP) announced that more detailed results from the 48 week off-therapy follow-up to the Phase 2 clinical trial of teprotumumab for people living with moderate-to-severe active thyroid eye disease (TED) were presented at the American Academy of Ophthalmology (AAO) Annual Meeting, Oct. 27 – 30, 2018, in Chicago, Ill. The data was presented in an oral session, *Diplopia Response in a Controlled Trial with Teprotumumab, an IGF-1 Receptor Antagonist Antibody for Thyroid Eye Disease*, at 4:57 p.m. CT today.

During active TED, which can last up to three years, the insulin-like growth factor 1 receptor (IGF-1R) is overexpressed on orbital fibroblasts, resulting in local inflammation and tissue expansion. This can lead to proptosis, or bulging of the eye, and depending on the degree of proptosis, pressure is created on the eyeball within a tight orbital space that can cause multiple eye symptoms. Displacement of the eye muscles subsequently cause ocular misalignment, or strabismus; as a result of which, many people living with TED also endure challenges with double vision, known as diplopia.

“Diplopia is viewed as a hallmark for more serious TED, resulting from swelling and thickening of the extraocular muscles, causing the eyes to move out of alignment,” 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. “The objectives of this analysis were to examine the diplopia findings in this 24-week controlled trial as well as the additional 48-week long-term follow-up after medicine discontinuation.”

The analysis of this Phase 2 exploratory endpoint shows that 69.2 percent (18/26 patients) of those with diplopia improvements of at least one grade at week 24 maintained these improvements at week 72 (48 weeks following treatment period). The Phase 3 confirmatory trial and extension studies will evaluate diplopia in people with moderate-to-severe active TED. Teprotumumab is an investigational medicine and its safety and efficacy have not been established.

“These data are one of the few presentations selected for the oral sessions at this year’s AAO meeting, which speaks to the growing interest we see in the potential role that teprotumumab may have in the treatment of active TED,” said Elizabeth Thompson, Ph.D., vice president, clinical development, rare diseases, Horizon Pharma plc. “We understand there are many challenges for those living with active TED and our ongoing clinical trial and extension study are exploring the potential of teprotumumab to have a significant impact on the treatment approach for these patients.”

About Thyroid Eye Disease

Thyroid eye disease is a rare autoimmune disease that can be 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. Depending on the degree of proptosis, pressure is created on the eyeball within a tight orbital space that can cause multiple eye symptoms. Lid retraction and inability to close the eyelids subsequently lead to dry eye symptoms, corneal ulcerations, infections and impaired vision. Displacement of the eye muscles subsequently cause ocular misalignment, or strabismus; as a result of which, many people living with TED also endure challenges with double vision, known as diplopia. In severe cases, pressure on the optic nerve that is responsible for vision, may compromise blood supply and potentially cause blindness. Once TED is no longer active, the orbital muscles and tissues become fibrotic, and, for some, the resulting exophthalmos and diplopia can only be corrected with complicated surgical procedures which may not always successfully reverse patients’ eye conditions.

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 clinical activity score (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 (≥ 5 percent) reported with teprotumumab compared to placebo and not dose limiting 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 expectations regarding the Phase 3 trial and other studies of teprotumumab for 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 Pharma experiences delays in completing the Phase 3 trial or other planned studies, 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 medicine 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](https://twitter.com/HZNPplc) on Twitter, like us on [Facebook](https://www.facebook.com/horizonpharma) or explore career opportunities on [LinkedIn](https://www.linkedin.com/company/horizonpharma).

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