TEPEZZA® (teprotumumab-trbw) Data from the Phase 2 Clinical Trial Evaluate Longer-Term Responses in People Living with Thyroid Eye Disease (TED)

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-- New findings presented during the Academy of Managed Care Pharmacy Nexus 2020 Virtual Meeting showed most patients had at least some improvement in one or more disease parameters for up to one year following TEPEZZA treatment for TED, and are supported by recently announced long-term follow-up data from the Phase 3 OPTIC clinical trial --

DUBLIN--(BUSINESS WIRE)--Oct. 14, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced new long-term follow-up data from the Phase 2 clinical trial of TEPEZZA® (teprotumumab-trbw), which showed a sustained response up to one year following completion of treatment for Thyroid Eye Disease (TED). These data will be presented as part of the Academy of Managed Care Pharmacy (AMCP) Nexus 2020 Virtual Meeting. TEPEZZA is the first and only medicine approved by the U.S. Food and Drug Administration (FDA) for the treatment of TED – a serious, progressive and vision-threatening rare autoimmune disease.[1]

In the Phase 2 and Phase 3 clinical trials, TEPEZZA demonstrated clinically significant improvements in several key indicators of TED, including proptosis (eye bulging), diplopia (double vision) and clinical activity score (CAS), at Week 24. To understand the long-term benefits of TEPEZZA, patients from the Phase 2 clinical trial were followed for 51 weeks (study Week 72) after their last infusion of TEPEZZA. Study findings only include patients who had Week 72 data (n=37). The study assessed the percent of patients who received TEPEZZA and had any improvement in proptosis, diplopia or CAS, as well as the percent with disease inactivation, as measured by a CAS of 0 or 1 point at the end of the study. Four patients received non-TEPEZZA therapy (corticosteroids and/or orbital decompression surgery) during this follow-up period and were counted as improved in the study.

Key findings include the following:

- All patients with Week 72 data (37/37) reported some improvement in at least one of the study outcomes from baseline.
- 97 percent (36/37) had an improvement in CAS (decrease of at least 1 point).
- 86 percent (31/36) had any decrease in proptosis. One patient chose elective TED surgery at Week 70 and did not have proptosis measurements at Week 72.
- Of patients with baseline diplopia, 70 percent (23/33) had an improvement of at least one grade.
- 70 percent (26/37) had disease inactivation (CAS of 0 or 1 point).

“These findings indicate this medication can provide relief at least a year after the last dose, including improvements in proptosis and diplopia, which are especially difficult symptoms to manage,” said Roger A. Dailey, M.D., F.A.C.S., trial investigator and professor of ophthalmology at Oregon Health & Science University’s Casey Eye Institute.

This study adds to the body of evidence supporting the long-term effects of TEPEZZA, including data recently announced from the Phase 3 OPTIC 48-week off-treatment follow-up period. In that analysis, the majority of TEPEZZA patients who were proptosis responders at Week 24 in OPTIC maintained their response at Week 72 (19/34; 56 percent) without receiving additional TED treatment. Of the 15 patients who did not qualify as maintaining a proptosis response, eight patients were at least 2 mm better than baseline at the time of their last assessment in the OPTIC 48-week off-treatment follow-up period. There were no new safety concerns in the OPTIC 48-week off-treatment follow-up period. Additional data from the OPTIC trial will be presented at future medical congresses.

“We continue to evaluate existing and new data from our clinical development program and are pleased with the continuing evidence supporting potential for sustained benefit,” said Elizabeth H.Z. Thompson, Ph.D., group vice president, development and external search, research and development, Horizon. “For a patient population who has had no options aside from difficult and complicated surgeries, the potential for lasting benefit can really bring hope to patients.”

About the Phase 2 Clinical Trial

The Phase 2 clinical trial was designed to evaluate the efficacy and safety of TEPEZZA 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 at least 2 points and reduction of proptosis of at least 2 mm at Week 24 without corresponding deterioration in the fellow eye. In the intent-to-treat population, 69 percent (29/42) of patients receiving TEPEZZA and 20 percent (9/45) of patients receiving placebo were responders at Week 24 ($p<0.001$). The most frequent adverse events (at least 5 percent) reported with TEPEZZA and greater than in the placebo group 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*.

About Thyroid Eye Disease (TED)

TED is a serious, progressive and vision-threatening rare autoimmune disease.[1] TED often occurs in people living with hyperthyroidism or Graves’ disease; however, it is a distinct disease that is caused by autoantibodies activating an IGF-1R-mediated signaling complex on cells within the retro-orbital space.[2,3] This leads to a cascade of negative effects, which may cause long-term, irreversible damage. As TED progresses, the serious

damage it can cause includes proptosis (eye bulging), strabismus (misalignment of the eyes) and diplopia (double vision) – and in some cases can lead to blindness.[4,5]

About TEPEZZA

INDICATION

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Infusion Reactions: TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain. Infusion reactions may occur during an infusion or within 1.5 hours after an infusion. In patients who experience an infusion reaction, consideration should be given to premedicating with an antihistamine, antipyretic, or corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

Preexisting Inflammatory Bowel Disease: TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

Hyperglycemia: Increased blood glucose or hyperglycemia may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be managed with medications for glycemic control, if necessary. Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

Adverse Reactions

The most common adverse reactions (incidence ≥5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache and dry skin.

For additional information on TEPEZZA, please see Full Prescribing Information at TEPEZZAhcp.com.

About Horizon

Horizon is focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare and rheumatic 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 statements regarding the potential benefits of TEPEZZA as a treatment of TED. These forward-looking statements are based on management 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 whether TEPEZZA is successfully commercialized and adopted by physicians and patients, as well as those described in Horizon'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 does not undertake any obligation to update or revise these statements, except as may be required by law.

References

1. Barrio-Barrio J, et al. Graves' Ophthalmopathy: VISA versus EUGOGO Classification, Assessment, and Management. *Journal of Ophthalmopathy*. 2015;2015:1-16.
2. Weightman DR, et al. Autoantibodies to IGF-1 Binding Sites in Thyroid Associated Ophthalmopathy. *Autoimmunity*. 1993;16(4):251–257.
3. Pritchard J, et al. Immunoglobulin Activation of T Cell Chemoattractant Expression in Fibroblasts from Patients with Graves’ Disease Is Mediated Through the Insulin-Like Growth Factor 1 Receptor Pathway. *J Immunol*. 2003;170:6348-6354.
4. Bahn. Graves' Ophthalmopathy. *New England Journal of Medicine*. 2010;362:726-38.
5. McKeag D, et al. Clinical features of dysthyroid optic neuropathy: a European Group on Graves' Orbitopathy (EUGOGO) survey. *Br J Ophthalmol*. 2007;91:455-458.

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