New Data Build on Growing Evidence Supporting TEPEZZA® (teprotumumab-trbw) Efficacy in Thyroid Eye Disease (TED), Including in Patients With Less Severe Disease and Longer Disease Duration

November 13, 2020

-- Presentation during American Academy of Ophthalmology Annual Meeting (AAO 2020 Virtual) demonstrates clinical improvement in the less severe eye --

-- Additional data from OPTIC 48-week follow-up study and OPTIC-X extension trial, including findings showing that the majority of TEPEZZA patients who were diplopia (double vision) responders in OPTIC at week 24 maintained their response at week 72, nearly a year off-treatment --

-- Patients who received placebo during the OPTIC Phase 3 clinical trial and then received TEPEZZA in the OPTIC-X extension trial also achieved clinically significant diplopia improvement with an average of 12 months of disease, compared with six months in OPTIC --

DUBLIN--(BUSINESS WIRE)--Nov. 13, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced new TEPEZZA® (teprotumumab-trbw) data presented at the American Academy of Ophthalmology Annual Meeting (AAO 2020 Virtual), including findings suggesting benefits of TEPEZZA in the less severe eye of patients with Thyroid Eye Disease (TED), and new data from the OPTIC 48-week follow-up study and OPTIC-X clinical trial. 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]

"We continue to analyze our existing clinical trials and pursue new research to fully understand the impact TEPEZZA has on this challenging disease," said Elizabeth H.Z. Thompson, Ph.D., group vice president, development and external search, Horizon. "Our data demonstrating the effect of TEPEZZA at varying stages of the disease, including in the less severely affected eye and in patients who have had Thyroid Eye Disease for a longer period of time, will help advance the science of Thyroid Eye Disease and instill greater understanding of the role TEPEZZA can play in improving patient outcomes."

Compelling Response in Less Severe TED

Improvement in Fellow Eye of Patients with TED: Pooled Analyses from Teprotumumab Studies (PO305)

In patients with TED, one eye can have more severe symptoms than the other. The TEPEZZA Phase 2 clinical trial and OPTIC Phase 3 confirmatory clinical trial designated the more severely affected eye as the "study eye". [2,3] This new analysis focused specifically on efficacy of TEPEZZA in treating the less severe eye, or "fellow eye", of patients in the TEPEZZA Phase 2 and 3 trials. Researchers analyzed the intent-to-treat (ITT) population in the Phase 2 and Phase 3 studies, defined as all patients randomized to receive TEPEZZA (n=84) and all patients randomized to receive placebo (n=87). The fellow eye was less proptotic than the study eye in both the TEPEZZA (21.61 mm vs. 23.02 mm) and placebo (21.97 mm vs. 23.15 mm) groups, indicating less severe disease. Additionally, the fellow eye, on average, demonstrated less inflammation based on the clinical activity score (CAS) than the study eye in both the TEPEZZA (CAS: 4.3 vs. 5.1 points) and placebo (CAS: 4.7 vs. 5.3 points) groups.

Findings suggest that TEPEZZA may offer benefits in patients with less severe TED:

- At Week 24, more TEPEZZA patients were proptosis (eye bulging) responders (≥2 mm reduction) in the fellow eye than placebo patients (63.1 percent vs. 8.0 percent, p<0.001), with a mean reduction in proptosis of 2.39 mm for TEPEZZA patients and a mean increase in proptosis of 0.15 mm for placebo patients (p<0.001).
- 30 patients (34.5 percent) in the placebo group had a worsening of proptosis at Week 24 in the fellow eye compared to 0 patients (0 percent) in the TEPEZZA group.
- CAS in the fellow eye decreased from baseline by a mean of -3.42 points in the TEPEZZA group compared to -2.00 points in the placebo group (p<0.001) at Week 24.
- More TEPEZZA patients (63.1 percent) than placebo patients (26.4 percent) had a CAS of 0 or 1 – signifying disease inactivation – in the fellow eye at Week 24 (p<0.001).

"We know from the clinical development program that TEPEZZA significantly reduces proptosis and Thyroid Eye Disease-related inflammation in patients with moderate-to-severe disease, and now with this new analysis of the Phase 2 and 3 data, we have evidence pointing to efficacy in patients with less severe disease as well," said Raymond Douglas, M.D., Ph.D., study author and director of the Orbital and Thyroid Eye Disease Program, Cedars-Sinai Medical Center. "We believe this robust effect is the result of the mechanism of TEPEZZA that effectively targets the underlying molecular pathways that cause Thyroid Eye Disease."

Additional Findings from the OPTIC 48-Week Follow-Up Study and OPTIC-X Clinical Trial

Long Term Assessment of Proptosis and Diplopia from the OPTIC Trial of Teprotumumab in Thyroid Eye Disease (PA038)

Additional data from the OPTIC Phase 3 confirmatory clinical trial and the OPTIC-X open-label extension clinical trial were also included in an abstract and presented during AAO, supplementing the topline results on proptosis response announced in July 2020. The OPTIC trial included a 24-week treatment period (treatment every three weeks for a total of eight infusions) and a 48-week off-treatment follow-up period. OPTIC-X evaluated TEPEZZA in patients who were enrolled in OPTIC and were either proptosis non-responders at Week 24 or were proptosis responders at Week 24 but flared during the 48-week off-treatment follow-up period.

New OPTIC 48-week off-treatment follow-up study findings include the following:

- The majority of TEPEZZA patients who had at least 1 grade of diplopia (double vision) improvement at Week 24 in OPTIC maintained their response at Week 72 (11/19; 58 percent) without receiving additional TED treatment.
- 50 percent of TEPEZZA patients (8/16) who had a diplopia score of 0 at Week 24 in OPTIC maintained a diplopia score of 0 at Week 72 without receiving additional TED treatment.

New OPTIC-X findings include the following:

- 61 percent of patients (14/23) who received placebo during the OPTIC trial and then entered OPTIC-X and received TEPEZZA were considered diplopia responders (≥1 grade improvement) at Week 24. This is consistent with results from the OPTIC trial, where 68 percent of patients (19/28) who received TEPEZZA had a change from baseline of at least 1 grade in diplopia at Week 24. OPTIC-X patients had an average of 12 months of TED compared with six months in OPTIC.
- Five patients who received placebo during the OPTIC trial and then entered OPTIC-X had a CAS of 0 or 1, which means they had minimal or no inflammation. Of those, 60 percent (3/5) were proptosis responders at Week 24 (≥2 mm improvement in proptosis from baseline in the study eye without deterioration in the fellow eye at Week 24).

There were no new safety concerns in OPTIC-X or the OPTIC 48-week off-treatment follow-up period, including in patients who received additional TEPEZZA treatment.

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.[4,5] 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.[6,7]

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 less severe 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 risks associated with future clinical development, whether TEPEZZA will be adopted as a treatment for less severe TED, 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

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