



## **New Topline TEPEZZA® (teprotumumab-trbw) Data Underscore its Efficacy in Longer Disease Duration, Long-Term Durability and Potential for Retreatment in People Living with Thyroid Eye Disease (TED)**

July 31, 2020

*-- 89 percent of patients who received placebo during the OPTIC Phase 3 clinical trial and then received TEPEZZA in the OPTIC-X extension trial achieved clinically significant proptosis reduction with an average of 12 months of disease, compared with six months in OPTIC --*

*-- Majority of TEPEZZA patients who were proptosis responders in OPTIC at week 24 maintained their response at week 72, nearly a year off treatment --*

*-- For the small number of TEPEZZA patients who relapsed during the OPTIC follow-up period, the majority experienced improvements in proptosis with an additional course of TEPEZZA in OPTIC-X --*

*-- Horizon will host an investor webcast on July 31, 2020, at 9 a.m. ET --*

DUBLIN--(BUSINESS WIRE)--Jul. 31, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced positive topline data from two clinical trials that add to the growing body of evidence supporting the efficacy and safety of TEPEZZA® (teprotumumab-trbw) for the treatment of Thyroid Eye Disease (TED). 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.<sup>1</sup>

The [OPTIC](#) Phase 3 confirmatory clinical trial and the [OPTIC-X](#) open-label extension clinical trial are part of Horizon's development program to evaluate the safety and efficacy of TEPEZZA in people living with TED. The OPTIC Phase 3 confirmatory clinical trial included a 24-week treatment period and a 48-week off-treatment follow-up period. The OPTIC 24-week treatment period evaluated patients who received TEPEZZA or placebo once every three weeks for a total of eight infusions. The primary endpoint was a 2 mm or more reduction of proptosis (eye bulging) from baseline in the study eye (without deterioration in the fellow eye) at Week 24. At Week 24 of OPTIC, proptosis responders entered into a 48-week off-treatment follow-up period, without receiving additional TED treatment, including TEPEZZA.

OPTIC-X evaluated the safety and efficacy of TEPEZZA in TED patients who were enrolled in OPTIC and were either proptosis non-responders at Week 24 of OPTIC, or were proptosis responders at Week 24 but relapsed during the 48-week off-treatment follow-up period. Non-responders were defined as patients who did not achieve at least a 2 mm proptosis improvement from baseline at Week 24 of OPTIC. Relapse was defined as patients who lost at least 2 mm of their Week 24 proptosis improvement during the 48-week off-treatment follow-up period – even if their proptosis was still substantially better than at baseline of OPTIC – or who had a substantial increase in the number of inflammatory signs or symptoms without worsening proptosis. Patients could qualify as relapsing at any point during the 48-week off-treatment follow-up period of OPTIC.

Topline data include the following:

- 89 percent of patients (33/37) who received placebo during the OPTIC trial and then entered OPTIC-X and received TEPEZZA achieved the primary endpoint of a 2 mm or more reduction in proptosis at Week 24 (average reduction of -3.5 mm). This is consistent with results from the OPTIC trial, where 83 percent of TEPEZZA patients (n=41) had a proptosis reduction of 2 mm or more at Week 24 (average reduction of -3.3 mm).<sup>2</sup>
- The results for other OPTIC-X endpoints, including diplopia and Clinical Activity Score (CAS), are similar to what was observed in OPTIC.<sup>2</sup>
- These patients who received placebo in OPTIC and their first course of TEPEZZA in OPTIC-X had a TED diagnosis for an average of one year and as long as 16 months, compared with an average of six months in the OPTIC trial.
- In the OPTIC 48-week off-treatment follow-up period, the majority of TEPEZZA patients who were proptosis responders at Week 24 in OPTIC maintained their proptosis 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. The 15 patients include four who prematurely discontinued the study, two who had worsened slightly but not enough to qualify as relapsed for OPTIC-X and nine who met the OPTIC-X criteria for relapse prior to Week 72 of the off-treatment follow-up period (eight of whom entered OPTIC-X for retreatment and one who did not enroll in OPTIC-X).
- Similar durability from Week 24 to Week 72 was demonstrated for other endpoints in the OPTIC 48-week off-treatment follow-up period, including diplopia and CAS.
- For relapsed patients who were retreated with an additional course of TEPEZZA, more than 60 percent had a 2 mm or more proptosis improvement from OPTIC-X baseline at Week 24.
- Only five patients had not achieved a proptosis response after completing a full course of TEPEZZA in OPTIC. Of these,

two achieved a 2 mm or more proptosis reduction in OPTIC-X after an additional course of TEPEZZA.

- 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.

“Data from OPTIC-X provide evidence supporting the potential for TEPEZZA to meaningfully reduce proptosis in patients who have had TED for a longer period of time than what was originally studied in the Phase 2 and Phase 3 clinical trials,” said Elizabeth H.Z. Thompson, Ph.D., group vice president, development and external search, research and development, Horizon. “It is also promising to see that there are patients who may benefit from additional therapy with TEPEZZA, and the data suggest that they can experience these improvements without added safety concerns. We look forward to continuing our development program and further understanding the efficacy and safety of TEPEZZA among patients who are at various stages of their TED journey, from early diagnosis to chronic (inactive) patients.”

“The similarity in results between those who received TEPEZZA in the OPTIC trial and those who transitioned from placebo in OPTIC to TEPEZZA in OPTIC-X is remarkable,” said Raymond Douglas, M.D., Ph.D., the trial’s co-principal investigator and director of the Orbital and Thyroid Eye Disease Program, Cedars-Sinai Medical Center. “Previously, people diagnosed with TED had no FDA-approved treatments and could expect to experience many years of life-altering symptoms while undergoing multiple surgeries in an attempt to restore their vision. Data from the OPTIC and OPTIC-X clinical trials, as well as observations from our real-world use of TEPEZZA following the FDA approval, have provided very compelling reasons to completely change expectations for people living with TED.”

Detailed data will be presented at a future medical congress.

### **About the OPTIC 48-Week Follow-Up Period**

OPTIC (Treatment of Graves’ Orbitopathy [Thyroid Eye Disease] to Reduce Proptosis with Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study) was a multicenter, randomized, double-blind, placebo-controlled trial. This Phase 3 confirmatory clinical trial included a 24-week treatment period and a 48-week off-treatment follow-up period. At the end of the 24-week treatment period, patients who were proptosis responders entered into the 48-week off-treatment follow-up period, without receiving additional TED treatment, including TEPEZZA. Clinic visits were scheduled for Weeks 28, 36, 48, 60, and 72 (Months 7, 9, 12, 15, and 18). Sustained proptosis response in the OPTIC 48-week off-treatment follow-up period was defined as a 2 mm or more proptosis improvement from OPTIC baseline at Week 24, a 2 mm or more proptosis improvement from OPTIC baseline at Week 72 and no additional TED treatment, including TEPEZZA.

### **About OPTIC-X**

OPTIC-X (Treatment of Graves’ Orbitopathy [Thyroid Eye Disease] to Reduce Proptosis with Teprotumumab Infusions in an Open-Label Clinical Extension Study) was designed to better understand whether certain patients may benefit from retreatment or longer treatment (more than 6 months) with TEPEZZA. OPTIC-X was a 48-week, open-label extension trial in which patients who participated in the OPTIC Phase 3 clinical trial received eight additional infusions of TEPEZZA (10 mg/kg for the first infusion followed by 20 mg/kg for the remaining seven infusions). Trial patients had to either be a proptosis non-responder at Week 24 of OPTIC or a proptosis responder at Week 24 of OPTIC who relapsed during the OPTIC 48-week off-treatment follow-up period. Relapse was defined as an increase in proptosis of 2 mm or more in the study eye since Week 24 of OPTIC or an increase in CAS of at least 2 points since Week 24 with an absolute CAS of at least 4 in the study eye following Week 24 of OPTIC. The primary endpoint was proptosis responder rate, which is defined as the percentage of participants with a 2 mm or more proptosis reduction since baseline of OPTIC-X in the study eye without deterioration of proptosis in the fellow eye (2 mm or more increase) at Week 24.

### **About Thyroid Eye Disease (TED)**

TED is a serious, progressive and vision-threatening rare autoimmune disease.<sup>1</sup> 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.<sup>3,4</sup> 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.<sup>5,6</sup>

### **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  $\geq 5\%$  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](http://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](http://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 and Horizon's further development plans with respect to TEPEZZA. 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, risks related to clinical development, 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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