



FDA Approves TEPEZZA (TM) (teprotumumab-trbw) for the Treatment of Thyroid Eye Disease (TED)

January 21, 2020

-- First and only FDA-approved medicine for TED, a serious, progressive, vision-threatening rare disease --

-- Clinical improvements were seen as early as six weeks, with continued improvement across the 24-week treatment period --

-- Approval comes ahead of the Prescription Drug User Fee Act (PDUFA) goal date of March 8, 2020 --

-- Horizon to host investor webcast Tuesday, January 21 at 5:00 p.m. ET --

DUBLIN--(BUSINESS WIRE)--Jan. 21, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced that the U.S. Food and Drug Administration (FDA) has approved TEPEZZA™ (teprotumumab-trbw) for the treatment of Thyroid Eye Disease (TED). TEPEZZA is the first and only FDA-approved medicine for the treatment of TED, a serious, progressive and vision-threatening rare autoimmune disease that is associated with proptosis (eye bulging), diplopia (double vision), blurred vision, pain, inflammation and facial disfigurement. TEPEZZA is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the insulin-like growth factor-1 receptor (IGF-1R) that is administered to patients once every three weeks for a total of eight infusions.

"Today is a great day for people living with Thyroid Eye Disease, a rare, vision-threatening disease that previously had no FDA-approved treatment options," said Timothy Walbert, chairman, president and chief executive officer, Horizon. "The TED community has gone far too long without an FDA-approved therapy, and we are grateful to the people living with TED and physicians who partnered with us on the clinical development program that led to today's approval of TEPEZZA. This also marks the early approval of Horizon's first Biologics License Application – a key step in our evolution to an innovation-focused biopharma company, developing new medicines for debilitating diseases with few or no treatment options."

The FDA approval of TEPEZZA comes ahead of the Prescription Drug User Fee Act (PDUFA) goal date of March 8, 2020. The medicine received Priority Review, Orphan Drug, Fast Track and Breakthrough Therapy designations from the FDA.

"The FDA approval of TEPEZZA is momentous for the TED community and has the potential to change the treatment paradigm for TED – providing new hope for people who are living with this horrible, vision-threatening disease," said Raymond Douglas, M.D., Ph.D., director of the Orbital and Thyroid Eye Disease Program, Cedars-Sinai Medical Center and co-principal investigator of the TEPEZZA Phase 3 confirmatory clinical trial. "Today's news brings forward a medicine for patients that targets the underlying biology of the disease and has been shown to significantly improve eye bulging and double vision, which are the most debilitating aspects of the disease."

"TEPEZZA is a much-needed breakthrough for a community of people who have historically had to struggle in pain as their symptoms progress – risking permanent damage to their eyes and making it extremely difficult to go about their daily lives," said Jeff Todd, president and chief executive officer, [Prevent Blindness](#). "This approval is meaningful to our organization because we are committed to helping patients with vision impairment and those who are at significant risk."

The FDA approval of TEPEZZA is supported by a robust body of clinical evidence, including statistically significant, positive results from the [Phase 2 clinical study](#), as well as the Phase 3 confirmatory clinical study [OPTIC](#) (Treatment of Graves' Orbitopathy [Thyroid Eye Disease] to Reduce Proptosis with Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study). The OPTIC study found that significantly more patients treated with TEPEZZA (82.9%) had a meaningful improvement in proptosis (≥ 2 mm) as compared with placebo patients (9.5%) ($p < 0.001$) without deterioration in the fellow eye at Week 24. Additional secondary endpoints were also met, including a change from baseline of at least one grade in diplopia (double vision) in 67.9% of patients receiving TEPEZZA compared to 28.6% of patients receiving placebo ($p = 0.001$) at Week 24. In a related analysis of the Phase 2 and Phase 3 clinical studies, there were more patients with complete resolution of diplopia among those treated with TEPEZZA (53%) compared with those treated with placebo (25%). The majority of adverse events experienced with TEPEZZA treatment were graded as mild to moderate and were manageable in the trials, with few discontinuations or therapy interruptions.

Horizon will conduct a post-marketing study to evaluate safety in a larger patient population as was discussed at the Dermatologic and Ophthalmic Drugs Advisory Committee (DODAC) FDA Advisory Committee meeting on December 13, 2019, where the committee voted unanimously (12-0) that TEPEZZA demonstrated a positive benefit risk profile. This study will also evaluate retreatment rates relative to how long patients receive the medicine.

TEPEZZA is expected to be available in the United States in the coming weeks. To speak with a Nurse Advocate about TED, patients can call 1-833-483-7399. To learn more about TEPEZZA, visit [TEPEZZA.com](#).

As a result of the FDA approval of TEPEZZA, Horizon will make approximately \$105 million in milestone payments during the first half of 2020.

Investor Webcast Information

Horizon will discuss the FDA approval of TEPEZZA during an investor webcast Tuesday, January 21 at 5:00 p.m. ET. The live webcast and a replay may be accessed at <http://ir.horizontherapeutics.com>. Please connect to Horizon's website at least 15 minutes prior to the live webcast to ensure adequate time for any software download that may be needed to access the webcast. A replay of the webcast will be available approximately two hours after the live webcast.

About Thyroid Eye Disease

Thyroid Eye Disease (TED) is a serious, progressive and vision-threatening rare autoimmune disease.¹ While TED often occurs in people living with hyperthyroidism or Graves' disease, 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, it causes serious damage – including proptosis (eye bulging), strabismus (misalignment of the eyes) and diplopia (double vision) – and in some cases can lead to blindness.^{4,5} Historically, patients have had to live with TED until the inflammation subsides, after which they are often left with permanent and vision-impairing consequences.^{1,6}

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](#).

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, follow us [@HorizonNews](#) on Twitter, like us on [Facebook](#) or explore career opportunities on [LinkedIn](#).

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the timing of TEPEZZA's availability in the United States, the potential benefits of TEPEZZA as a treatment of TED, plans to conduct post-marketing clinical trials and expected milestone payment obligations. 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 Horizon's ability to launch TEPEZZA in the United States, whether TEPEZZA is successfully commercialized and adopted by physicians and patients, the extent to which reimbursement is available for TEPEZZA, and potential delays in initiating and completing clinical trials, 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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