



TEPEZZA™ (teprotumumab-trbw) Significantly Reduces Proptosis (Eye Bulging), a Key Marker of Thyroid Eye Disease, Across Patient Subtypes

March 31, 2020

-- Data presented as part of ENDO 2020 demonstrates proptosis response regardless of age, gender and smoking status --

DUBLIN--(BUSINESS WIRE)--Mar. 31, 2020-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced new pooled efficacy data from the Phase 2 and 3 clinical trials of TEPEZZA™ (teprotumumab-trbw) showing that the recently approved medicine effectively reduces proptosis (eye bulging) in patients with Thyroid Eye Disease (TED) regardless of age, gender and smoking status. The analysis was accepted for presentation during an oral session at ENDO 2020, the Endocrine Society's annual meeting, and will also be published in a special supplemental section of the *Journal of the Endocrine Society*. TEPEZZA – the first and only medicine approved by the U.S. Food and Drug Administration (FDA) for TED – is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the insulin-like growth factor-1 receptor (IGF-1R).

"Proptosis is one of the most debilitating symptoms of TED, especially given the accompanying pain, vision impairment and emotional distress," said George Kahaly, M.D., Ph.D., of the Johannes Gutenberg University Medical Center in Mainz, Germany, and lead study author. "This analysis provides further evidence for physicians to consider when determining what type of patient to treat with TEPEZZA. For instance, smoking is a risk factor for TED and can make it more difficult to manage. It's exciting to see in this analysis that 70 percent of smokers were proptosis responders, with a mean reduction of almost 3 millimeters – which is comparable to results seen in non-smokers."

Prior analyses of combined data from two 24-week, randomized, double-masked, parallel-group clinical trials (Phase 2 and Phase 3) for TEPEZZA have demonstrated a proptosis response (≥ 2 mm reduction) rate of 77.4 percent in TEPEZZA patients compared to only 14.9 percent in placebo patients ($p < 0.001$) at Week 24.^{1,2,3} This new analysis was conducted to determine if there are any differences in proptosis response based on patient demographic characteristics, including age, gender and smoking status.

At Week 24 of treatment, across all subgroups, significantly more patients receiving TEPEZZA (n=84) experienced an improvement of at least 2 millimeters in proptosis compared to those receiving placebo (n=87) ($p < 0.001$ for all):

- Younger than age 65 (n=145): 76.1% vs. 16.2%
- Age 65 and older (n=26): 84.6% vs. 7.7%
- Male (n=46): 73.1% vs. 5.0%
- Female (n=125): 79.3% vs. 17.9%
- Smoker (n=46): 70.0% vs. 23.1%
- Non-smoker (n=125): 79.7% vs. 11.5%

The mean reduction in proptosis from baseline was also significantly greater at Week 24 in TEPEZZA-treated patients compared to placebo-treated patients (male: -3.34 vs. -0.07 mm; female: -3.10 vs. -0.42 mm; smokers: -2.99 vs. -0.72 mm; non-smokers: -3.20 vs. -0.31 mm; younger: -3.10 vs. -0.39 mm; older: -3.55 vs. -0.22 mm; all $p < 0.001$). The majority of adverse events experienced with TEPEZZA were manageable in the trials, with few discontinuations or therapy interruptions.^{1,2}

"From our work in the TED community, we know that the disease has several known risk factors, including age, gender and smoking status, which is why it is so encouraging to see that all of these patient types had similar proptosis reductions with TEPEZZA," said Elizabeth H.Z. Thompson, Ph.D., group vice president, clinical development and external search, Horizon. "We are committed to ongoing research, including analyses like this, to inform physicians as they decide how to use this new, breakthrough medicine."

About Thyroid Eye Disease

TED is a serious, progressive and vision-threatening rare autoimmune disease.⁴ 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.^{5,6} 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.^{7,8} Until the recent FDA approval of TEPEZZA, patients had to live with TED until the inflammation subsided, after which they were often left with permanent and vision-impairing consequences.^{4,9}

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 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

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