Horizon Therapeutics plc Announces Positive Topline Data from TEPEZZA® (teprotumumab-trbw) Phase 4 Clinical Trial in Patients with Chronic/Low Clinical Activity Score (CAS) Thyroid Eye Disease (TED)

April 10, 2023

-- At Week 24, patients treated with TEPEZZA achieved a 2.41 mm reduction in proptosis from baseline compared with 0.92 mm for those receiving placebo --

-- 62% of patients treated with TEPEZZA had a clinically meaningful improvement in proptosis at Week 24 (≥ 2 mm) compared with 25% of patients receiving placebo --

DUBLIN--(BUSINESS WIRE)--Apr. 10, 2023-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced positive and statistically significant topline results from its randomized, double-masked, placebo-controlled Phase 4 clinical trial (NCT04583735) evaluating TEPEZZA for the treatment of adults with chronic TED and low CAS, which is a measure of disease activity. The totality of clinical trial data continues to strongly support the efficacy of TEPEZZA across a broad spectrum of TED patients regardless of disease activity or duration, with a well-established safety profile. 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, debilitating and potentially vision-threatening rare autoimmune disease.[1]

The Phase 4 trial evaluated patients with an initial diagnosis of TED between two to 10 years (mean duration of 5.2 years; SD 1.77) and low levels of disease activity (mean CAS of 0.4; SD 0.49), whereas the prior pivotal trials (Phase 2 and 3) that formed the basis of the original FDA approval of TEPEZZA evaluated patients with disease duration of nine months or less and higher levels of disease activity.

“We are thrilled with the topline results, which reinforce that TEPEZZA significantly reduces proptosis in people living with Thyroid Eye Disease, regardless of their disease activity or duration, and underscores what we learned from our initial trials and what we have seen through more than three years of real-world use of TEPEZZA,” said Elizabeth H.Z. Thompson, Ph.D., executive vice president, research and development, Horizon. “With TEPEZZA, physicians have a medicine that can be used in a broad range of Thyroid Eye Disease patients, including those with long-duration disease of more than 5 years on average in this trial, which is important because we know the negative impact of the disease can be significant across all types of Thyroid Eye Disease patients. We look forward to discussing these data with the FDA to determine our next steps.”

Topline Data Overview

At Week 24, topline data per the pre-specified primary analysis method (intent-to-treat) demonstrated that the primary endpoint was met, and patients treated with TEPEZZA achieved a statistically significant reduction in proptosis from baseline compared to those receiving placebo. In addition, in the pre-specified per-protocol analysis, the differences between patients treated with TEPEZZA and patients treated with placebo increased.

Reduction in Proptosis – Week 24 – (Primary Endpoint)

	TEPEZZA	Placebo	p-value
Intent-to-treat	2.41 mm	0.92 mm	p=0.0004
Per protocol	2.44 mm	0.69 mm	p=0.0006

Proptosis Responder Rate – Week 24 – (≥ 2 mm) (Key Secondary Endpoint)

Intent-to-treat	62%	25%	p=0.0134
Per protocol	63%	7%	p=0.0008

No new safety signals were observed.

The Company plans to present these data at a future medical congress and publish them in a peer-reviewed medical journal to help educate key stakeholders, including physicians, patients and payors.

“Given this new and positive clinical evidence in patients with long-duration Thyroid Eye Disease and low CAS, it is important for physicians to thoroughly assess all of their Thyroid Eye Disease patients to determine whether TEPEZZA might be an option,” said Raymond Douglas, M.D., Ph.D., the trial’s principal investigator and director of the Orbital and Thyroid Eye Disease Program, Cedars-Sinai Medical Center in Los Angeles. “It is important to specifically ask patients if their symptoms are interfering with their ability to work, socialize and go about daily activities. These conversations can help physicians uncover the true burden of the disease and need for treatment, regardless of how much inflammation they have behind the eye or how long they have been living with the disease.”

Trial Design

This randomized, double-masked, placebo-controlled, parallel-group, multicenter trial evaluated the efficacy, safety, and tolerability of TEPEZZA (n=42) compared to placebo (n=20) in adults with chronic TED (two to 10 years duration prior to the study) and low CAS. The primary efficacy objective was to measure the effect of TEPEZZA versus placebo in the change of proptosis measurements in the study eye from baseline at Week 24. All study participants were required to have an initial diagnosis of TED two to 10 years prior to screening, and a CAS of ≤1 in both eyes for at least one year prior to screening or all of the following one year prior to screening: no progression in proptosis, no progression in diplopia and no new inflammatory TED symptoms. Participants could not have had prior orbital irradiation, orbital decompression surgery or strabismus surgery. The mean duration of disease for TEPEZZA and placebo patients was 5.1 years (SD 1.88) and 5.4 years (SD 1.61), respectively. The mean CAS for TEPEZZA and placebo patients was 0.3 (SD 0.47) and 0.5 (SD 0.51), respectively.

About Thyroid Eye Disease (TED)

TED is a serious, progressive, debilitating and potentially vision-threatening rare autoimmune disease.[1] TED often occurs in people living with Graves' disease, but 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, including blindness. Signs and symptoms of TED may include dry eyes and grittiness; redness, swelling and excessive tearing; eyelid retraction; proptosis; pressure and/or pain behind the eyes; and diplopia.[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 controlled with medications for glycemic control, if necessary. Assess patients for elevated blood glucose and symptoms of hyperglycemia prior to infusion and continue to monitor while on treatment with TEPEZZA. Ensure patients with hyperglycemia or preexisting diabetes are under appropriate glycemic control before and while 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, dry skin, weight decreased, nail disorders, and menstrual disorders.

Please see Full Prescribing Information or visit TEPEZZAhcp.com for more information.

About Horizon

Horizon is focused on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory 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, 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 benefits of TEPEZZA as a treatment of chronic/low CAS 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 regarding whether additional clinical trial results or data analyses will be consistent with preliminary results or results of other trials or Horizon's expectations, the risks associated with adoption of novel medicines and factors that may change physician treatment strategies, 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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