New Data from Teprotumumab Phase 3 OPTIC Study Shows Significantly Reduced Double Vision and Improved Quality of Life for People with Active Thyroid Eye Disease

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DUBLIN--(BUSINESS WIRE)--Oct. 11, 2019-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced new data from the Phase 3 OPTIC confirmatory clinical trial showing that teprotumumab provided significant benefit on several devastating effects of active thyroid eye disease (TED) compared with placebo, including diplopia (double vision), quality of life (QoL) and clinical activity score (CAS). These data were presented during the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) 50th Anniversary 2019 Fall Scientific Symposium, and build upon data presented earlier this year that demonstrated the significant benefit of teprotumumab on proptosis (bulging eyes).

Teprotumumab is an investigational medicine for the treatment of active TED and is currently under review by the U.S. Food and Drug Administration (FDA). The teprotumumab Biologics License Application (BLA) was recently granted Priority Review by the FDA and if approved, teprotumumab would be the first FDA-approved medicine for the treatment of active TED. The Prescription Drug User Fee Act (PDUFA) goal date is March 8, 2020.

“Thyroid eye disease commonly causes a variety of vision impairments, with double vision reported in about half of all people living with the disease, and almost 70 percent of patients enrolled in the OPTIC study,” said Raymond Douglas, M.D., Ph.D., of Cedars Sinai Medical Center and lead investigator of the OPTIC study. “People suffering from double vision often lose the ability to perform daily tasks, like reading and driving, impacting their ability to work and causing depression. The results of this study are very encouraging, showing that 68 percent of patients had an improvement of at least one grade in double vision, and also improved on other measures including quality of life and CAS score.”

Previously presented primary endpoint data from OPTIC (Treatment of Graves’ **O**rbitopathy (Thyroid Eye Disease) to Reduce **P**roptosis with **T**eprotumumab **I**nfusions in a Randomized, Placebo-Controlled, **C**linical Study) showed that significantly more patients treated with teprotumumab had a meaningful improvement in proptosis, the primary study endpoint, as compared with placebo (82.9% of teprotumumab patients compared to 9.5% of placebo patients; p<0.001).

The following new data on three secondary endpoints were presented at ASOPRS:

- Diplopia: At Week 24, 68% of patients receiving teprotumumab had an improvement from baseline of at least one grade in diplopia, compared to 29% of patients receiving placebo (p=0.001). This endpoint measured the percentage of patients who reported at least some diplopia at baseline in the study eye and who had a reduction of ≥ 1 grade with no corresponding deterioration (≥ 1 grade worsening) in the fellow eye at Week 24.
- Quality of Life: Patients receiving teprotumumab had a mean change of 13.79 on the Graves' Ophthalmopathy Quality of Life (GO-QoL) scale compared with a change of 4.43 for patients receiving placebo (p<0.001). These scores indicate a statistical and clinically meaningful improvement over placebo in these QoL measures. The GO-QoL scale consists of two subscales to evaluate the quality of life of TED (Graves’ Ophthalmology) patients, including impacts on visual function and self-assessment of appearance. A change of 6 points is considered clinically significant.[1]
- CAS Score: At Week 24, more patients achieved a CAS value of 0 or 1 with teprotumumab treatment (59% vs 21% of placebo participants) (p<0.001). CAS is a scale used to assess the disease activity of TED, and measures the degree of inflammation, including pain, swelling and redness. The CAS scale ranges from 0 to 7, with a score of 0 representing no swelling or activity.[2]
- Significant improvement in other secondary endpoints, including average change in proptosis and overall response rate over the 24-week treatment period, were presented during the 2019 American Association of Clinical Endocrinologists (AACE) Annual Scientific & Clinical Congress.

As previously reported, teprotumumab was generally well tolerated; the majority of adverse events were mild or moderate, manageable and resolved during or after treatment. The earlier Phase 2 study results were published in *The New England Journal of Medicine* in May 2017.

“The Phase 3 data further illustrate the potential for teprotumumab to benefit the most prominent and challenging characteristics of active thyroid eye disease, most notably the vision impairment and subsequent detrimental effect on daily life,” said Shao-Lee Lin, M.D., Ph.D., executive vice president, head of research and development and chief scientific officer, Horizon. “With the findings of our Phase 3 clinical trial demonstrating benefit across all of the ranked endpoints studied, we are one step closer to addressing the unmet need in the TED community for an FDA-approved medicine.”

About Thyroid Eye Disease

Thyroid eye disease (TED) is a serious, progressive and vision-threatening autoimmune disease with a limited window of activity that can last up to three years.[3,4,5] 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 orbit.[6,7] This leads to a cascade of negative effects, which may cause long-term, irreversible damage. Active TED lasts for up to three years and is characterized by inflammation and tissue expansion behind the

eye.[3,8] 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.[4,9] TED has only been shown to respond to pharmacotherapy while the disease is active and inflammation is ongoing.[10] Currently, patients must live with active TED until the disease becomes inactive – often left with permanent and vision-impairing consequences.[3,8]

About Teprotumumab

Teprotumumab is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the insulin-like growth factor 1 receptor (IGF-1R). Teprotumumab has received Priority Review, Orphan Drug, Fast Track, and Breakthrough Therapy designations from the FDA. The clinical development program for teprotumumab in the treatment of TED includes positive results from the Phase 3 OPTIC confirmatory clinical trial as well as positive Phase 2 results, which were published in The New England Journal of Medicine. The OPTIC trial was conducted at leading centers in the U.S., Germany and Italy, with co-principal investigators Raymond Douglas, M.D., Ph.D., Cedars-Sinai Medical Center; and George Kahaly, M.D., Ph.D., Johannes Gutenberg University Medical Center. Horizon is also conducting the OPTIC-X extension trial to gather further insight into the long-term efficacy and safety of teprotumumab.

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 potential availability and benefits of teprotumumab to patients. 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 the actual timing and process of review of the teprotumumab BLA and whether the BLA is ultimately approved, 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

1. Terwee CB. *Clinical Endocrinology* 2001; 54: 391-398.
2. Wiersinga WM, Perros P, Kahaly GJ, et al. Clinical assessment of patients with Graves’ orbitopathy: the European Group on Graves’ Orbitopathy recommendations to generalists, specialists and clinical researchers. *Eur J Endocrinol* 2006; 155: 387-9.
3. Graves’ Ophthalmopathy: VISA versus EUGOGO Classification, Assessment, and Management. *Journal of Ophthalmology.* 2015. https://www.hindawi.com/journals/joph/2015/249125/cta/. Accessed Feb 22, 2019.
4. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy. *European Thyroid Journal.*2 March 2016. https://www.ncbi.nlm.nih.gov/pubmed/27099835. Accessed Feb 22, 2019.
5. Shan SJ, Douglas RS. The Pathophysiology of Thyroid Eye Disease. *Journal of Neuro-Ophthalmology*. 2014; 34: 177-185.
6. Graves' Ophthalmopathy. *The New England Journal of Medicine.* 25 February 2010. https://www.nejm.org/doi/full/10.1056/NEJMra0905750. Accessed Feb 22, 2019.
7. Igs from patients with Graves' disease induce the expression of T cell chemoattractants in their fibroblasts. *The Journal of Immunology.* 15 January 2002. https://www.ncbi.nlm.nih.gov/pubmed/11777993. Accessed Feb 22, 2019.
8. Update on thyroid eye disease and management. *Clinical Ophthalmology.* 19 October 2009. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2770865/. Accessed Feb 22, 2019.
9. Clinical features of dysthyroid optic neuropathy: a European Group on Graves' Orbitopathy (EUGOGO) survey. *British Journal of Ophthalmology.* 11 October 2006. https://www.ncbi.nlm.nih.gov/pubmed/17035276. Accessed Feb 22, 2019.
10. Mamoojee Y, Pearce SHS. Natural History. In: Wiersinga WM, Kahaly GJ (eds): *Graves’ Orbitopathy: A Multidisciplinary Approach – Questions and Answers.* Basel, Karger. 2017:93-104.

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