



Horizon Therapeutics plc Submits Teprotumumab Biologics License Application (BLA) for the Treatment of Active Thyroid Eye Disease (TED)

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DUBLIN--(BUSINESS WIRE)--Jul. 10, 2019-- Horizon Therapeutics plc (Nasdaq: HZNP) announced today that it has submitted a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for its investigational medicine teprotumumab for the treatment of active thyroid eye disease (TED). Teprotumumab has Breakthrough Therapy, Orphan Drug and Fast Track designations from the FDA. Horizon requested priority review for the application, which, if granted, could result in a six-month review process. The FDA has a 60-day filing review period to determine whether the BLA is complete and acceptable for filing.

"There is a major unmet need for an effective therapy for active thyroid eye disease, a painful and sight-threatening disease with no FDA-approved treatment options," said Timothy Walbert, chairman, president and chief executive officer, Horizon. "Our BLA submission is an important step toward our goal of making teprotumumab available as soon as possible for patients with this debilitating disease."

The teprotumumab BLA submission includes results from the Phase 3 confirmatory clinical trial, called OPTIC (Treatment of Graves' Orbitopathy (Thyroid Eye Disease) to Reduce Proptosis with Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study), as well as positive Phase 2 results. Results from OPTIC were [presented](#) at the 2019 American Association of Clinical Endocrinologists (AACE) Scientific and Clinical Congress. The study met its primary endpoint, showing that significantly more patients treated with teprotumumab compared with placebo had a meaningful improvement in proptosis, or bulging of the eye: 82.9 percent of teprotumumab patients compared to 9.5 percent of placebo patients achieved the primary endpoint of a 2 mm or more reduction in proptosis ($p < 0.001$). All secondary endpoints were also met. Teprotumumab was generally well tolerated; the majority of adverse events were mild or moderate, manageable and resolved during or after treatment. The confirmatory OPTIC study was initiated after clinically meaningful and highly statistically significant results from a Phase 2 study, published in *The New England Journal of Medicine* on May 4, 2017. Teprotumumab is an investigational medicine and its safety and efficacy have not been established.

About Thyroid Eye Disease (TED)

TED is a progressive and debilitating autoimmune disease with a limited window of active disease during which it may respond to medical intervention.^{1,2} 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 signalling complex on cells within the orbit.^{3,4} 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.^{5,1} 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.^{2,6} Currently, patients must suffer through Active TED until the disease becomes inactive – often left with permanent and sight-impairing consequences.^{5,1} People living with TED often experience long-term functional, psychological and economic burdens, including inability to work and perform activities of daily living.^{7,8} There are currently no FDA-approved treatments for Active TED.

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 Breakthrough Therapy, Orphan Drug and Fast Track 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., 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 FDA's review of the teprotumumab BLA, potential regulatory approval of teprotumumab and the potential for teprotumumab as a treatment for TED. 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. These forward-looking statements are based on management's 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, but are not limited to, risks regarding whether the FDA will accept the planned BLA for filing or approve the BLA, whether the FDA grants priority review for the BLA, risks associated with clinical development of medicine candidates and whether Horizon will be able to successfully commercialize teprotumumab, if

approved. For a further description of these and other risks facing Horizon, please see the risk factors 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 undertakes no obligation to update or revise these statements, except as may be required by law.

References

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