New Data Suggest UPLIZNA® (inebilizumab-cdon) for the Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD) Did Not Increase the Risk of COVID-19 Infection or Reduce Antibody Levels From Childhood Vaccines

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-- Analyses suggest the B-cell-depleting mechanism of UPLIZNA did not interfere with important immune activity, including COVID-19 infection defenses and antibody levels from childhood vaccines --

DUBLIN--(BUSINESS WIRE)--Feb. 23, 2023-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced new data from two post-hoc analyses of the N-MOmentum clinical trial of UPLIZNA for the treatment of neuromyelitis optica spectrum disorder (NMOSD) will be presented at the eighth annual Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum, February 23-25, 2023, in San Diego. These data suggest UPLIZNA does not increase susceptibility to COVID infection or deplete childhood vaccine-generated antibodies. UPLIZNA is the first and only B-cell-depleting monotherapy approved by the U.S. Food and Drug Administration and the European Commission for the treatment of NMOSD in adults who are anti-aquaporin-4 immunoglobulin G seropositive (AQP4-IgG+).

“UPLIZNA prevents NMOSD attacks by targeting CD19-expressing B cells that are a key driver of NMOSD activity,” said Bruce Cree, M.D., Ph.D., MAS, study author and professor of Clinical Neurology at the University of California San Francisco Weill Institute for Neurosciences. “Through ongoing studies and clinical use, we are learning that UPLIZNA’s impact on NMOSD activity is very focused and may not interfere with certain other immune responses. Patients treated with UPLIZNA appear to not be more susceptibile to COVID-19 infections or to develop waning immunity from prior vaccinations due to treatment.”

Low Rate of COVID Infections Reported in UPLIZNA-Treated Patients

This analysis sought to evaluate any correlation between UPLIZNA treatment and COVID infection risk and outcomes. Reports of COVID infections were analyzed for 182 participants who received UPLIZNA during the Phase 3 pivotal trial (March-November 2020) and in the post-approval U.S. safety database (data cutoff July 31, 2022).

In total, the analysis found a low incidence rate of infections (0.024 events per patient year) among UPLIZNA-treated patients. A total of 17 confirmed COVID infections were reported (two infections before November 2020, prior to the availability of COVID vaccines, and 15 additional infections as of July 31, 2022). Ten of these events were reported as serious, though vaccine status was not known. Of the 10 patients with known outcomes, six were reported as “recovered/resolved,” two as not recovered/resolved and two patients died. Of the two fatalities, one was unvaccinated; the other had an unknown vaccination status and a history of deep vein thrombosis that was complicated by a pulmonary embolism.

Long-term UPLIZNA Treatment Did Not Affect Vaccine-Generated Antibodies in NMOSD Patients

This analysis aimed to evaluate whether long-term B-cell depletion in patients being treated with UPLIZNA affects antibody levels from childhood vaccinations against measles, mumps, rubella, varicella-zoster and tetanus. Assay assessments were conducted to measure antibody titers associated with each vaccine at week 156 of the N-MOmentum trial, comparing the change from baseline among UPLIZNA-treated versus placebo-treated participants. Overall, vaccine titers showed no meaningful reduction after 3.5 years of treatment with UPLIZNA.

“The N-MOmentum trial has provided a rich body of data that we are mining to better understand the mechanisms of UPLIZNA and its impact among people with NMOSD beyond protection against attacks,” said Kristina Patterson, M.D., PhD, medical director, neuroimmunology, Horizon. “The results of these analyses provide further support that UPLIZNA is an effective long-term treatment for NMOSD with a favorable safety profile.”

About Neuromyelitis Optica Spectrum Disorder (NMOSD)

NMOSD is a unifying term for neuromyelitis optica (NMO) and related syndromes. NMOSD is a rare, severe, relapsing, neuroinflammatory autoimmune disease that attacks the optic nerve, spinal cord, brain and brain stem.[1,2] Approximately 80% of all patients with NMOSD test positive for anti-AQP4 antibodies.[3] AQP4-IgG binds primarily to astrocytes in the central nervous system and triggers an escalating immune response that results in lesion formation and astrocyte death.[4]

Anti-AQP4 autoantibodies are produced by plasmablasts and some plasma cells. These B-cell populations are central to NMOSD disease pathogenesis, and a large proportion of these cells express CD19.[5] Depletion of these CD19+ B-cells is thought to remove an important contributor to inflammation, lesion formation and astrocyte damage. Clinically, this damage presents as an NMOSD attack, which can involve the optic nerve, spinal cord and brain.[4,6] Loss of vision, paralysis, loss of sensation, bladder and bowel dysfunction, nerve pain and respiratory failure can all be manifestations of the disease.[7] Each NMOSD attack can lead to further cumulative damage and disability.[8,9] NMOSD occurs more commonly in women and may be more common in individuals of African and Asian descent.[10,11]

About UPLIZNA

INDICATION

UPLIZNA is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

IMPORTANT SAFETY INFORMATION

UPLIZNA is contraindicated in patients with:

- A history of life-threatening infusion reaction to UPLIZNA
- Active hepatitis B infection
- Active or untreated latent tuberculosis

WARNINGS AND PRECAUTIONS

Infusion Reactions: UPLIZNA can cause infusion reactions, which can include headache, nausea, somnolence, dyspnea, fever, myalgia, rash or other symptoms. Infusion reactions were most common with the first infusion but were also observed during subsequent infusions. Administer pre-medication with a corticosteroid, an antihistamine and an anti-pyretic.

Infections: The most common infections reported by UPLIZNA-treated patients in the randomized and open-label periods included urinary tract infection (20%), nasopharyngitis (13%), upper respiratory tract infection (8%) and influenza (7%). Delay UPLIZNA administration in patients with an active infection until the infection is resolved.

Increased immunosuppressive effects are possible if combining UPLIZNA with another immunosuppressive therapy.

The risk of Hepatitis B Virus (HBV) reactivation has been observed with other B-cell-depleting antibodies. Perform HBV screening in all patients before initiation of treatment with UPLIZNA. Do not administer to patients with active hepatitis.

Although no confirmed cases of Progressive Multifocal Leukoencephalopathy (PML) were identified in UPLIZNA clinical trials, JC virus infection resulting in PML has been observed in patients treated with other B-cell-depleting antibodies and other therapies that affect immune competence. At the first sign or symptom suggestive of PML, withhold UPLIZNA and perform an appropriate diagnostic evaluation.

Patients should be evaluated for tuberculosis risk factors and tested for latent infection prior to initiating UPLIZNA.

Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B-cell repletion.

Reduction in Immunoglobulins: There may be a progressive and prolonged hypogammaglobulinemia or decline in the levels of total and individual immunoglobulins such as immunoglobulins G and M (IgG and IgM) with continued UPLIZNA treatment. Monitor the level of immunoglobulins at the beginning, during, and after discontinuation of treatment with UPLIZNA until B-cell repletion especially in patients with opportunistic or recurrent infections.

Fetal Risk: May cause fetal harm based on animal data. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping UPLIZNA.

Adverse Reactions: The most common adverse reactions (at least 10% of patients treated with UPLIZNA and greater than placebo) were urinary tract infection and arthralgia.

For additional information on UPLIZNA, please see the Full Prescribing Information at www.UPLIZNA.com.

About Horizon

Horizon is a global biotechnology company 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 potential benefits of UPLIZNA and Horizon's research and development plans. 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 future results of clinical trials will be consistent with preliminary results or results of prior trials or other data or Horizon's expectations. 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.

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