New Analysis Published in Multiple Sclerosis and Related Disorders Supports the Efficacy of UPLIZNA® (inebilizumab-cdon) in Patients Previously Treated with Rituximab for Neuromyelitis Optica Spectrum Disorder (NMOSD)

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-- Post hoc analysis of UPLIZNA Phase 2/3 trial shows all seven patients who had attacks while receiving rituximab were attack-free after switching to UPLIZNA --

DUBLIN--(BUSINESS WIRE)--Nov. 22, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced that a new post hoc analysis of the UPLIZNA N-MOmentum Phase 2/3 pivotal trial has been published in *Multiple Sclerosis and Related Disorders* showing that prior rituximab exposure did not impact the efficacy of UPLIZNA, and that UPLIZNA demonstrated comparable efficacy to trial participants without prior exposure to rituximab.

UPLIZNA is the first and only B-cell-depleting humanized monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) for the treatment of NMOSD in adults who are anti-aquaporin-4 (AQP4) antibody positive. UPLIZNA is a next-generation B-cell-depleting therapy engineered for optimized efficacy and tolerability. UPLIZNA specifically targets and depletes CD19-expressing B cells, including plasmablasts and some plasma cells not targeted by anti-CD20 therapies like rituximab. Rituximab is not approved by the FDA for the treatment of NMOSD.

This analysis assessed the efficacy and safety of UPLIZNA among participants who were previously treated with rituximab to determine any impact of prior treatment on rates of adjudicated attacks, secondary efficacy outcomes and treatment-emergent adverse events. Of the 17 participants who had previously been treated with rituximab, 13 were randomly assigned to the UPLIZNA treatment group. Notably, all seven participants who had pre-study attacks despite rituximab use (annualized attack rate, 0.78 attacks per person year) did not experience any attacks after being treated with UPLIZNA.

“It is encouraging to see that in this analysis, none of the seven patients who experienced breakthrough attacks while previously being treated with rituximab went on to experience an attack while taking UPLIZNA,” said Eoin P. Flanagan, M.B., B.Ch., a neurology specialist at the Mayo Clinic and study author. “Although UPLIZNA and rituximab both target B cells, UPLIZNA targets a broader range of B cells, and may explain why patients in the study who had attacks while being treated with rituximab did not experience attacks with UPLIZNA.”

Key analysis findings:

- 92% of participants previously treated with rituximab did not experience an NMOSD attack while being treated with UPLIZNA during the randomized-controlled period (RCP) of N-MOmentum (hazard ratio vs all placebo, 0.16; 95% confidence interval: 0.02-1.20) and remained attack-free through the open-label extension period (OLP).
- Annualized attack rate reduced to 0.08 attacks per person year after the first administration of UPLIZNA, similar to recipients without prior rituximab exposure (0.10 attacks per person year).
- Two participants previously treated with rituximab each experienced an attack during the OLP, both of whom originally received placebo during the RCP.
- Two participants with prior rituximab use experienced serious treatment-emergent adverse events related to UPLIZNA, and three experienced serious or grade ≥3 infections.
- UPLIZNA had a similar safety profile in participants with and without prior rituximab use.

“Physicians who are considering transitioning their patients from rituximab to UPLIZNA are eager for evidence that this can be done safely and effectively,” said Kristina Patterson, M.D., Ph.D., medical director, neuroimmunology, Horizon. “This analysis may suggest that appropriate patients can successfully transition from rituximab to UPLIZNA, which is particularly important for physicians who have been hesitant to transition patients to a different medicine because they don’t want to trigger an attack.”

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 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 descents.[10,11]

About UPLIZNA

INDICATION

UPLIZNA (inebilizumab-cdon) 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 Full Prescribing 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, 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 UPLIZNA in treating NMOSD patients that have previously been treated with rituximab. 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 additional data from clinical trials or other analyses will be consistent with prior 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.

References

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