New Data Reinforce the Relationship Between B-Cell Depletion and Improved Outcomes in People Receiving UPLIZNA® (inebilizumab-cdon) for Neuromyelitis Optica Spectrum Disorder (NMOSD)

October 13, 2021

-- Findings presented at ECTRIMS 2021 suggest that deep, persistent B-cell depletion is linked to reduced disease activity --

DUBLIN--(BUSINESS WIRE)--Oct. 13, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced results from a new analysis of the UPLIZNA pivotal Phase 2/3 N-MOmentum trial indicating a correlation between the depth of B-cell depletion and improved NMOSD patient outcomes. The data are being presented at the virtual 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS 2021). UPLIZNA is the first and only FDA-approved anti-CD19 B-cell-depleting humanized monoclonal antibody for the treatment of adult patients with anti-aquaporin-4 (AQP4) antibody positive NMOSD.

“This analysis provides additional evidence that B cells play a central role in NMOSD, and that there is a link between the depth of B cell depletion in the blood and long-term clinical outcomes,” said Jeffrey Bennett, M.D., Ph.D., University of Colorado and study author. “We found that B-cell levels at the end of the 28-week randomized, placebo-controlled period of the N-MOmentum trial were predictive of stable and deep B-cell depletion continuing through long-term exposure.”

The N-MOmentum trial included a randomized-controlled period (RCP) of up to 28 weeks, followed by an optional open-label period (OLP) of at least two years. During the trial, B-cell counts were determined using high-resolution flow cytometry (captured as cells/µL). Disease activity was measured using annualized attack rate (AAR) and the number of new or enlarging T2 lesions in the brain or spine.

Key analysis findings include (P028):

- All participants had B-cell reductions at one week from first treatment.
- At Week 4 of the RCP, median (interquartile range [IQR]) B-cell counts were 2.5 (1.0–7.6) cells/µL in the inebilizumab group and 112.3 (96.3–176.9) cells/µL in the placebo group.
- At Week 156 of the OLP, median (IQR) B-cell count was 0.33 (< LLoQ–1.0) cells/µL with inebilizumab.
- UPLIZNA provided sustained B-cell depletion after 2.5 years and decreased NMOSD activity in treated patients, with a 97% reduction in AAR and a 73% reduction in new/enlarging lesions when compared to the placebo group.
- Participants with B-cell counts ≤ 4 cells/µL had persistently deeper B-cell depletion compared with those with B-cell counts > 4 cells/µL
- While all participants saw significant treatment effect, those whose B-cell counts were ≤ 4 cells/µL (n=139/200) at Week 28 had reduced rates of AAR (rate ratio 0.4) and new/enlarging lesions (0.36) versus those with B-cell counts > 4 cells/µL.

“These data contribute to our mechanistic understanding of NMOSD as a B-cell-mediated disease and provide greater evidence that UPLIZNA is working directly against those underlying disease mechanisms known to have the greatest impact on patient outcomes,” said Quinn Dinh, M.D., vice president, international medical affairs and pipeline launch strategy for Horizon. “Our ongoing research efforts in this area aim to improve care for patients today while also preventing the damage of NMOSD over time.”

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 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 Full Prescribing Information at **www.UPLIZNA.com**.

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 and Horizon's plans with respect to future research. 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 data analyses or clinical evidence will be consistent with existing data from the Phase 2/3 N-MOmentum clinical trial 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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Source: Horizon Therapeutics plc