Horizon Therapeutics plc Announces Data Showing UPLIZNA® (inebilizumab-cdon) Also Produces Rapid and Sustained B-Cell Depletion in African Americans with Neuromyelitis Optica Spectrum Disorder (NMOSD)

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-- Analysis of 20 African Americans from the pivotal study presented at the 15th World Congress on Controversies in Neurology --

DUBLIN--(BUSINESS WIRE)--Sep. 23, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced results of a retrospective analysis of the pivotal Phase 2/3 N-MOmentum clinical trial, indicating UPLIZNA may provide durable efficacy and a favorable safety profile for African Americans with NMOSD. These data were presented during the 15th World Congress on Controversies in Neurology (CONy Virtual), Sept. 23-26, 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.

"Studies have shown that African Americans diagnosed with NMOSD often have a distinct experience managing this disease, including an earlier age of onset and more severe relapses compared with Caucasians, as well as different responses to targeted therapeutics," said Evanthia Bernitsas, M.D., Department of Neurology at Wayne State University School of Medicine and lead study author. "This analysis provides useful information about how African Americans may benefit from UPLIZNA's CD19 B-cell depleting mechanism to help reduce the incidence of acute attacks."

N-MOmentum consisted of a 28-week randomized controlled period (RCP), in which study participants received UPLIZNA or placebo, followed by an optional open-label period (OLP) during which all participants received UPLIZNA for at least two years. This analysis represents the experience of 20 African Americans who participated in the RCP (15 received UPLIZNA, five received placebo) and the OLP (20 received UPLIZNA).

Key analysis findings (P-045):

- Among African American participants who received UPLIZNA during the RCP and/or OLP, three of 19 had attacks 18, 29 and 104 days after their first UPLIZNA dose
- Annualized attack rate (AAR) for African Americans was 0.06 compared with 0.09 in the overall group with any UPLIZNA exposure
    - Median AAR in the African American group in the two years before enrollment was 1.38
- In African American participants, UPLIZNA produced rapid and sustained B-cell depletion, consistent with other N-MOmentum trial participants
- During the RCP, African American participants in the UPLIZNA group developed fewer infections (26.7%) than those in the placebo group (60%), although one participant in the treatment arm developed cytopenia that resolved in four weeks

"NMOSD is a complex and often unpredictable disease that can be challenging to manage, especially in subpopulations that are disproportionally and more severely affected," said Quinn Dinh, M.D., vice president, international medical affairs and pipeline launch strategy, Horizon. "Ongoing research with UPLIZNA can help inform treatment decisions in the clinic as physicians work to reduce the debilitating effects of this disease for their patients."

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 and spinal cord, as well as the brain and brain stem.[1,2] Approximately 80 percent of all patients with NMOSD test positive for anti-AQP4 antibodies.[3] AQP4-IgG bind primarily to astrocytes in the central nervous system and trigger 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. 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.[4,5] Loss of vision, paralysis, loss of sensation, bladder and bowel dysfunction, nerve pain, and respiratory failure can all be manifestations of the disease.[6] Each NMOSD attack can lead to further cumulative damage and disability.[7,8] NMOSD occurs more commonly in women and may be more common in individuals of African and Asian descent.[9,10]

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 **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 African Americans with NMOSD. 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 the sub-analysis 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.

References

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