New Analysis Finds UPLIZNA® (inebilizumab-cdon) Effective for People with Newly-Presenting Neuromyelitis Optica Spectrum Disorder (NMOSD)

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-- Separate analysis being presented at the AAN Annual Meeting shows UPLIZNA reduced pain associated with NMOSD over three years --

DUBLIN--(BUSINESS WIRE)--Mar. 31, 2022-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced the presentation of a post-hoc analysis from the N-MOmentum Phase 3 pivotal trial of UPLIZNA, showing that the medicine was safe and effective in NMOSD patients who were treated with UPLIZNA after having only one attack. These data are being presented during a poster session at the American Academy of Neurology (AAN) 2022 Annual Meeting in Seattle April 2-7 and virtually April 24-26, 2022. UPLIZNA is the first and only FDA-approved CD19+ B-cell-depleting monotherapy proven to reduce the risk of attacks in adults with NMOSD who are anti-aquaporin-4 (AQP4) antibody positive.

This analysis aimed to clarify how prior history of attacks might affect the response to UPLIZNA by evaluating the medicine's effect among individuals with newly-presenting NMOSD who were enrolled in the 28-week randomized, placebo-controlled period of the trial after their first attack compared to individuals with a history of two or more attacks.

Key analysis findings:

- Of the 37 study participants who had experienced only one attack before joining the study, 4.2% (1/24) of those who were treated with UPLIZNA experienced an attack compared to 23.1% (3/13) of those who were treated with placebo.
- Of the 176 study participants who had experienced more than one attack before joining the study, 12.4% (17/137) of those who were treated with UPLIZNA experienced an attack compared to 48.7% (19/39) of those who were treated with placebo.
- No significant differences in attacks or Expanded Disability Status Scale (EDSS) worsening were found between participants with one pre-study attack and those with two or more pre-study attacks.
- Treatment-emergent adverse events among those enrolled after their first attack were consistent with pivotal trial outcomes.

"These data are important because physicians see NMOSD patients at varying stages of their illness and it is helpful to understand how UPLIZNA might benefit patients at disease onset as well as those who have had more than one attack," said Bruce Cree, M.D., Ph.D., MAS, professor of clinical neurology at the University of California San Francisco Weill Institute for Neurosciences and primary study investigator. "In this sub-analysis of the N-MOmentum pivotal trial, which is the largest clinical trial conducted in NMOSD, UPLIZNA shows comparable efficacy in patients who had only one attack to those who have had two or more attacks. With this information, physicians can feel confident that patients may stop experiencing attacks after being treated with UPLIZNA regardless of how many previous attacks they experienced."

In addition, an analysis from the N-MOmentum trial will be presented showing long-term treatment with UPLIZNA improved pain outcomes in patients with NMOSD. Pain is a common, debilitating symptom of NMOSD that can dramatically impact daily activities. Previously presented data demonstrated improvements in pain scores after treatment with UPLIZNA. The new analysis builds on those findings by showing a durable, long-term benefit in managing pain, with year-over-year improvements from baseline (average of 6.57 points after one year, 7.08 after two years and 7.96 after three years) as measured by the 36-item short-form survey body pain subscore (SF36-BPS).

"These rigorous analyses from the UPLIZNA pivotal trial provide compelling insights into the real value that UPLIZNA may provide as a novel option for people living with NMOSD," said Kristina Patterson, M.D., Ph.D., medical director, neuroimmunology, Horizon. "As physicians gain more experience with UPLIZNA, they can see how these clinical data translate into outcomes within their practices and potentially help more patients gain greater control over this challenging disease."

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 percent 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 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, 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 patients 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 analyses from the 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

1. Ajmera MR, Boscoe A, Mauskopf J, Candrilli SD, Levy M. Evaluation of comorbidities and health care resource use among patients with highly active neuromyelitis optica. *J Neurol Sci*. 2018;384:96-103.
2. What is NMO? Guthyjacksonfoundation.org. www.guthyjacksonfoundation.org/neuromyelitis-optica-nmo/ Accessed April 15, 2021.

3. Layman's Guide to NMO. Sumairafoundation.org. https://www.sumairafoundation.org/laymans-guide-to-nmo/ Accessed April 25, 2021.
4. Liu Y, et al. A tract-based diffusion study of cerebral white matter in neuromyelitis optica reveals widespread pathological alterations. *Mult Scler*. 2011;18(7):1013-1021.
5. Chihara N, et al. Interleukin 6 signaling promotes anti-aquaporin-4 autoantibody production from plasmablasts in neuromyelitis optica. *PNAS*. 2011;108(9):3701-3706.
6. Duan T, Smith AJ, Verkamn AS. Complement-independent bystander injury in AQP4-IgG seropositive neuromyelitis optica produced by antibody dependent cellular cytotoxicity. *Acta Neuropathologica Comm*. 2019;7(112).
7. Beekman J, et al. Neuromyelitis optica spectrum disorder: patient experience and quality of life. *Neural Neuroimmunol Neuroinflamm*. 2019;6(4):e580.
8. Kimbrough DJ, et al. Treatment of neuromyelitis optica: review and recommendations. *Mult Scler Relat Disord*. 2012;1(4):180-187.
9. Baranello RJ, Avasarala, JR. Neuromyelitis optica spectrum disorders with and without aquaporin 4 antibody: Characterization, differential diagnosis, and recent advances. *J Neuro Ther.* 2015;1(1):9-14.
10. Wingerchuk DM. Neuromyelitis optica: effect of gender. *J Neurol Sci.* 2009;286(1-2):18-23.
11. Flanagan EP, et al. Epidemiology of aquaporin-4 autoimmunity and neuromyelitis optica spectrum. *Ann Neurol.* 2016;79(5):775-783.

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