New Analysis Published in Multiple Sclerosis Journal Assesses Long-Term Use of UPLIZNA® (inebilizumab-cdon) for the Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD)

October 4, 2021

-- Data show notable decline in disease-related attacks after the first year of treatment in patients receiving UPLIZNA for four or more years --

-- Consistent safety profile maintained throughout long-term study period with no treatment discontinuations --

DUBLIN--(BUSINESS WIRE)--Oct. 4, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced the publication of a post-hoc analysis from the N-MOmentum phase 2/3 pivotal trial of UPLIZNA, which highlights a sustained effect on attack risk with no new safety signals in people with NMOSD who received the treatment for four or more years. These data are published in the *Multiple Sclerosis Journal*.

NMOSD is a rare, severe autoimmune disease that attacks the optic nerve, spinal cord and brain stem. The attacks are often recurrent and can cause irreversible damage to the nerves, leading to cumulative visual and motor disabilities over time. 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 long-term study is important because NMOSD is a chronic disease that requires lifelong management. Physicians need to understand the implications of prolonged treatment,” 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. “It is highly encouraging to see that most patients in this study were attack-free after the first year of UPLIZNA treatment and that new safety concerns were not observed. The data demonstrate that long-term UPLIZNA use is associated with a reduced risk of NMOSD attacks – possibly due to the depth and extent of B-cell depletion with repeated doses.”

The post-hoc analysis represents the experience of 75 people with AQP4 antibody positive NMOSD who were treated with UPLIZNA for four or more years during the open-label extension period of the N-MOmentum trial.

Key study findings include the following:

- A total of 18 attacks occurred in 13 people, with an annualized attack rate of 0.052 attacks per person year.
- The small number of total attacks decreased significantly after the first year of treatment with UPLIZNA.
    - 67% of attacks occurred within the first year (12 attacks).
    - 92% of patients were attack-free in subsequent years (two attacks each during years two to four).
- The infection rate did not increase over time on treatment with UPLIZNA.
- UPLIZNA was generally well tolerated, with few treatment-related dose interruptions and no treatment discontinuations.

“NMOSD is a complex and often unpredictable B-cell-mediated disease that presents significant challenges to both patients and physicians,” said Kristina Patterson, M.D., Ph.D., medical director, neuroimmunology, Horizon. “With recent treatment advancements, the NMOSD community now has more options than ever before – including UPLIZNA, which is engineered for broad, deep and durable B-cell depletion. We are fully committed to increasing our understanding of this disease so we can continue to improve patient care.”

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, 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 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, the risks associated with clinical development and adoption of novel medicines and risks related to competition or other factors that may change physician treatment strategies. 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20211004005304/en/

Tina Ventura
Senior Vice President, Investor Relations
Investor-relations@horizontherapeutics.com

Ruth Venning
Executive Director, Investor Relations
Investor-relations@horizontherapeutics.com

U.S. Media Contact:
Rachel Vann
Director, Product Communications
media@horizontherapeutics.com

Ireland Media Contact:
Gordon MRM
Ray Gordon
ray@gordonmrm.ie

Source: Horizon Therapeutics plc