New Long-Term Data for UPLIZNA® (inebilizumab-cdon) in People Living with Neuromyelitis Optica Spectrum Disorder (NMOSD)

April 16, 2021

-- Presentation at American Academy of Neurology's 73rd Annual Meeting shows no new safety signals with prolonged use of UPLIZNA --

-- UPLIZNA continues to lower the rate of NMOSD attacks throughout the four-year open-label period (OLP) --

-- Results from NMOSD patient survey describe long and daunting journey to diagnosis --

DUBLIN--(BUSINESS WIRE)--Apr. 16, 2021-- Horizon Therapeutics plc (Nasdaq: HZNP) today announced new UPLIZNA (inebilizumab-cdon) data being presented at the American Academy of Neurology's 73rd Annual Meeting being held virtually April 17-22, 2021 (AAN 2021), including new, end-of-study data from the open-label extension period of the pivotal N-MOmentum trial in patients with NMOSD. 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.

"The goal of the open-label extension period was to better understand the long-term administration of UPLIZNA beyond the 28-week time frame that was originally studied in the randomized controlled period of the trial," 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. "These data are important because they provide further evidence that UPLIZNA can safely be used by NMOSD patients for an extended period of time, for at least four years, and that the medicine provides a sustained effect on attack risk."

Outcomes Maintained Throughout the Four-Year Open-Label Period

The N-MOmentum Phase 2/3 clinical trial consisted of a 28-week randomized controlled period (RCP), where study participants received UPLIZNA or placebo. Following the completion of this period, patients could enter into the OLP for at least two years, during which all patients (n=216) received UPLIZNA 300 mg every six months, with follow-up visits at Weeks 2, 4, 13, 26 and 39 of the OLP and every 26 weeks thereafter.

Key OLP findings include (P15.076)*:

- Long-term UPLIZNA treatment provided a sustained reduction in NMOSD attack risk from baseline, regardless of when treatment was initiated: 87.7 percent of patients who originally received UPLIZNA in the RCP (n=165) and 83.4 percent of patients who originally received placebo in the RCP (n=51) remained attack-free during the OLP for at least four years.
- The vast majority of attacks occurred in the first year of treatment.
- UPLIZNA treatment was associated with lesion reduction shown by MRI. The mean number of active lesions was similar during the OLP to the number observed in patients who received UPLIZNA during the RCP.

Key OLP safety findings include (P15.100)*:

- Treatment with UPLIZNA was generally well-tolerated for at least four years.
- No new safety signals were identified with prolonged UPLIZNA treatment and UPLIZNA-mediated B-cell depletion.
- Rates of infection or serious infection did not increase with prolonged UPLIZNA treatment.
- Levels of immunoglobins declined over time and continued to fall up to five years after the start of the OLP. No clear association between low IgG levels and severe infection can be established.
- Infusion-related reactions during the N-MOmentum trial were generally mild, with no unexpected safety concerns identified during continued dosing in the OLP (P15.211).

Data from the OLP were also recently presented at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) 2021 Forum. Of note, one poster featured data with UPLIZNA in NMOSD patients who had previous rituximab exposure. Seventeen subjects who enrolled in the N-MOmentum study had previous rituximab treatment. The annual relapse rate for those with prior rituximab exposure was .083 compared to an annual relapse rate of .102 for those without prior rituximab exposure.

"For people living with NMOSD, attacks can cause devastating and often permanent disability, including blindness and paralysis," said Quinn Dinh, vice president, medical affairs, Horizon. "Having a treatment that can be administered twice a year after the initial doses and that has supportive long-term data, is an important advancement for the NMOSD community."

A separate study presented at AAN (P2.017)* evaluated patient-reported pain scores for each of five body areas (eyes, arms, legs, upper back and lower back) in the previous 24 hours, every four weeks during the RCP of the N-MOmentum trial, as well as during NMOSD attacks. The study used the 11-point Pain Numeric Rating Scale (NRS-11), where 0 equals no pain and 10 equals the worst pain. Across the five body areas, patients in both groups reported episodic, rather than persistent pain during the RCP. Also in the RCP, fewer patients who received UPLIZNA (56 percent) than

placebo (77 percent) reported a ≥3-point worsening in NRS-11 score relative to baseline.

**Note: These abstracts only provide interim results, full posters provide end-of-study results.*

Patient Attitudes Towards NMOSD Diagnosis and Treatment

To improve understanding of NMOSD patients' experience throughout the course of their disease, a comprehensive survey was administered to 151 people living with NMOSD. The survey results demonstrate the importance of finding the right specialist who can identify appropriate screening tests that will lead to an earlier diagnosis and progression toward better patient outcomes.

Key findings include (P2.106):

- The average time to NMOSD diagnosis was 2.2 years, and over 10 years for some.
- Only 11 percent of survey participants were diagnosed with NMOSD when symptoms first appeared.
- 34 percent first shared their symptoms with an emergency room doctor and 34 percent first shared their symptoms with a primary care physician.
- Fear (57 percent) and frustration (40 percent) were the most-commonly reported emotions experienced during initial visits with a medical provider.

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 and brain stem.[1,3] Approximately 80 percent of all patients with NMOSD test positive for anti-AQP4 antibodies.[4]

B cells play a critical role in the pathogenesis of NMOSD. Depletion of CD19+ B cells has an overall impact on the ability of the immune system to trigger damage to the astrocytes, which are at the center of this disease. AQP4 autoantibodies are produced by plasmoblasts and plasma cells, and most are CD19+ B cells. AQP4-IgG bind primarily to astrocytes in the central nervous system and trigger an escalating immune response that results in severe damage to astrocytes and neurons. [5] Clinically, this damage presents as an NMOSD attack, which can involve the optic nerve, spinal cord and brain.[5,6] 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 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

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, but not limited to, statements related to the potential benefits of UPLIZNA and business and other statements that are not historical facts. These forward-looking statements are based on Horizon's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to Horizon's ability in increase adoption of UPLIZNA; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; risks relating to Horizon's ability to successfully implement its business strategies; risks in the ability to recruit, train and retain qualified personnel; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information.

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