UPLIZNA® (INEBILIZUMAB-CDON) IS NOW THE FIRST AND ONLY FDA-APPROVED TREATMENT FOR IGG4-RELATED DISEASE

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Breakthrough CD19+ B-Cell Targeted Therapy Delivered an 87% Reduction in the Risk of Flares Versus Placebo

UPLIZNA Shown to Deliver Corticosteroid-Free, Flare-Free, Complete Remission for Patients in the MITIGATE Trial

Advances Amgen's Leadership in CD19 Directed, B-Cell Depletion Therapies for Serious Autoimmune Diseases Including NMOSD, IgG4-RD and gMG

THOUSAND OAKS, Calif., April 3, 2025 /PRNewswire/ -- Amgen (NASDAQ:AMGN) announced today that the U.S. Food and Drug Administration (FDA) has approved UPLIZNA as the first and only treatment for adults living with Immunoglobulin G4-related disease (IgG4-RD). IgG4-RD is a chronic and debilitating immune-mediated inflammatory condition that can affect multiple organs. The FDA granted Breakthrough Therapy Designation to UPLIZNA for the treatment of IgG4-RD, recognizing the high unmet medical need in this serious condition and the medicine's potential to benefit patients.

"The FDA approval of UPLIZNA marks a significant turning point for IgG4-RD patients and physicians who now have a proven treatment that targets a key driver of the disease, reducing the risk of flares and reliance on harmful long-term steroid use," said Jay Bradner, M.D., executive vice president of Research and Development at Amgen. "We are proud to deliver a therapy that has the potential to significantly improve care for patients with IgG4-RD and remain encouraged by UPLIZNA's broader potential in other immune-mediated diseases, including neuromyelitis optica spectrum disorder and generalized myasthenia gravis. This approval underscores Amgen's ongoing commitment and leadership in developing innovative treatments targeting CD19+ B-cells across multiple therapeutic areas."

IgG4-RD can occur in multiple organs and lead to fibrosis and permanent organ damage.[1,2] Understanding how organ damage manifests is critically important to inform the timely diagnosis of IgG4-RD. The disease mimics other diseases due to the heterogeneous and unpredictable inflammatory flares that can occur.[3] Over time, IgG4-RD can affect virtually any organ system.[1]

"Targeting CD19+ B cells with UPLIZNA has proven to be a highly effective approach to help address the pathophysiology of IgG4-RD," said John Stone, M.D., M.P.H., principal investigator, and a professor of medicine at Harvard Medical School and the Edward A. Fox Chair in Medicine at the Massachusetts General Hospital. "The clinical community now has an FDA-approved therapeutic innovation for patients that targets underlying disease mechanisms and helps to control disease activity by reducing flares in IgG4-RD. Now, our work begins in raising awareness of this disease so that patients can access the right treatment as early as possible, avoiding a long and often harmful diagnostic journey."

The approval of UPLIZNA for IgG4-RD is supported by data from the MITIGATE trial, the first randomized, double-blind, placebo-controlled trial conducted in IgG4-RD.[1] This trial demonstrated the potential of UPLIZNA to decrease disease activity by reducing flares in patients, while maintaining its efficacy and established safety profile.[1]

This is the second approved indication for UPLIZNA, which was previously approved by the FDA for the treatment of adult patients with AQP4-IgG+ Neuromyelitis Optica Spectrum Disorder (NMOSD) in June 2020. The FDA also granted UPLIZNA Orphan Drug Designation for the treatment of generalized myasthenia gravis (gMG). Regulatory filing activities are underway for gMG with submission anticipated to be complete in H1 2025.

Amgen is committed to supporting patients with IgG4-RD and helping appropriate patients with access to UPLIZNA. Patients and caregivers who need support, tools or resources can contact Amgen By Your Side.

About the MITIGATE Trial
MITIGATE is a randomized, double-blind, placebo-controlled, parallel-group, multicenter trial designed to evaluate the efficacy and safety of UPLIZNA compared to placebo in reducing the risk of flares in adults with IgG4-RD.[1]

The primary endpoint was time to first treated and adjudicated IgG4-RD flare.[1] The three key secondary endpoints were annualized flare rate; flare-free, treatment-free complete remission; and flare-free, corticosteroid-free complete remission.[1] The MITIGATE trial also includes an optional three-year open-label treatment period and a safety follow-up period after UPLIZNA discontinuation of up to two years.

Key findings from the MITIGATE trial include (p values are formatted to align with New England Journal of Medicine standards):[1]

- An 87% reduction in the risk of IgG4-RD flare compared to placebo (Hazard Ratio 0.13, p<0.001) during the 52-week placebo-controlled period; 10.3% (7 of 68) of participants receiving UPLIZNA experienced a flare compared to 59.7% (40 of 67) of participants receiving placebo.
- A reduction in annualized flare rate for treated and adjudication committee-determined flares during the placebo-controlled period; 0.10 for participants receiving UPLIZNA compared to 0.71 for participants receiving placebo (p<0.001).
- 57.4% (39 of 68) of participants receiving UPLIZNA achieved flare-free, treatment-free, and complete remission at Week 52 compared to 22.4% (15 of 67) of participants receiving placebo (p<0.001).
- 58.8% (40 of 68) of participants receiving UPLIZNA achieved flare-free, corticosteroid-free, and complete remission at Week 52 compared to 22.4% (15 of 67) of participants receiving placebo (p<0.001).
- 89.7% (61 of 68) of UPLIZNA-treated patients required no glucocorticoid treatment for disease control during the placebo-controlled period, outside of the planned glucocorticoid tapering, compared to 37.3% (25 of 67) of patients on placebo.

- UPLIZNA-treated patients experienced a ten-fold reduction in mean total glucocorticoid use for disease control per patient relative to placebo (118 mg vs. 1385 mg, respectively) during the placebo-controlled period.

The most common adverse reactions in patients with IgG4-RD (at least 10% of patients treated with UPLIZNA and greater than placebo) were urinary tract infection (12%) and lymphopenia (19%).

About Immunoglobulin G4-related disease (IgG4-RD)
Immunoglobulin G4-related disease (IgG4-RD) is a chronic, systemic, immune-mediated, fibroinflammatory disease which can affect numerous and generally multiple organs of the body.[1] It is a progressive disease that can affect a variety of organ systems and often affects multiple organs over time. It is characterized by periods of remission and unpredictable disease flares.[4,5] IgG4-RD can cause permanent organ damage with or without the presence of symptoms.[2] Awareness of how organ damage manifests is critically important to inform the timely diagnosis of IgG4-RD. B cells are central to the pathogenesis of IgG4-RD.[1] In IgG4-RD, CD19-expressing (CD19+) B cells are thought to drive inflammatory and fibrotic processes and interact with other immune cells that contribute to disease activity.[1,2]

The prevalence is estimated at 20,000 people in the United States (5 in 100,000 worldwide), although the number of IgG4-RD patients is difficult to determine based on limited epidemiology data.[1,2] The typical age of onset of IgG4-RD is between 50 and 70 years old and, unlike many other immune-mediated diseases, IgG4-RD is more likely to occur in men than women.[4]

About UPLIZNA® (inebilizumab-cdon)
UPLIZNA is a humanized monoclonal antibody (mAb) that causes targeted and sustained depletion of key cells that contribute to underlying disease process (autoantibody-producing CD19+ B cells, including plasmablasts and some plasma cells). The precise mechanism by which UPLIZNA exerts its therapeutic effects in IgG4-RD is unknown. After two initial infusions, patients need one dose of UPLIZNA every six months.

UPLIZNA® (inebilizumab-cdon) U.S. INDICATION

INDICATIONS
UPLIZNA® (inebilizumab-cdon) is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive.

UPLIZNA® is indicated for the treatment of Immunoglobulin G4-related disease (IgG4-RD) in adult patients.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
UPLIZNA® (inebilizumab-cdon) is contraindicated in patients with a history of a life-threatening infusion reaction to UPLIZNA, active hepatitis B infection, or active or untreated latent tuberculosis.

WARNINGS AND PRECAUTIONS

- **Infusion Reactions**: Can cause infusion reactions, including anaphylaxis. Symptoms can include headache, nausea, somnolence, dyspnea, fever, myalgia, rash, or palpitations. During the randomized clinical trial period (RCP), infusion reactions were observed with the first course of UPLIZNA in 9.3% of NMOSD patients. Infusion reactions of UPLIZNA were observed in 7.4% of IgG4-RD patients during the RCP. 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 antipyretic. For life-threatening infusion reactions, immediately and permanently stop UPLIZNA and administer appropriate supportive treatment. For less severe infusion reactions, management may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

- **Infections**: An increased risk of infections has been observed with other B-cell depleting therapies. The most common infections reported by UPLIZNA-treated patients in the NMOSD RCP and open-label clinical trial periods were urinary tract infection (20%), nasopharyngitis (13%), upper respiratory tract infection (8%), and influenza (7%). In the IgG4-RD RCP and open-label period, the most common infections reported by UPLIZNA-treated patients were upper respiratory tract infection (11%), nasopharyngitis (10%), urinary tract infection (9%), and influenza (6%). Delay UPLIZNA administration in patients with an active infection until the infection is resolved.

Possible Increased Risk of Immunosuppressant Effects with Other Immunosuppressants: UPLIZNA has not been studied in combination with other immunosuppressants. If combining UPLIZNA with another immunosuppressive therapy, consider the potential for increased immunosuppressive effects.

Hepatitis B Virus (HBV) Reactivation: Risk of HBV reactivation has been observed with other B-cell depleting antibodies. There have been no cases of HBV reactivation in patients treated with UPLIZNA, but patients with chronic HBV infection were excluded from clinical trials. Perform HBV screening in all patients before initiation of treatment. Do not administer to patients with active hepatitis. For patients who are chronic carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment.

Progressive Multifocal Leukoencephalopathy (PML): Although no confirmed cases of 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. In UPLIZNA clinical trials one subject died following the development of new brain lesions for which a definitive diagnosis could not be established,

though the differential diagnosis included an atypical NMOSD relapse, PML, or acute disseminated encephalomyelitis. At the first sign or symptom suggestive of PML, withhold UPLIZNA and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

Tuberculosis
Patients should be evaluated for tuberculosis risk factors and tested for latent infection prior to initiating UPLIZNA. Consider anti-tuberculosis therapy prior to initiation of UPLIZNA in patients with a history of latent active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection. Consult infectious disease experts regarding whether initiating anti-tuberculosis therapy is appropriate before starting treatment.

Vaccinations
Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of UPLIZNA. The safety of immunization with live or live-attenuated vaccines following UPLIZNA therapy has not been studied, and vaccination with live-attenuated or live vaccines is not recommended during treatment and until B-cell repletion.

Vaccination of Infants Born to Mothers Treated with UPLIZNA During Pregnancy
In infants of mothers exposed to UPLIZNA during pregnancy, do not administer live or live-attenuated vaccines before confirming recovery of B-cell counts in the infant. Depletion of B-cells in these exposed infants may increase the risks from live or live-attenuated vaccines. Non-live vaccines, as indicated, may be administered prior to recovery from B-cell and immunoglobulin level depletion, but consultation with a qualified specialist should be considered to assess whether a protective immune response was mounted.

- **Reductions 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 levels of quantitative serum immunoglobulins during treatment with UPLIZNA, especially in patients with opportunistic or recurrent infections, and until B-cell repletion after discontinuation of therapy. Consider discontinuing UPLIZNA therapy if a patient with low immunoglobulin G or M develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.
- **Fetal Risk**: Based on animal data, UPLIZNA can cause fetal harm due to B-cell lymphopenia and reduce antibody response in offspring exposed to UPLIZNA even after B-cell repletion. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other B-cell depleting antibodies during pregnancy. Advise females of reproductive potential to use effective contraception while receiving UPLIZNA and for at least 6 months after the last dose.

ADVERSE REACTIONS

- The most common adverse reactions in NMOSD (at least 10% of patients treated with UPLIZNA and greater than placebo) were urinary tract infection and arthralgia.
- The most common adverse reactions in IgG4-RD (at least 10% of patients treated with UPLIZNA and greater than placebo) were urinary tract infections and lymphopenia.

Please see UPLIZNA® full Prescribing Information.

About Amgen
Amgen discovers, develops, manufactures and delivers innovative medicines to help millions of patients in their fight against some of the world's toughest diseases. More than 40 years ago, Amgen helped to establish the biotechnology industry and remains on the cutting-edge of innovation, using technology and human genetic data to push beyond what's known today. Amgen is advancing a broad and deep pipeline that builds on its existing portfolio of medicines to treat cancer, heart disease, osteoporosis, inflammatory diseases and rare diseases.

In 2024, Amgen was named one of the "World's Most Innovative Companies" by Fast Company and one of "America's Best Large Employers" by Forbes, among other external recognitions. Amgen is one of the 30 companies that comprise the Dow Jones Industrial Average®, and it is also part of the Nasdaq-100 Index®, which includes the largest and most innovative non-financial companies listed on the Nasdaq Stock Market based on market capitalization.

For more information, visit Amgen.com and follow Amgen on X, LinkedIn, Instagram, YouTube and Threads.

Amgen Forward-Looking Statements
This news release contains forward-looking statements that are based on the current expectations and beliefs of Amgen. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including any statements on the outcome, benefits and synergies of collaborations, or potential collaborations, with any other company (including BeiGene, Ltd. or Kyowa Kirin Co., Ltd.), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), Amgen's acquisitions of Teneobio, Inc., ChemoCentryx, Inc., or Horizon Therapeutics plc (including the prospective performance and outlook of Horizon's business, performance and opportunities, any potential strategic benefits, synergies or opportunities expected as a result of such acquisition, and any projected impacts from the Horizon acquisition on Amgen's acquisition-related expenses going forward), as well as estimates of revenues, operating margins, capital expenditures, cash, other financial metrics, expected legal, arbitration, political, regulatory or clinical results or practices, customer and prescriber patterns or practices, reimbursement activities and outcomes, effects of pandemics or other widespread health problems on Amgen's business, outcomes, progress and other such estimates and results. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission reports filed by Amgen, including its most recent annual report on Form 10-K and any subsequent periodic reports on Form 10-Q and current reports on Form 8-K. Unless otherwise noted, Amgen is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this

document as a result of new information, future events or otherwise.

No forward-looking statement can be guaranteed and actual results may differ materially from those Amgen projects. Amgen's results may be affected by its ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing its products and global economic conditions. In addition, sales of Amgen's products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen or others could identify safety, side effects or manufacturing problems with its products, including its devices, after they are on the market. Amgen's business may be impacted by government investigations, litigation and product liability claims. In addition, Amgen's business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If Amgen fails to meet the compliance obligations in the corporate integrity agreement between Amgen and the U.S. government, Amgen could become subject to significant sanctions. Further, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors, or Amgen may fail to prevail in present and future intellectual property litigation. Amgen performs a substantial amount of its commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depends on third parties for a portion of its manufacturing activities, and limits on supply may constrain sales of certain of its current products and product candidate development. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for Amgen's manufacturing activities, the distribution of Amgen's products, the commercialization of Amgen's product candidates, and Amgen's clinical trial operations, and any such events may have a material adverse effect on Amgen's product development, product sales, business and results of operations. Amgen relies on collaborations with third parties for the development of some of its product candidates and for the commercialization and sales of some of its commercial products. In addition, Amgen competes with other companies with respect to many of its marketed products as well as for the discovery and development of new products. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third-party suppliers. Certain of Amgen's distributors, customers and payers have substantial purchasing leverage in their dealings with Amgen. The discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on its business and results of operations. Amgen's efforts to collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology Amgen has acquired, may not be successful. There can be no guarantee that Amgen will be able to realize any of the strategic benefits, synergies or opportunities arising from the Horizon acquisition, and such benefits, synergies or opportunities may take longer to realize than expected. Amgen may not be able to successfully integrate Horizon, and such integration may take longer, be more difficult or cost more than expected. A breakdown, cyberattack or information security breach of Amgen's information technology systems could compromise the confidentiality, integrity and availability of Amgen's systems and Amgen's data. Amgen's stock price may be volatile and may be affected by a number of events. Amgen's business and operations may be negatively affected by the failure, or perceived failure, of achieving its environmental, social and governance objectives. The effects of global climate change and related natural disasters could negatively affect Amgen's business and operations. Global economic conditions may magnify certain risks that affect Amgen's business. Amgen's business performance could affect or limit the ability of the Amgen Board of Directors to declare a dividend or its ability to pay a dividend or repurchase its common stock. Amgen may not be able to access the capital and credit markets on terms that are favorable to it, or at all.

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