AMGEN PRESENTS NEW DATA ACROSS RARE INFLAMMATORY DISEASES AT ACR 2024

November 14, 2024

MITIGATE Phase 3 Study Results Reinforce Promise of UPLIZNA® as the First Potential Treatment tor IgG4-RD

Phase 4 AGILE Data Support Shortening KRYSTEXXA® Infusion Time

THOUSAND OAKS, Calif., Nov. 14, 2024 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced the presentation of new data across its rare disease portfolio and pipeline at the annual American College of Rheumatology (ACR) Convergence 2024 conference in Washington, D.C., Nov. 14-19, 2024. New data showcase reduction in disease activity by UPLIZNA® (inebilizumab-cdon) in Immunoglobulin G4-Related Disease (IgG4-RD) and support shorter infusion times for KRYSTEXXA® (pegloticase) co-administered with weekly oral methotrexate 15 mg.

"These data add to the growing body of evidence for UPLIZNA and KRYSTEXXA and strengthen our commitment to developing new treatment options for rare diseases like IgG4-RD and uncontrolled gout," said Jay Bradner, M.D., executive vice president of Research and Development and chief scientific officer at Amgen. "Patients living with these debilitating conditions deserve new approaches targeting the underlying causes of disease, potentially improving outcomes and enhancing the overall treatment experience."

Key presentations include:

A Phase 3, Randomized, Double-Blind, Multicenter, Placebo-Controlled Study of Inebilizumab in IgG4-Related Disease (MITIGATE): Primary Efficacy and Safety Findings
Abstract #0775, Abstract Session: Saturday, Nov. 16 from 1:00 p.m. – 1:15 p.m. ET

MITIGATE, the first randomized, double-blind, placebo-controlled study ever conducted in IgG4-RD, evaluated the safety and efficacy of CD19+ B-cell depletion with UPLIZNA.

Key findings include*:

- A clinically meaningful and statistically significant 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; seven of 68 participants receiving UPLIZNA experienced a flare compared to 40 of 67 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, complete remission at Week 52 compared to 22.4% (15 of 67) participants receiving placebo (p<0.001).
- 58.8% (40 of 68) of participants receiving UPLIZNA achieved flare-free, corticosteroid-free, complete remission at Week 52 compared to 22.4% (15 of 67) participants receiving placebo (p<0.001).
- Confirmation of the unique mechanism of action of UPLIZNA to deliver rapid and sustained depletion of peripheral B cells leading to lowered levels of disease biomarkers. Flares are indicative of high disease activity.

Notably, 89.7% (61 of 68) of UPLIZNA-treated patients required no glucocorticoid treatment for disease control during the placebo-controlled period, compared to 37.3% (25 of 67) of patients on placebo. After Week 8, UPLIZNA-treated patients experienced a ten-fold reduction in total glucocorticoid use relative to placebo.

The safety results in the placebo-controlled period were consistent with the established safety profile of UPLIZNA. The most common treatment-emergent adverse events included COVID-19, lymphopenia, urinary tract infection, and headache.

The data were simultaneously published in the *New England Journal of Medicine*. In August, the U.S. Food and Drug Administration granted Breakthrough Therapy Designation for UPLIZNA in IgG4-RD based on data from the MITIGATE study, and regulatory filing activities are currently underway.

**All p-values follow the New England Journal of Medicine reporting guidelines; values smaller than 0.001 are presented as 0.001.*

Safety, Tolerability and Efficacy of Pegloticase Administered with a Shorter Infusion Duration in Subjects with Uncontrolled Gout Receiving Methotrexate: Primary Findings of the AGILE Open-label Trial
Abstract #2012, Poster Session C: Monday, Nov. 18 from 10:30 p.m. – 12:30 p.m. ET

The AGILE trial assessed the safety, tolerability and efficacy of KRYSTEXXA administered with a shorter infusion duration in patients with uncontrolled gout receiving methotrexate as co-administration.

Safety and efficacy data from the 60-minute infusion duration cohort of the AGILE trial are similar to the MIRROR randomized clinical trial and current administration of KRYSTEXXA with methotrexate over at least 120 minutes.

Key findings include:

- 67.2% (78 of 116) of participants receiving a 60-minute infusion duration of KRYSTEXXA with methotrexate achieved and maintained a response during Month 6, defined as a urate level of < 6mg/dL for ≥80% of the time.

- 6.0% (7 of 116) of participants receiving a 60-minute infusion duration of KRYSTEXXA with methotrexate experienced an infusion reaction, including anaphylaxis (1.7%; 2 of 116 participants), based on adjudicated results.

Regulatory filings for the AGILE study findings are currently underway.

About Uncontrolled Gout

Gout is a chronic, progressive inflammatory form of arthritis that is caused by high urate levels in the body. Tiny needle-like crystals can form and build up almost anywhere in the body. Patients with uncontrolled gout continue to have high levels of uric acid and ongoing symptoms of gout despite the use of oral urate-lowering therapies. Uncontrolled gout is a chronic, systemic disease, and if not addressed can have significant clinical consequences.

About KRYSTEXXA® (pegloticase)

KRYSTEXXA is the first and only biologic approved by the FDA to treat adults living with uncontrolled gout, a painful and debilitating inflammatory condition with which people continue to have abnormally high levels of uric acid and symptoms despite the use of conventional therapies.

In 2022, the FDA approved expanding labeling to include co-administration with the immunomodulator methotrexate, based on results from the MIRROR randomized controlled trial, which showed significant improvements in efficacy and safety, including a reduction in infusion reactions.

KRYSTEXXA® (pegloticase) U.S. Indication

KRYSTEXXA is indicated for the treatment of chronic gout in adult patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Limitations of Use: KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

KRYSTEXXA U.S. Important Safety Information

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS, G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

- **Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA.**
- **Anaphylaxis may occur with any infusion, including a first infusion and generally manifests within 2 hours of the infusion. Delayed hypersensitivity reactions have also been reported.**
- **KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions.**
- **Premedicate with antihistamines and corticosteroids and closely monitor for anaphylaxis for an appropriate period after administration of KRYSTEXXA.**
- **Monitor serum uric acid levels prior to each infusion and discontinue treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL are observed.**
- **Screen patients at risk for glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. KRYSTEXXA is contraindicated in patients with G6PD deficiency.**

CONTRAINDICATIONS

- In patients with G6PD deficiency.
- In patients with history of serious hypersensitivity reactions, including anaphylaxis, to KRYSTEXXA or any of its components.

WARNINGS AND PRECAUTIONS

Gout Flares: An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including KRYSTEXXA. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

Congestive Heart Failure: KRYSTEXXA has not been formally studied in patients with congestive heart failure, but some patients in the pre-marketing placebo-controlled clinical trials experienced exacerbation. Exercise caution in patients who have congestive heart failure and monitor patients closely following infusion.

ADVERSE REACTIONS

The most commonly reported adverse reactions (≥5%) are:

- **KRYSTEXXA co-administration with methotrexate:** gout flares, arthralgia, COVID-19, nausea and fatigue; KRYSTEXXA alone: gout flares, arthralgia, COVID-19, nausea, fatigue, infusion reactions, pain in extremity, hypertension and vomiting.
- **KRYSTEXXA pre-marketing placebo-controlled trials:** gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.

Please see Full Prescribing Information, including Boxed Warning.

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. It is a progressive disease affecting new organs over time either consecutively or simultaneously and is characterized by periods of remission and unpredictable disease flares. IgG4-RD can cause irreversible organ damage with or without the presence of symptoms. 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. 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.

The incidence is estimated at 1-5 in 100,000 although the number of IgG4-RD patients is difficult to determine based on limited epidemiology data. 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.

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). After two initial infusions, patients need one dose of UPLIZNA every six months.

UPLIZNA is currently approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive in the United States and other countries around the world.

UPLIZNA® (inebilizumab-cdon) U.S. 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 the Full Prescribing Information at **www.UPLIZNA.com**.

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, TikTok, YouTube and Threads.

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), our 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 our 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 our 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 our 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 we project. 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, preclinical results do not guarantee safe and effective performance of product candidates in humans. The complexity of the human body cannot be perfectly, or sometimes, even adequately modeled by computer or cell culture systems or animal models. The length of time that it takes for us to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and we expect similar variability in the future.

Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. We develop product candidates internally and through licensing collaborations, partnerships and joint ventures. Product candidates that are derived from relationships may be subject to disputes between the parties or may prove to be not as effective or as safe as we may have believed at the time of entering into such relationship. Also, we or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market.

Our results may be affected by our 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 our products and global economic conditions. In addition, sales of our 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, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our 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 our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our 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 we have acquired, may not be successful. There can be no guarantee that we 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. We 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 our information technology systems could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business and operations may be negatively affected by the failure, or perceived failure, of achieving our environmental, social and governance objectives. The effects of global climate change and related natural disasters could negatively affect our business and operations. Global economic conditions may magnify certain risks that affect our business. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative. Further, any scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration for the products. The products are not approved for the investigational use(s) discussed in this news release, and no conclusions can or should be drawn regarding the safety or effectiveness of the products for these uses.

CONTACT: Amgen, Thousand Oaks
Madison Howard, 773-635-4910 (media)
Elissa Snook, 609-251-1407 (media)
Justin Claeys, 805-313-9775 (investors)

View original content to download multimedia:https://www.prnewswire.com/news-releases/amgen-presents-new-data-across-rare-inflammatory-diseases-at-acr-2024-302306359.html

SOURCE Amgen