FDA APPROVES RIABNI™ (RITUXIMAB-ARRX), A BIOSIMILAR TO RITUXAN® (RITUXIMAB), FOR ADULTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

June 6, 2022

New Indication for Amgen's Fifth FDA-approved Biosimilar

Now Approved to Treat All Available Rituxan® Indications

THOUSAND OAKS, Calif., June 6, 2022 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved RIABNI™ (rituximab-arrx), a biosimilar to Rituxan®, in combination with methotrexate for adults with moderate to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. RIABNI is already approved for the treatment of adult patients with Non-Hodgkin's Lymphoma (NHL), Chronic Lymphocytic Leukemia (CLL), Granulomatosis with Polyangiitis (GPA) (also called Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA).

"The approval of RIABNI is an important advancement for adults living with moderate to severe rheumatoid arthritis, a chronic inflammatory joint disease, who now have access to a proven and affordable treatment option," said Murdo Gordon, executive vice president of Global Commercial Operations at Amgen. "Our fully integrated portfolio of innovative and biosimilar medicines for inflammatory diseases reinforces our commitment to providing patients with high-quality and affordable treatment options that deliver substantial value to our healthcare system."

RIABNI, a CD20-directed cytolytic antibody, was proven to be highly similar to, with no clinically meaningful differences in safety or efficacy from, Rituxan (rituximab) based on totality of evidence, which included comparative analytical, non-clinical and clinical data.

The randomized, double-blind, comparative clinical study compared the efficacy, safety, pharmacokinetics and immunogenicity of RIABNI versus rituximab reference product (RP) in patients with moderate to severe RA. Overall, 311 patients were randomized and treated with RIABNI, rituximab RP approved in the EU (rituximab-EU) or rituximab RP approved in the US (rituximab-US). The rituximab-US group transitioned to RIABNI in period 2 of the study. The primary efficacy endpoint, the change in disease activity score 28 using C-reactive protein (DAS28-CRP) from baseline at week 24, was within the predefined equivalence margin indicating equivalence in clinical efficacy between RIABNI and rituximab RP. Safety, pharmacokinetics and immunogenicity of RIABNI were similar to rituximab RP.

Amgen has a total of 11 biosimilars in its portfolio including potential treatments for chronic inflammatory diseases and cancer. There are currently five biosimilars approved in the U.S. and three approved in the European Union (EU) in Amgen's portfolio.

About RIABNI™ (rituximab-arrx) in the U.S.
RIABNI is a biosimilar to Rituxan, an anti-CD20 monoclonal antibody. The active ingredient of RIABNI is a monoclonal antibody that has the same amino acid sequence as Rituxan. RIABNI also has the same strength as Rituxan, and the dosage form and route of administration are identical to Rituxan. RIABNI is not currently indicated as a treatment for children with mature B-cell Non-Hodgkin's lymphoma, mature B-cell acute leukemia, MPA, or GPA. RIABNI is not indicated in adult patients with moderate to severe pemphigus vulgaris (PV), for which Rituxan has orphan status.

In the U.S., RIABNI is approved for:

Non-Hodgkin's Lymphoma (NHL)
RIABNI (rituximab-arrx) is indicated for the treatment of adult patients with:

- Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent.
- Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy.
- Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy.
- Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens.

Chronic Lymphocytic Leukemia (CLL)
RIABNI, in combination with fludarabine and cyclophosphamide (FC), is indicated for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.

Rheumatoid Arthritis (RA)

RIABNI, in combination with methotrexate, is indicated for the treatment of adult patients with moderately- to severely- active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)
RIABNI, in combination with glucocorticoids, is indicated for the treatment of adult patients with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA).

IMPORTANT SAFETY INFORMATION

BOXED WARNINGS: FATAL INFUSION-RELATED REACTIONS, SEVERE MUCOCUTANEOUS REACTIONS, HEPATITIS B VIRUS

REACTIVATION, PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

- **Infusion-Related Reactions: Rituximab product administration can result in serious, including fatal, infusion-related reactions. Deaths within 24 hours of rituximab infusion have occurred. Approximately 80% of fatal infusion-related reactions occurred in association with the first infusion. Monitor patients closely. Discontinue RIABNI™ infusion for severe reactions and provide medical treatment for Grade 3 or 4 infusion-related reactions.**
- **Severe Mucocutaneous Reactions: Severe, including fatal, mucocutaneous reactions can occur in patients receiving rituximab products. Discontinue RIABNI™ in patients who experience a severe mucocutaneous reaction. The safety of readministration of RIABNI™ to patients with severe mucocutaneous reactions has not been determined.**
- **Hepatitis B Virus (HBV) Reactivation: HBV reactivation can occur in patients treated with rituximab products, in some cases resulting in fulminant hepatitis, hepatic failure, and death. Screen all patients for HBV infection before treatment initiation, and monitor patients during and after treatment with RIABNI™. Discontinue RIABNI™ and concomitant medications in the event of HBV reactivation.**
- **Progressive Multifocal Leukoencephalopathy (PML), including fatal PML, can occur in patients receiving rituximab products. Discontinue RIABNI™ and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.**

Warnings and Precautions

Infusion-Related Reactions (IRR)

- Rituximab products can cause severe, including fatal, infusion-related reactions. Severe reactions typically occurred during the first infusion with time to onset of 30-120 minutes.
- Rituximab product-induced infusion-related reactions and sequelae include urticaria, hypotension, angioedema, hypoxia, bronchospasm, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, anaphylactoid events, or death.
- Premedicate patients with an antihistamine and acetaminophen prior to dosing. For patients with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA), methylprednisolone 100 mg intravenously or its equivalent is recommended 30 minutes prior to each infusion. Institute medical management (eg, glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion-related reactions as needed. Depending on the severity of the infusion-related reaction and the required interventions, temporarily or permanently discontinue RIABNI.™ Resume infusion at a minimum of 50% reduction in rate after symptoms have resolved.
- Closely monitor the following patients: those with pre-existing cardiac or pulmonary conditions, those who experienced prior cardiopulmonary adverse reactions, and those with high numbers of circulating malignant cells (≥25,000/mm^3).

Severe Mucocutaneous Reactions

- Mucocutaneous reactions, some with fatal outcome, can occur in patients receiving rituximab products. These reactions include paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.
- The onset of these reactions has been variable and includes reports with onset on the first day of rituximab exposure. Discontinue RIABNI in patients who experience a severe mucocutaneous reaction. The safety of readministration of rituximab products to patients with severe mucocutaneous reactions has not been determined.

Hepatitis B Virus (HBV) Reactivation

- Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs classified as CD20-directed cytolytic antibodies, including rituximab products. Cases have been reported in patients who are hepatitis B surface antigen (HBsAg) positive and also in patients who are HBsAg negative but are hepatitis B core antibody (anti-HBc) positive. Reactivation also has occurred in patients who appear to have resolved hepatitis B infection (i.e., HBsAg negative, anti-HBc positive and hepatitis B surface antibody [anti-HBs] positive).
- HBV reactivation is defined as an abrupt increase in HBV replication manifesting as a rapid increase in serum HBV DNA level or detection of HBsAg in a person who was previously HBsAg negative and anti-HBc positive. Reactivation of HBV replication is often followed by hepatitis, i.e., increase in transaminase levels. In severe cases, increase in bilirubin levels, liver failure, and death can occur.

- Screen all patients for HBV infection by measuring HBsAg and anti-HBc before initiating treatment with RIABNI.™ For patients who show evidence of prior hepatitis B infection (HBsAg positive [regardless of antibody status] or HBsAg negative but anti-HBc positive), consult with physicians with expertise in managing hepatitis B regarding monitoring and consideration for HBV antiviral therapy before and/or during RIABNI treatment.

- Monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis or HBV reactivation during and for several months following RIABNI™ therapy. HBV reactivation has been reported up to 24 months following completion of rituximab therapy.

- In patients who develop reactivation of HBV while on RIABNI™, immediately discontinue RIABNI™ and any concomitant chemotherapy, and institute appropriate treatment. Insufficient data exist regarding the safety of resuming rituximab product treatment in patients who develop HBV reactivation. Resumption of RIABNI™ treatment in patients whose HBV reactivation resolves should be discussed with physicians with expertise in managing HBV.

Progressive Multifocal Leukoencephalopathy (PML)

- JC virus infection resulting in multifocal leukoencephalopathy (PML) and death can occur in rituximab product-treated patients with hematologic malignancies or with autoimmune diseases. The majority of patients with hematologic malignancies diagnosed with PML received rituximab in combination with chemotherapy or as part of a hematopoietic stem cell transplant. The patients with autoimmune diseases had prior or concurrent immunosuppressive therapy. Most cases of PML were diagnosed within 12 months of their last infusion of rituximab.

- Consider the diagnosis of PML in any patient presenting with new-onset neurologic manifestations. Evaluation of PML includes, but is not limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Discontinue RIABNI™ and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML.

Tumor Lysis Syndrome (TLS)

- Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia from tumor lysis, sometimes fatal, can occur within 12-24 hours after the first infusion of RIABNI™ in patients with non–Hodgkin's Lymphoma (NHL). A high number of circulating malignant cells (≥25,000/mm^3), or high tumor burden, confers a greater risk of TLS.

- Administer aggressive intravenous hydration and anti-hyperuricemic therapy in patients at high risk for TLS. Correct electrolyte abnormalities, monitor renal function and fluid balance, and administer supportive care, including dialysis, as indicated.

Infections

- Serious, including fatal, bacterial, fungal, and new or reactivated viral infections can occur during and following the completion of rituximab product-based therapy. Infections have been reported in some patients with prolonged hypogammaglobulinemia (defined as hypogammaglobulinemia >11 months after rituximab exposure).

- New or reactivated viral infections included cytomegalovirus, herpes simplex virus, parvovirus B19, varicella zoster virus, West Nile virus, and hepatitis B and C. Discontinue RIABNI™ for serious infections and institute appropriate anti-infective therapy.

- RIABNI™ is not recommended for use in patients with severe, active infections.

Cardiovascular Adverse Reactions

- Cardiac adverse reactions, including ventricular fibrillation, myocardial infarction, and cardiogenic shock may occur in patients receiving rituximab products. Discontinue infusions for serious or life-threatening cardiac arrhythmias. Perform cardiac monitoring during and after all infusions of RIABNI™ for patients who develop clinically significant arrhythmias, or who have a history of arrhythmia or angina.

Renal Toxicity

- Severe, including fatal, renal toxicity can occur after rituximab product administration in patients with NHL. Renal toxicity has occurred in patients who experience TLS and in patients with NHL administered concomitant cisplatin therapy during clinical trials. The combination of cisplatin and RIABNI™ is not an approved treatment regimen. Monitor closely for signs of renal failure and discontinue RIABNI™ in patients with a rising serum creatinine or oliguria.

Bowel Obstruction and Perforation

- Abdominal pain, bowel obstruction and perforation, in some cases leading to death, can occur in patients receiving rituximab products in combination with chemotherapy. In postmarketing reports, the mean time to documented gastrointestinal perforation was 6 (range 1−77) days in patients with NHL. Evaluate if symptoms of obstruction such as abdominal pain or repeated vomiting occur.

Immunization

- The safety of immunization with live viral vaccines following rituximab product therapy has not been studied, and vaccination with live virus vaccines is not recommended before or during treatment.
- For patients treated with RIABNI™, physicians should review the patient's vaccination status and patients should, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating RIABNI and administer non-live vaccines at least 4 weeks prior to a course of RIABNI.™
- The effect of rituximab products on immune responses was assessed in a randomized, controlled study in patients with RA treated with rituximab and methotrexate (MTX) compared to patients treated with MTX alone.
- A response to pneumococcal vaccination (a T-cell independent antigen) as measured by an increase in antibody titers to at least 6 of 12 serotypes was lower in patients treated with rituximab plus MTX as compared to patients treated with MTX alone (19% vs 61%). A lower proportion of patients in the rituximab plus MTX group developed detectable levels of anti-keyhole limpet hemocyanin antibodies (a novel protein antigen) after vaccination compared to patients on MTX alone (47% vs 93%).
- A positive response to tetanus toxoid vaccine (a T-cell dependent antigen with existing immunity) was similar in patients treated with rituximab plus MTX compared to patients on MTX alone (39% vs 42%). The proportion of patients maintaining a positive Candida skin test (to evaluate delayed type hypersensitivity) was also similar (77% of patients on rituximab plus MTX vs 70% of patients on MTX alone).
- Most patients in the rituximab-treated group had B-cell counts below the lower limit of normal at the time of immunization. The clinical implications of these findings are not known.

Embryo-Fetal Toxicity

- Based on human data, rituximab products can cause fetal harm due to B-cell lymphocytopenia in infants exposed in utero. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception with RIABNI™ and for 12 months after the last dose.

Concomitant Use with Biologic Agents and DMARDs Other Than MTX

- Limited data are available on the safety of the use of biologic agents or DMARDs other than MTX in RA patients exhibiting peripheral B-cell depletion following treatment with rituximab. Observe patients closely for signs of infection if biologic agents and/or DMARDs are used concomitantly. Use of concomitant immunosuppressants other than corticosteroids has not been studied in GPA, MPA, or PV patients exhibiting peripheral B-cell depletion following treatment with rituximab products.

Use in Patients With RA Who Had No Prior Inadequate Response to Tumor Necrosis Factor (TNF) Antagonists

- While the efficacy of rituximab was supported in 4 controlled trials in patients with RA with prior inadequate responses to nonbiologic DMARDs and in a controlled trial in MTX-naïve patients, a favorable risk-benefit relationship has not been established in these populations. The use of RIABNI™ in patients with RA who have not had prior inadequate response to one or more TNF antagonists is not recommended.

Additional Important Safety Information

Adverse Reactions

Clinical Trials Experience in NHL and CLL

- The most common Grade 3 or 4 adverse reactions in clinical trials of NHL and chronic lymphocytic leukemia (CLL) were infusion-related reactions, neutropenia, leukopenia, anemia, thrombocytopenia, and infections. Additionally, lymphopenia and lung disorder were seen in NHL trials; and febrile neutropenia, pancytopenia, hypotension, and hepatitis B were seen in CLL trials.
- The most common adverse reactions (incidence ≥25%) in clinical trials of NHL and CLL were infusion-related reactions. Additionally, fever, lymphopenia, chills, infection, and asthenia were seen in NHL trials; and neutropenia was seen in CLL trials.

Clinical Trials Experience in RA

- Among all exposed patients, adverse reactions reported in greater than 10% of patients include infusion-related reactions, upper respiratory tract infection, nasopharyngitis, urinary tract infection, and bronchitis.
- In placebo-controlled studies, adverse reactions reported in ≥5% of patients were hypertension (8% vs 5%), nausea (8% vs 5%), upper respiratory tract infection (7% vs 6%), arthralgia (6% vs 4%), pyrexia (5% vs 2%), and pruritus (5% vs 1%) of rituximab-treated vs placebo, respectively.

Infusion-Related Reactions

- In the rituximab RA pooled, placebo-controlled studies, incidence of any adverse event within 24 hours of an infusion was 32% vs 23% after the first infusion, and 11% vs 13% after the second infusion in the rituximab-treated patients and placebo group, respectively. Incidence of acute infusion-related reactions was 27% vs 19% after the first infusion, 9% vs 11% after the second infusion in the rituximab-treated patients and placebo group, respectively.
- Serious acute infusion-related reactions were experienced by <1% of patients in either treatment group. Acute infusion-related reactions required dose modification (stopping, slowing, or interruption of the infusion) in 10% and 2% of patients receiving rituximab or placebo, respectively, after the first course.

Infections

- In the pooled, placebo controlled studies, incidence of any type of infection was 39% vs 34%, rituximab-treated vs placebo. The most common infections were nasopharyngitis, upper respiratory tract infections, urinary tract infections, bronchitis, and sinusitis. The incidence of serious infections was 2% vs 1%, rituximab-treated vs placebo group.
- In the experience with rituximab in 2578 RA patients, the rate of serious infection was 4.31 per 100 patient-years. The most common serious infections (≥0.5%) were pneumonia or lower respiratory tract infections, cellulitis, and urinary tract infections. Fatal serious infections included pneumonia, sepsis, and colitis. Rates of serious infection remain stable in patients receiving subsequent courses.
- In 185 rituximab-treated RA patients with active disease, subsequent treatment with a biologic DMARD, the majority of which were TNF antagonists, did not appear to increase the rate of serious infection.

Cardiovascular Adverse Reactions

- In the pooled, placebo-controlled studies, incidence of serious cardiovascular reactions was 1.7% vs 1.3% rituximab-treated vs placebo. Three cardiovascular deaths occurred during the double-blind period of the RA studies including all rituximab regimens (3/769=0.4%) compared to none in the placebo treatment group (0/389).
- In the experience with rituximab in 2578 RA patients, the rate of myocardial infarction (MI) was consistent with MI rates in the general RA population. RIABNI should be discontinued in the event of a serious or life-threatening cardiac event.

Hypophosphatemia and Hyperuricemia

- In the pooled, placebo-controlled studies, newly occurring hypophosphatemia (<2.0 mg/dL) was 12% vs 10%, rituximab-treated vs placebo, respectively. Hypophosphatemia was more common in patients who received corticosteroids. Newly occurring hyperuricemia (>10 mg/dL) was observed in 1.5% vs 0.3%, rituximab-treated vs placebo, respectively.

Retreatment in Patients With RA

- In the experience with rituximab in RA patients, 2578 patients have been exposed to rituximab and have received up to 10 courses of rituximab in RA clinical trials, with 1890, 1043, and 425 patients having received at least 2, 3, and 4 courses, respectively. Most of the patients who received additional courses did so 24 weeks or more after the previous course and none were retreated sooner than 16 weeks. The rates and types of adverse reactions reported for subsequent courses of rituximab were similar to rates and types seen for a single course of rituximab. In RA Study 2, where all patients initially received rituximab, the safety profile of patients who were retreated with rituximab was similar to those who were retreated with placebo.

Immunogenicity

- A total of 273/2578 (11%) patients with RA tested positive for anti-rituximab antibodies at any time after receiving rituximab. Anti-rituximab antibody positivity was not associated with increased infusion-related reactions or other adverse reactions. Upon further treatment, the proportions of patients with infusion-related reactions were similar between anti-rituximab antibody positive and negative patients, and most reactions were mild to moderate.

- Four anti-rituximab antibody positive patients had serious infusion-related reactions, and the temporal relationship between anti-rituximab antibody positivity and infusion-related reaction was variable. The clinical relevance of anti-rituximab antibody formation in rituximab-treated patients is unclear.

Clinical Trials Experience in GPA and MPA

- Adverse reactions reported in ≥15% of rituximab-treated patients were infections, nausea, diarrhea, headache, muscle spasms, anemia, peripheral edema, infusion-related reactions.

Induction Treatment of Patients with Active GPA/MPA (GPA/MPA Study 1)

Infusion-Related Reactions

- In GPA/MPA Study 1, 12% vs 11% (rituximab-treated vs cyclophosphamide) of patients experienced at least one infusion-related reaction. Infusion-related reactions included cytokine release syndrome, flushing, throat irritation, and tremor. In the rituximab group, the proportion of patients experiencing an infusion-related reaction was 12%, 5%, 4%, and 1% following the first, second, third, and fourth infusions, respectively. Patients were premedicated with antihistamine and acetaminophen before each rituximab infusion and were on background oral corticosteroids, which may have mitigated or masked an infusion-related reaction; however, there is insufficient evidence to determine whether premedication diminishes the frequency or severity of infusion-related reactions.

Infections

- In GPA/MPA Study 1, 62% vs 47% (rituximab-treated vs cyclophosphamide-treated, respectively) of patients experienced an infection by Month 6. The most common infections in the rituximab group were upper respiratory tract infections, urinary tract infections, and herpes zoster. The incidence of serious infections was 11% vs 10% (rituximab-treated vs cyclophosphamide, respectively), with rates of approximately 25 and 28 per 100 patient-years, respectively. The most common serious infection was pneumonia.

Hypogammaglobulinemia

- Hypogammaglobulinemia (IgA, IgG, or IgM below the lower limit of normal) has been observed in patients with GPA and MPA treated with rituximab in GPA/MPA Study 1. At 6 months, in the rituximab group, 27%, 58%, and 51% of patients with normal immunoglobulin levels at baseline had low IgA, IgG, and IgM levels, respectively compared to 25%, 50%, and 46% in cyclophosphamide group.

Immunogenicity

- A total of 23/99 (23%) rituximab-treated patients with GPA or MPA tested positive for anti-rituximab antibodies by 18 months in GPA/MPA Study 1. The clinical relevance of anti-rituximab antibody formation in rituximab-treated patients is unclear.

Treatment of Patients with GPA/MPA who have Achieved Disease Control with Induction Treatment (GPA/MPA Study 2)

- In GPA/MPA Study 2, the safety profile was consistent with the known safety profile of rituximab in immunologic indications.

Infusion-Related Reactions

- In GPA/MPA Study 2, 7/57 (12%) patients in the non-U.S.-licensed rituximab arm reported infusion-related reactions. The incidence of IRR symptoms was highest during or after the first infusion (9%) and decreased with subsequent infusions (<4%). One patient had two serious IRRs, two IRRs led to a dose modification, and no IRRs were severe, fatal, or led to withdrawal from the study.

Infections

- In GPA/MPA Study 2, 30/57 (53%) patients in the non-U.S.-licensed rituximab arm and 33/58 (57%) in the azathioprine arm reported infections. The incidence of all grade infections was similar between the arms. The incidence of serious infections was similar in both arms (12%). The most commonly reported serious infection in the group was mild or moderate bronchitis.

Pregnancy and Nursing Mothers

- Based on human data, rituximab products can cause adverse developmental outcomes including B-cell lymphocytopenia in infants exposed in utero. Advise pregnant women of the risk to a fetus. There are limited data on the presence of rituximab products in human milk and the effect on the breastfed child, and there are no data on the effect on milk

production. Rituximab is detected in the milk of lactating cynomolgus monkeys, and maternal IgG is present in human breast milk. Rituximab has also been reported to be excreted at low concentrations in human breast milk. Given that the clinical significance of this finding for children is not known, advise women not to breastfeed during treatment with RIABNI™ and for 6 months after the last dose due to the potential for serious adverse reactions in breastfed children.

Attention Healthcare Provider: Provide Medication Guide to patient prior to RIABNI™ infusion and advise patients to read guide.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Amgen at 1-800-772-6436.

Please see the full Prescribing Information, including BOXED WARNINGS and Medication Guide, for additional Important Safety Information.

About Amgen Biosimilars
Amgen is committed to building upon Amgen's experience in the development and manufacturing of innovative human therapeutics to expand Amgen's reach to patients with serious illnesses. Biosimilars help to maintain Amgen's commitment to connect patients with vital medicines, and Amgen is well positioned to leverage its nearly four decades of experience in biotechnology to create high-quality biosimilars and reliably supply them to patients worldwide.

For more information, visit www.amgenbiosimilars.com.

About Amgen
Amgen is committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing and delivering innovative human therapeutics. This approach begins by using tools like advanced human genetics to unravel the complexities of disease and understand the fundamentals of human biology.

Amgen focuses on areas of high unmet medical need and leverages its expertise to strive for solutions that improve health outcomes and dramatically improve people's lives. A biotechnology pioneer since 1980, Amgen has grown to be one of the world's leading independent biotechnology companies, has reached millions of patients around the world and is developing a pipeline of medicines with breakaway potential.

Amgen is one of the 30 companies that comprise the Dow Jones Industrial Average and is also part of the Nasdaq-100 index. In 2021, Amgen was named one of the 25 World's Best Workplaces™ by Fortune and Great Place to Work™ and one of the 100 most sustainable companies in the world by Barron's.

For more information, visit www.amgen.com and follow us on www.twitter.com/amgen.

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., Kyowa-Kirin Co., Ltd., or any collaboration to manufacture therapeutic antibodies against COVID-19), the performance of Otezla® (apremilast) (including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion), the Five Prime Therapeutics, Inc. acquisition, or the Teneobio, Inc. acquisition, 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 such as the ongoing COVID-19 pandemic on our business, 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. A breakdown, cyberattack or information security breach 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.

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