FDA Approves Amgen's AVSOLA™ (infliximab-axxq), For The Same Indications As Remicade® (infliximab)

December 6, 2019

Amgen's Fourth FDA Approval From Biosimilars Portfolio

THOUSAND OAKS, Calif., Dec. 6, 2019 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has approved AVSOLA™ (infliximab-axxq) for all approved indications of the reference product, Remicade® (infliximab): for the treatment of moderate-to-severe rheumatoid arthritis (RA), moderate-to-severe Crohn's Disease (CD) in the adult and pediatric population, moderate-to-severe ulcerative colitis (UC) in the adult and pediatric population, chronic severe plaque psoriasis (PsO), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

"The approval of AVSOLA represents an important milestone across our biosimilar and inflammation portfolios," said Murdo Gordon, executive vice president of Global Commercial Operations at Amgen. "Following July's exciting launches of our two biosimilars in oncology, AVSOLA highlights Amgen's long-term commitment to providing more affordable biological treatment options to patients across critical disease states, including chronic inflammatory conditions."

AVSOLA, an anti-tumor necrosis factor alpha (anti-TNF) monoclonal antibody, was proven to be highly similar to Remicade with no clinically meaningful differences based on a totality of evidence which included comparative analytical, nonclinical and clinical data. The data package was composed of, in part, results from a pharmacokinetic (PK) similarity study conducted in healthy subjects, and a comparative clinical study conducted in patients with moderate to severe RA.

The randomized, double-blind comparative clinical study evaluated the efficacy and safety of AVSOLA compared to Remicade in patients with moderate-to-severe RA. There were 558 patients enrolled and randomized (1:1) to receive either AVSOLA or Remicade at a dose of 3 mg/kg administered as an infusion on day 1, at weeks 2 and 6, and every 8 weeks thereafter. The primary endpoint was the response difference (RD) of 20% improvement in American College of Rheumatology core set measurements (ACR20) at week 22. Key secondary endpoints included DAS28-CRP change from baseline, RD of ACR20, ACR50 and ACR70 at weeks 2, 6, 14, 22, 30, 34, 38, 46 and 50. The study also incorporated the evaluation of a single transition in 119 subjects from Remicade to AVSOLA at week 22, which demonstrated similar safety and immunogenicity in patients who were previously on Remicade.

Amgen has a total of 10 biosimilars in its portfolio, four of which have been approved in the U.S., and 3 that are approved in the European Union (EU).

About AVSOLA™(infliximab-axxq) in the U.S.
AVSOLA is a biosimilar to Remicade, an anti-tumor necrosis factor alpha (anti-TNF) monoclonal antibody. The active ingredient of AVSOLA is an anti-TNF monoclonal antibody that has the same amino acid sequence as Remicade. AVSOLA also has the same pharmaceutical dosage form and strength as Remicade.

AVSOLA is currently not available commercially. This is not an offer for sale. The following information is derived from the approved label in the U.S.

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

Rheumatoid Arthritis

AVSOLA, in combination with methotrexate, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis.

Crohn's Disease

AVSOLA is indicated for

- reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy.
- reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.

Pediatric Crohn's Disease

AVSOLA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy.

Ulcerative Colitis

AVSOLA is indicated for reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.

Pediatric Ulcerative Colitis

AVSOLA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy.

Plaque Psoriasis

AVSOLA is indicated for the treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. AVSOLA should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

Psoriatic Arthritis

AVSOLA is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.

Ankylosing Spondylitis

AVSOLA is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

AVSOLA ™U.S. Important Safety Information

SERIOUS INFECTIONS

Patients treated with infliximab products are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Discontinue AVSOLA if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before AVSOLA use and during therapy. Treatment for latent infection should be initiated prior to AVSOLA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, pneumocystosis, and cryptococcosis. Patients may present with disseminated, rather than localized, disease. Empiric antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral and other infections due to opportunistic pathogens, including Legionella, Listeria and Salmonella.**

The risks and benefits of treatment with AVSOLA™ should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with AVSOLA™, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy, who are on treatment for latent TB, or who were previously treated for TB infection.

Risk of infection may be higher in patients greater than 65 years of age, pediatric patients, patients with co-morbid conditions and/or patients taking concomitant immunosuppressant therapy. In clinical trials, other serious infections observed in patients treated with infliximab products included pneumonia, cellulitis, abscess, and skin ulceration.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including infliximab products. Approximately half of these cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of malignancies, including rare malignancies that are usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. The malignancies occurred after a median of 30 months after the first dose of therapy. Most of the patients were receiving concomitant immunosuppressants.

Postmarketing cases of hepatosplenic T-cell lymphoma, a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including infliximab products. These cases have had a very aggressive disease course and have been fatal. The majority of reported cases have occurred in patients with Crohn's disease or ulcerative colitis and most were in adolescent and young adult males. Almost all patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF-blocker at or prior to diagnosis. Carefully assess the risks and benefits of treatment with AVSOLA™, especially in these patient types.

In clinical trials of all TNF inhibitors, more cases of lymphoma were observed compared with controls and the expected rate in the general population. However, patients with Crohn's disease, rheumatoid arthritis, or plaque psoriasis may be at higher risk for developing lymphoma. In clinical trials of some TNF inhibitors, including infliximab products, more cases of other malignancies were observed compared with controls. The rate of these malignancies among patients treated with infliximab products was similar to that expected in the general population, whereas the rate in control patients was lower than expected. Cases of acute and chronic leukemia have been reported with postmarketing TNF-blocker use. As the potential role of TNF inhibitors in the development of malignancies is not known, caution should be exercised when considering treatment of patients with a current or a past history of malignancy or other risk factors such as chronic obstructive pulmonary disease (COPD).

Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-blocker therapy, including infliximab products. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.

A population-based retrospective cohort study found a 2- to 3-fold increase in the incidence of invasive cervical cancer in women with rheumatoid arthritis treated with infliximab compared to biologics-naïve patients or the general population, particularly those over 60 years of age. A causal relationship between infliximab products and cervical cancer cannot be excluded. Periodic screening should continue in women treated with AVSOLA.

CONTRAINDICATIONS

AVSOLA is contraindicated in patients with moderate to severe (NYHA Class III/IV) congestive heart failure (CHF) at doses greater than 5 mg/kg. Higher mortality rates at the 10 mg/kg dose and higher rates of cardiovascular events at the 5 mg/kg dose have been observed in these patients.

AVSOLA should be used with caution and only after consideration of other treatment options. Patients should be monitored closely. Discontinue AVSOLA if new or worsening CHF symptoms appear. AVSOLA should not be (re)administered to patients who have experienced a severe hypersensitivity reaction or to patients with hypersensitivity to murine proteins or other components of the product.

HEPATITIS B REACTIVATION

TNF inhibitors, including infliximab products, have been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases were fatal. Patients should be tested for HBV infection before initiating AVSOLA. For patients who test positive, consult a physician with expertise in the treatment of hepatitis B. Exercise caution when prescribing AVSOLA for patients identified as carriers of HBV and monitor closely for active HBV infection during and following termination of therapy with AVSOLA. Discontinue AVSOLA in patients who develop HBV reactivation and initiate antiviral therapy with appropriate supportive treatment. Exercise caution when considering resumption of TNF blocker- therapy and monitor patients closely.

HEPATOTOXICITY

Severe hepatic reactions, including acute liver failure, jaundice, hepatitis and cholestasis, have been reported in patients receiving infliximab products postmarketing. Some cases were fatal or required liver transplant. Aminotransferase elevations were not noted prior to discovery of liver injury in many cases. Patients with symptoms or signs of liver dysfunction should be evaluated for evidence of liver injury. If jaundice and/or marked liver enzyme elevations (e.g., ≥5 times the upper limit of normal) develop, AVSOLA should be discontinued, and a thorough investigation of the abnormality should be undertaken.

HEMATOLOGIC REACTIONS

Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia (some fatal) have been reported in patients receiving infliximab products. The causal relationship to infliximab product therapy remains unclear. Exercise caution in patients who have ongoing or a history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs and symptoms of blood dyscrasias or infection. Consider discontinuation of AVSOLA in patients who develop significant hematologic abnormalities.

HYPERSENSITIVITY

Infliximab products have been associated with hypersensitivity reactions that differ in their time of onset. Anaphylaxis, urticaria, dyspnea, and hypotension have occurred in association with infusions of infliximab products. Medications for the treatment of hypersensitivity reactions should be available.

CARDIOVASCULAR AND CEREBROVASCULAR REACTIONS DURING AND AFTER INFUSION

Serious cerebrovascular accidents, myocardial ischemia/infarction (some fatal), hypotension, hypertension, and arrhythmias have been reported during and within 24 hours of initiation of infliximab product infusion. Cases of transient visual loss have been reported during or within 2 hours of infusion of infliximab. Monitor patients during infusion and if a serious reaction occurs, discontinue infusion. Manage reactions according to signs and symptoms.

NEUROLOGIC REACTIONS

Agents that inhibit TNF have been associated with CNS manifestation of systemic vasculitis, seizure and new onset or exacerbation of CNS demyelinating disorders, including multiple sclerosis and optic neuritis, and peripheral demyelinating disorders, including Guillain-Barré syndrome. Exercise caution when considering AVSOLA in patients with these disorders and consider discontinuation if these disorders develop.

AUTOIMMUNITY

Treatment with infliximab products may result in the formation of autoantibodies and in the development of a lupus-like syndrome. Discontinue treatment with AVSOLA if symptoms of a lupus-like syndrome develop.

ADVERSE REACTIONS

In clinical trials with infliximab products, the most common adverse reactions occurring in >10% of patients included infections (e.g., upper respiratory, sinusitis, and pharyngitis), infusion-related reactions, headache, and abdominal pain.

USE WITH OTHER DRUGS

Concomitant use of AVSOLA with anakinra, abatacept, tocilizumab, or other biologics used to treat the same conditions as AVSOLA is not recommended because of the possibility of an increased risk of infection. Care should be taken when switching from one biologic to another, since overlapping biological activity may further increase the risk of infection.

LIVE VACCINES/THERAPEUTIC INFECTIOUS AGENTS

Live vaccines or therapeutic infectious agents should not be given with AVSOLA™ due to the possibility of clinical infections, including disseminated infections.

Bring pediatric patients up to date with all vaccinations prior to initiating AVSOLA™. At least a 6-month waiting period following birth is recommended before the administration of any live vaccine to infants exposed *in utero* to infliximab products.

Please see full Prescribing Information, including **Boxed WARNINGS**, at www.Amgen.com.

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 will 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 and follow us on www.twitter.com/amgenbiosim.

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.

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 collaboration with any other company, including BeiGene, Ltd. or the acquisition of Otezla® (apremilast), including anticipated Otezla sales growth and the timing of non-GAAP EPS accretion, 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 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. 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 acquire other companies or products and to integrate the operations of companies 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 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.

CONTACT: Amgen, Thousand Oaks
Kelley Davenport, 202-585-9637 (media)
Trish Hawkins, 805-447-5631 (media)
Arvind Sood, 805-447-1060 (investors)

View original content to download multimedia:http://www.prnewswire.com/news-releases/fda-approves-amgens-avsola-infliximab-axxq-for-the-same-indications-as-remicade-infliximab-300970785.html

SOURCE Amgen