Amgen Receives Positive CHMP Opinion For ABP 501 (Biosimilar Adalimumab) For The Treatment Of Certain Inflammatory Diseases

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First Adalimumab Biosimilar Candidate Recommended for EMA Approval

THOUSAND OAKS, Calif., Jan. 27, 2017 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion for the Marketing Authorization of ABP 501 (biosimilar adalimumab), recommending approval for all available indications. ABP 501 has been recommended for approval for the treatment of certain inflammatory diseases in adults, including moderate-to-severe rheumatoid arthritis, psoriatic arthritis, severe ankylosing spondylitis (AS), severe axial spondyloarthritis without radiographic evidence of AS, moderate-to-severe chronic plaque psoriasis, moderate-to-severe hidradenitis suppurativa, non-infectious intermediate, posterior and panuveitis, moderate-to-severe Crohn's disease and moderate-to-severe ulcerative colitis. The CHMP opinion also recommends approval for the treatment of certain pediatric inflammatory diseases, including moderate-to-severe Crohn's disease (ages six and older), severe chronic plaque psoriasis (ages four and older), enthesitis-related arthritis (ages six and older) and polyarticular juvenile idiopathic arthritis (ages two and older).

"The positive CHMP opinion for ABP 501 marks the first time an adalimumab biosimilar has been recommended for approval in the EU," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "This represents another significant milestone for our biosimilars portfolio and is an important step in our effort to develop high-quality biologic medicines for patients suffering from chronic inflammatory diseases."

The Marketing Authorization Application (MAA) submission for ABP 501 was based on a comprehensive data package supporting biosimilarity to adalimumab based on analytical, pharmacokinetic and clinical data, including results from two Phase 3 studies conducted in moderate-to-severe plaque psoriasis and moderate-to-severe rheumatoid arthritis patients. The Phase 3 studies each met their primary endpoint showing no clinically meaningful differences to adalimumab. Safety and immunogenicity of ABP 501 were also comparable to adalimumab. Data to support the transition of adalimumab patients to ABP 501 were also included in the submission.

The CHMP positive opinion will now be reviewed by the European Commission (EC), which has the authority to approve medicines for the European Union (EU). If approved, a centralized marketing authorization will be granted that will be valid in the 28 countries that are members of the EU. Norway, Iceland and Liechtenstein, as members of the European Economic Area (EEA), will take corresponding decisions on the basis of the decision of the EC.

ABP 501 was approved in the United States (U.S.) by the U.S. Food and Drug Administration (FDA) on Sept. 23, 2016, where it goes by the brand name AMJEVITA™ (adalimumab-atto).

About ABP 501
ABP 501 is a biosimilar candidate to adalimumab, an anti-TNF-α monoclonal antibody, which is approved in many regions for the treatment of several inflammatory diseases. The active ingredient of ABP 501 is an anti-TNF-α monoclonal antibody that has the same amino acid sequence as adalimumab.

About AMJEVITA™ (adalimumab-atto) in the U.S.
AMJEVITA is a biosimilar to adalimumab, an anti-TNF-α monoclonal antibody. The active ingredient of AMJEVITA is an anti-TNF-α monoclonal antibody that has the same amino acid sequence as, and has been determined by FDA to be highly similar to, adalimumab. AMJEVITA will be delivered in prefilled syringe and autoinjector presentations to support dosing in each of the approved indications.

AMJEVITA is indicated, alone or in combination with methotrexate or other non-biologic DMARDs, for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis.

AMJEVITA is indicated, alone or in combination with methotrexate, for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 4 years of age and older.

AMJEVITA is indicated, alone or in combination with non-biologic DMARDs, for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis.

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

AMJEVITA 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, and reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

AMJEVITA is indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine, or 6-mercaptopurine. The effectiveness of adalimumab products has not been established in patients who have lost response to or were intolerant to TNF blockers.

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

AMJEVITA 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.

AMJEVITA™ U.S. Important Safety Information

SERIOUS INFECTIONS

Patients treated with AMJEVITA™ 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 AMJEVITA™ if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before AMJEVITA™ use and during therapy. Initiate treatment for latent TB prior to AMJEVITA™ use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

Carefully consider the risks and benefits of treatment with AMJEVITA™ prior to initiating therapy in patients: 1. with chronic or recurrent infection, 2. who have been exposed to TB, 3. with a history of opportunistic infection, 4. who resided in or traveled in regions where mycoses are endemic, 5. with underlying conditions that may predispose them to infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with AMJEVITA™, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start AMJEVITA™ during an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- If an infection develops, monitor carefully and initiate appropriate therapy.
- Drug interactions with biologic products: A higher rate of serious infections has been observed in rheumatoid arthritis patients treated with rituximab who received subsequent treatment with a TNF blocker. An increased risk of serious infections has been seen with the combination of TNF blockers with anakinra or abatacept, with no demonstrated added benefit in patients with RA. Concurrent use of AMJEVITA™ with biologic DMARDs (e.g., anakinra or abatacept) or other TNF blockers is not recommended based on the possible increased risk for infections and other potential pharmacological interactions.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including adalimumab products. Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including adalimumab products. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

- Consider the risks and benefits of TNF-blocker treatment prior to initiating or continuing therapy in a patient with known malignancy.
- In clinical trials of some TNF-blockers, including adalimumab products, more cases of malignancies were observed among TNF-blocker-treated patients compared to control patients.
- Non-melanoma skin cancer (NMSC) was reported during clinical trials for adalimumab-treated patients. Examine all patients, particularly those with a history of prolonged immunosuppressant or PUVA therapy, for the presence of NMSC prior to and during treatment with AMJEVITA ™ .
- In adalimumab clinical trials, there was an approximate 3-fold higher rate of lymphoma than expected in the general U.S. population. Patients with chronic inflammatory diseases, particularly those with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at higher risk of lymphoma than the general population, even in the absence of TNF blockers.
- Postmarketing cases of acute and chronic leukemia were reported with TNF blocker use. Approximately half of the postmarketing cases of malignancies in children, adolescents, and young adults receiving TNF blockers were lymphomas; other cases included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents.

HYPERSENSITIVITY

Anaphylaxis and angioneurotic edema have been reported following administration of adalimumab products. If a serious allergic reaction occurs, stop AMJEVITA™ and institute appropriate therapy.

HEPATITIS B VIRUS REACTIVATION

Use of TNF blockers, including AMJEVITA™, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal. Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blocker therapy. Exercise caution in patients who are carriers of HBV and monitor them during and after AMJEVITA™ treatment. Discontinue AMJEVITA™ and begin antivira

therapy in patients who develop HBV reactivation. Exercise caution when resuming AMJEVITA™ after HBV treatment.

NEUROLOGIC REACTIONS
TNF blockers, including adalimumab products, have been associated with rare cases of new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, optic neuritis, and Guillain-Barré syndrome. Exercise caution when considering AMJEVITA™ for patients with these disorders; discontinuation of AMJEVITA™ should be considered if any of these disorders develop.

HEMATOLOGICAL REACTIONS
Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia has been infrequently reported with adalimumab products. Consider stopping AMJEVITA™ if significant hematologic abnormalities occur.

CONGESTIVE HEART FAILURE
Worsening and new onset congestive heart failure (CHF) has been reported with TNF blockers. Cases of worsening CHF have been observed with adalimumab products; exercise caution and monitor carefully.

AUTOIMMUNITY
Treatment with adalimumab products may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

IMMUNIZATIONS
Patients on AMJEVITA™ should not receive live vaccines. Pediatric patients, if possible, should be brought up to date with all immunizations before initiating AMJEVITA™ therapy. Adalimumab is actively transferred across the placenta during the third trimester of pregnancy and may affect immune response in the in utero exposed infant. The safety of administering live or live-attenuated vaccines in infants exposed to adalimumab products in utero is unknown. Risks and benefits should be considered prior to vaccinating (live or live-attenuated) exposed infants.

ADVERSE REACTIONS
The most common adverse reactions in adalimumab clinical trials (>10%) were: infections (e.g., upper respiratory, sinusitis), injection site reactions, headache, and rash.

Please see full Prescribing Information, including Medication Guide.

About Amgen Biosimilars
Amgen Biosimilars 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 more than 35 years 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.

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 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 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 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. We or others could identify safety, side effects or manufacturing problems with our products after they are on the market. 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 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. 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. 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. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all. We are increasingly dependent on information technology systems, infrastructure and data security. 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.

The scientific information discussed in this news release related to our product candidates is preliminary and investigative and specific to the European Union. Such product candidates are not approved by the European Commission, and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates in the European Union.

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