



## FDA Accepts Amgen's Supplemental Biologics License Application For The Expanded Use Of Enbrel® (Etanercept) To Treat Pediatric Patients With Chronic Severe Plaque Psoriasis

March 10, 2016

THOUSAND OAKS, Calif., March 10, 2016 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced that the U.S. Food and Drug Administration (FDA) has accepted for review Amgen's supplemental Biologics License Application (sBLA) for the expanded use of Enbrel® (etanercept) to treat pediatric patients with chronic severe plaque psoriasis.

"If approved, ENBREL would be the first systemic drug approved in the U.S. to treat chronic severe plaque psoriasis in pediatric patients," said Sean E. Harper, M.D., executive vice president of Research and Development at Amgen. "We hope to be able to provide pediatric patients with an important new treatment option where there is a clear unmet medical need."

The sBLA, submitted on Jan. 5, 2016, is based on results from a Phase 3 one-year study and its five-year open-label extension study to evaluate the safety and efficacy of ENBREL in pediatric patients with moderate to severe plaque psoriasis.

The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of Nov. 5, 2016, for the ENBREL sBLA application.

### About Psoriasis

Psoriasis is a serious, chronic inflammatory disease that causes raised, red, scaly patches to appear on the skin, typically affecting the outside of the elbows, knees or scalp, though it can appear on any location.<sup>1,2</sup> Approximately 125 million people worldwide have psoriasis and 80 percent of those patients have plaque psoriasis.<sup>3,4</sup> About one-third of psoriasis cases are pediatric.<sup>5</sup>

### About ENBREL® (etanercept)

ENBREL is a soluble form of a tumor necrosis factor (TNF) receptor with a clinical efficacy and safety profile established over 15 years of collective clinical experience. ENBREL was first approved in 1998 for moderate-to-severe rheumatoid arthritis. ENBREL was approved in 1999 to treat moderate-to-severe polyarticular juvenile idiopathic arthritis, in 2002 to treat psoriatic arthritis, for the treatment of patients with ankylosing spondylitis in 2003, and in 2004 to treat moderate-to-severe plaque psoriasis in adults. Prescription ENBREL is given by injection.

### ENBREL indications in the U.S.:

- ENBREL is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately-to-severely active rheumatoid arthritis (RA). ENBREL can be initiated in combination with methotrexate (MTX) or used alone.
- ENBREL is indicated for reducing signs and symptoms of moderately-to-severely active polyarticular juvenile idiopathic arthritis in patients ages two and older.
- ENBREL is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis. ENBREL can be used with or without methotrexate.
- ENBREL is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.
- ENBREL is indicated for the treatment of adult patients (18 years or older) with chronic moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

### Important Safety Information

**Patients treated with ENBREL 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 or were predisposed to infection because of their underlying disease. ENBREL should not be initiated in the presence of sepsis, active infections, or allergy to ENBREL or its components. ENBREL should be discontinued if a patient develops a serious infection or sepsis. Reported infections include: 1) Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before ENBREL use and periodically during therapy. Treatment for latent infection should be initiated prior to ENBREL use, 2) 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. Empiric antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness, and 3) Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

**The risks and benefits of treatment with ENBREL should be carefully considered prior to initiating therapy in patients 1) with chronic or recurrent infection, 2) who have been exposed to TB, 3) who have resided or traveled in areas of endemic TB or endemic mycoses, or 4) with underlying conditions that may predispose them to infections such as advanced or poorly controlled diabetes. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with ENBREL, including the possible development of TB in patients who tested negative for latent TB prior to initiating therapy.**

**Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including ENBREL.**

In adult clinical trials of all TNF blockers, more cases of lymphoma were seen compared to control patients. The risk of lymphoma may be up to several-fold higher in RA and psoriasis patients. The role of TNF blocker therapy in the development of malignancies is unknown. Cases of acute and

chronic leukemia have been reported in association with postmarketing TNF blocker use in RA and other indications. The risk of leukemia may be higher in patients with RA (approximately 2-fold) than the general population. Melanoma and non-melanoma skin cancer (NMSC) have been reported in patients treated with TNF blockers, including ENBREL. Periodic skin examinations should be considered for all patients at increased risk for skin cancer. In patients who initiated therapy at  $\leq 18$  years of age, approximately half of the reported malignancies were lymphomas (Hodgkin's and non-Hodgkin's lymphoma). Other cases included rare malignancies usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

Treatment with TNF-blocking agents, including ENBREL, has been associated with rare ( $< 0.1\%$ ) cases of new onset or exacerbation of central nervous system demyelinating disorders, some presenting with mental status changes and some associated with permanent disability, and with peripheral nervous system demyelinating disorders. Cases of transverse myelitis, optic neuritis, multiple sclerosis, Guillain-Barré syndromes, other peripheral demyelinating neuropathies, and new onset or exacerbation of seizure disorders have been reported in postmarketing experience with ENBREL therapy. Prescribers should exercise caution in considering the use of ENBREL in patients with preexisting or recent-onset central or peripheral nervous system demyelinating disorders.

Cases of worsening congestive heart failure (CHF) and, rarely, new-onset cases have been reported in patients taking ENBREL. Caution should be used when using ENBREL in patients with CHF. These patients should be carefully monitored. Rare cases of pancytopenia, including aplastic anemia, some fatal, have been reported. The causal relationship to ENBREL therapy remains unclear. Exercise caution when considering ENBREL in patients who have a previous history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection. Consider discontinuing ENBREL if significant hematologic abnormalities are confirmed. Reactivation of hepatitis B has been reported in patients who were previously infected with hepatitis B virus (HBV) and received concomitant TNF-blocking agents, including ENBREL. Most reports occurred in patients also taking immunosuppressive agents, which may contribute to hepatitis B reactivation. Exercise caution when considering ENBREL in these patients.

Allergic reactions associated with administration of ENBREL during clinical trials have been reported in  $< 2\%$  of patients. If an anaphylactic reaction or other serious allergic reaction occurs, administration of ENBREL should be discontinued immediately and appropriate therapy initiated. Live vaccines should not be administered to patients on ENBREL. JIA patients, if possible, should be brought up to date with all immunizations prior to initiating ENBREL. In patients with exposure to varicella virus, consider temporary discontinuation of ENBREL and prophylactic treatment with Varicella Zoster Immune Globulin. Autoantibodies may develop with ENBREL, and rarely lupus-like syndrome or autoimmune hepatitis may occur. These may resolve upon withdrawal of ENBREL. Stop ENBREL if lupus-like syndrome or autoimmune hepatitis develops. The use of ENBREL in patients with Wegener's granulomatosis receiving immunosuppressive agents (e.g., cyclophosphamide) is not recommended. Based on a study of patients treated for alcoholic hepatitis, exercise caution when using ENBREL in patients with moderate-to-severe alcoholic hepatitis.

The most commonly reported adverse events in RA clinical trials were injection site reaction, infection, and headache. In clinical trials of all other adult indications, adverse events were similar to those reported in RA clinical trials. In a JIA study, adverse reactions in pediatric patients were generally similar in frequency and type as those seen in adult patients. The types of infections reported in pediatric patients were generally mild and consistent with those commonly seen in the general pediatric population.

**Please see Prescribing Information and Medication Guide at [www.ENBREL.com](http://www.ENBREL.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 biologics manufacturing 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](http://www.amgen.com) and follow us on [www.twitter.com/amgen](https://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 Inc. and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements. Forward-looking statements involve significant risks and uncertainties, including those discussed below and more fully described in the Securities and Exchange Commission (SEC) reports filed by Amgen Inc., including Amgen Inc.'s 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 March 10, 2016, and expressly disclaims any duty to update information contained in this news release.

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. Even when clinical trials are successful, regulatory authorities may question the sufficiency for approval of the trial endpoints we have selected. In addition, 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. 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 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. We perform a substantial amount of our manufacturing activities at a few key manufacturing 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, sales of our products are affected by the 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. Government and others' regulations and reimbursement policies as well as political and public scrutiny may affect the development, usage and pricing of our 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. We believe that some of our newer products, product candidates or new indications for existing products, may face competition when and as they are approved and marketed. Our products may compete against products that have lower prices, established reimbursement, superior performance, are easier to administer, or that are otherwise competitive with our products. We expect to face increasing competition from biosimilars. In addition, while we routinely obtain patents for products and technology, the protection of our products offered by patents and patent applications may be challenged, invalidated or circumvented by competitors and there can be no guarantee of our ability to obtain or maintain patent protection for our products or product candidates or to prevail in intellectual property litigation. We cannot guarantee that we will be able to produce commercially successful products or maintain the commercial success of our existing products. Our stock price may be volatile and may be affected by actual or perceived market opportunity, competitive position, and success or failure of our products or product candidates. Further, 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 Amgen, or at all. 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 common stock.

The scientific information discussed in this news release related to new indications for Amgen's 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.

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References:

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- <sup>3</sup> International Federation of Psoriasis Associations. Psoriasis is a Serious Disease Deserving Global Attention: A report by the International Federation of Psoriasis Associations. [www.ifpa-pso.org/getfile.ashx?cid=279366&cc=3&refid=18](http://www.ifpa-pso.org/getfile.ashx?cid=279366&cc=3&refid=18). Accessed on February 19, 2016.
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