



## New Two-Year Data Show That Most Rheumatoid Arthritis Patients Treated with ENBREL Plus Methotrexate Had No Progression of Joint Damage

October 18, 2004

Additional Data Demonstrated that Patients Treated with ENBREL

Plus Methotrexate had Greater Improvement in Physical Function Scores

After Two Years Compared to Methotrexate Alone

THOUSAND OAKS, Calif. & COLLEGEVILLE, Pa.--(BUSINESS WIRE)--Oct. 18, 2004-- Nearly three quarters (74.2 percent) of rheumatoid arthritis (RA) patients treated with ENBREL(R) (etanercept) plus methotrexate combination therapy experienced no progression of joint damage over a continuous two-year span. These new two-year results from the ongoing TEMPO (Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes) study were presented today at the American College of Rheumatology's Annual Scientific Meeting in San Antonio, Texas.

"It is remarkable to see that a large majority of patients experienced no progression of joint damage while on ENBREL and methotrexate combination therapy. Moreover, the patients taking the combination therapy had better mean x-ray scores as a group after two years compared to baseline," said Desiree van der Heijde, M.D., professor of rheumatology, University of Maastricht in the Netherlands. "These data confirm the one year results and underscore the importance of aggressive treatment to help prevent long-term disability."

At two years, 74.2 percent of patients taking ENBREL and methotrexate combination therapy had no progression of joint damage as assessed by Total Sharp Scores (TSS). These validated scores are calculated by using x-ray measurements to assess joint damage. No progression is defined as a mean change from baseline in TSS less than or equal to 0. By comparison, 65.5 percent and 59.2 percent of ENBREL monotherapy and methotrexate monotherapy-treated patients, respectively, had no radiographic progression of joint damage at two years.

Further, data presented at ACR show that improvement in physical function scores were higher for the ENBREL combination group than those taking either therapy alone. Patients treated with ENBREL combination therapy experienced a 56 percent mean improvement in Health Assessment Questionnaire (HAQ) scores from baseline, compared to 39 percent mean improvement in patients treated with ENBREL alone and 36 percent mean improvement in patients treated with methotrexate alone. HAQ scores measure a patient's ability to perform activities of daily living such as dressing, walking and grooming.

The ENBREL TEMPO study randomized 686 patients with RA, of which 622 were included in the two-year radiographic analysis. Patients received either ENBREL (25 mg twice weekly), methotrexate (up to 20 mg once weekly), or ENBREL (25 mg twice weekly) plus methotrexate once weekly. Patients in the ENBREL TEMPO trial had active RA and an inadequate response to at least one disease-modifying antirheumatic drug (DMARD) other than methotrexate. The primary radiographic endpoint was the change from baseline in the van der Heijde-modified TSS at one year. Secondary radiographic endpoints included changes in total erosions, changes in total joint space narrowing, number of eroded joints and percent of patients with no radiographic progression.

Treatment with ENBREL therapy was generally well-tolerated.

ABOUT RA

More than two million Americans suffer from RA, which can cause stiffness, swelling and limitation in the motion and function of multiple joints. If RA is left untreated, patients can become disabled from joint damage caused by the disease, limiting their ability to function.

ABOUT ENBREL

ENBREL is the only fully human TNF receptor approved to reduce signs and symptoms, induce major clinical response, improve physical function, and inhibit the progression of structural damage in patients with moderately to severely active rheumatoid arthritis (RA). ENBREL is approved for first-line treatment of RA patients and can be used alone or in combination with methotrexate.

ENBREL is also indicated to reduce the signs and symptoms and inhibit the progression of structural damage of active arthritis in patients with psoriatic arthritis. It is approved to reduce the signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis (JRA) in patients who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). It is also the first biologic approved to treat the signs and symptoms in patients with active ankylosing spondylitis (AS). 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.

ENBREL has been used by more than 250,000 patients worldwide across indications.

ENBREL acts by binding TNF, one of the dominant inflammatory cytokines or regulatory proteins that play an important role in both normal immune function and the cascade of reactions involved in the inflammatory process of RA, JRA, psoriasis, psoriatic arthritis and AS. The binding of ENBREL to TNF renders the bound TNF biologically inactive, resulting in significant reduction in inflammatory activity.

Since the product was first introduced, the following have been reported in patients using ENBREL:

- Serious Infections
- Many occurred in people prone to infection, such as those with advanced or poorly controlled diabetes
- Some serious infections were fatal
- Rare cases of tuberculosis

- What to do/Not to do
- Do not start ENBREL if you have an infection or are allergic to ENBREL or its components.
- Tell your doctor if you are prone to infection.
- Stop ENBREL if a serious infection occurs.
- Contact your doctor if you have questions about ENBREL or develop an infection.
- Tell your doctor if you have ever been treated for heart failure.
- Serious nervous system disorders such as multiple sclerosis, seizures, or inflammation of the nerves of the eyes
- Tell your doctor if you have ever had any of these disorders or if you develop them after starting ENBREL.
- Rare reports of serious blood disorders (some fatal)
- Contact your doctor immediately if you develop symptoms such as persistent fever, bruising, bleeding, or paleness.
- In medical studies of all TNF-inhibitors, a higher rate of lymphoma (a type of cancer) was seen compared to the general population, however, the risk of lymphoma may be up to several fold higher in RA and psoriasis patients.
- The role of TNF-inhibitors in the development of lymphoma is unknown.
- The incidence of other cancers has not increased with extended exposure to ENBREL and is similar to the expected rate.
- ENBREL can also cause injection site reactions.
- In a medical study of patients with JRA, infections, headaches, abdominal pain, vomiting, and nausea occurred more frequently than in adults.
- The kinds of infections reported were generally mild and similar to those usually seen in children.
- Other serious adverse reactions were reported rarely, including serious infections (2 percent) and depression/personality disorder (1 percent).

Amgen Inc. and Wyeth Pharmaceuticals, a division of Wyeth, market ENBREL in North America. Wyeth markets ENBREL outside of North America. Immunex Corporation, a wholly owned subsidiary of Amgen, manufactures ENBREL. Additional information about ENBREL, including full Prescribing Information, can be found on the Web site sponsored by the companies at [www.enbrel.com](http://www.enbrel.com) or by calling toll free 888-4ENBREL (888-436-2735).

Amgen is a global biotechnology company that discovers, develops, manufactures and markets important human therapeutics based on advances in cellular and molecular biology. Wyeth Pharmaceuticals, a division of Wyeth, has leading products in the areas of women's health care, cardiovascular disease, central nervous system, inflammation, transplantation, hemophilia, oncology, vaccines and nutritional products. Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing, and marketing of pharmaceuticals, vaccines, biotechnology products and nonprescription medicines that improve the quality of life for people worldwide. The Company's major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare, and Fort Dodge Animal Health.

This news release contains forward-looking statements that involve significant risks and uncertainties, including those discussed below and others that can be found in Amgen's Form 10-K for the year ended December 31, 2003, and in Amgen's periodic reports on Form 10-Q and Form 8-K. 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 Amgen projects. 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 Amgen to complete clinical trials and obtain regulatory approval for product marketing has in the past varied and Amgen expects similar variability in the future.

Amgen develops 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 Amgen may have believed at the time of entering into such relationship. Also, Amgen or others could identify side effects or manufacturing problems with Amgen's products after they are on the market.

In addition, sales of Amgen's products are affected by the availability of reimbursement and the reimbursement policies imposed by third party payors, including governments, private insurance plans and managed care providers, and may be affected by domestic and international trends toward managed care and healthcare cost containment as well as possible U.S. legislation affecting pharmaceutical pricing and reimbursement. Government regulations and reimbursement policies may affect the development, usage and pricing of our products. In addition, Amgen competes with other companies with respect to some of Amgen's marketed products as well as for the discovery and development of new products. Amgen believes that some of its newer products, product candidates or new indications for existing products may face competition when and as they are approved and marketed. Amgen's products may compete against products that have lower prices, established reimbursement, superior performance, are easier to

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The scientific information discussed in this news release related to Amgen's product candidates is preliminary and investigative. Such product candidates are not approved by the U.S. Food and Drug Administration (FDA), and no conclusions can or should be drawn regarding the safety or effectiveness of the product candidates. Only the FDA can determine whether the product candidates are safe and effective for the use(s) being investigated. Further, the scientific information discussed in this news release relating to new indications for our products is preliminary and investigative and is not part of the labeling approved by the U.S. Food and Drug Administration (FDA) 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. Only the FDA can determine whether the products are safe and effective for these uses. Healthcare professionals should refer to and rely upon the FDA-approved labeling for the products, and not the information discussed in this news release.

The statements in this press release that are not historical facts are forward-looking statements based on current expectations of future events that involve risks and uncertainties including, without limitation, risks associated with the inherent uncertainty of pharmaceutical research, product development, manufacturing, and commercialization, and economic conditions, including interest and currency exchange rate fluctuations, the impact of competitive or generic products, product liability and other types of lawsuits, the impact of legislative and regulatory compliance and obtaining approvals, and patents, and other risks and uncertainties, including those detailed from time to time in Wyeth's periodic reports, including quarterly reports on Form 10-Q and the Annual Report on Form 10-K, filed with the Securities and Exchange Commission. Actual results may vary materially from the forward-looking statements. Wyeth assumes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

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**SOURCE: Amgen**