



## **Study Showed Half of Patients Treated with Enbrel(R) (etanercept) Plus Methotrexate Can Achieve DAS Clinical Remission and 80 Percent Had No Progression of Joint Damage in Active Early Rheumatoid Arthritis**

July 15, 2008

Data Demonstrated Benefits of Early Treatment in Patients with Moderate-to-Severe Rheumatoid Arthritis (RA)

COLLEGEVILLE, Pa. & THOUSAND OAKS, Calif.--(BUSINESS WIRE)--July 15, 2008--Wyeth Pharmaceuticals, a division of Wyeth (NYSE: WYE) and Amgen (NASDAQ:AMGN) today announced the publication of data from the COMET (COmbination of Methotrexate and ETanercept in Active Early Rheumatoid Arthritis) trial demonstrating that half of patients treated with the combination of ENBREL and methotrexate achieved Disease Activity Score (DAS) clinical remission and nearly all had no progression of joint damage. These findings were published online on July 15 by The Lancet, a leading global medical journal.

According to study results at one year, 50 percent of patients (n = 265) with active early moderate-to-severe rheumatoid arthritis who received a combination of ENBREL and methotrexate therapy achieved DAS clinical remission (DAS28 less than 2.6) versus 28 percent (n = 263) of those treated with methotrexate alone. DAS28 is a measure of joint swelling and tenderness (based on 28 joints), as well as overall disease activity measured by a global health assessment and an objective marker of inflammation (erythrocyte sedimentation rate). DAS28 is a modified measure of the DAS44, which is a validated tool used in clinical trials and serves as the basis for the European League Against Rheumatism (EULAR) response criteria.

"We hope that these data encourage physicians to use clinical remission as a new standard for evaluating symptom control in the treatment of early RA," said Paul Emery, M.D., lead COMET trial investigator and Professor of Rheumatology, University of Leeds, UK. "Clinical remission is highly relevant to patients' daily lives as they cope with their symptoms."

Additionally, at one year, 80 percent of patients (n = 246) receiving ENBREL and methotrexate had no evidence of progression of joint damage as seen on x-ray, compared to 59 percent (n = 230) of those treated with methotrexate alone.

Combination therapy with ENBREL plus methotrexate also helped patients remain more functionally active. Based on the Health Assessment Questionnaire (used to assess certain daily life activities), 61 percent (n = 256) of patients treated with combination therapy demonstrated improvement in their functionality versus 44 percent (n = 241) of those treated with only methotrexate. Further, the COMET trial showed that patients who were treated with combination therapy had a nearly three-fold reduction in work stoppage compared with those who received methotrexate alone.

"It's important for people living with a chronic disease like moderate to severe rheumatoid arthritis to be able to continue with their daily life activities," said Dr. Emery. "These data show that if patients receive combination treatment early, they are more likely to be able to continue with their daily activities, including going to work, than those treated with methotrexate alone."

American College of Rheumatology (ACR) scores were also assessed in the COMET study and were comparable to the DAS clinical remission data. Nearly half of patients receiving ENBREL plus methotrexate achieved an ACR 70 score, versus 28 percent of the methotrexate-only group. The percentage of patients who achieve an ACR 70 score represent those who achieve a 70 percent improvement in select RA symptoms, including joint swelling and tenderness, pain, level of disability, overall patient and physician disease assessment, and an objective marker of inflammation, such as erythrocyte sedimentation rate.

The COMET study is a 24-month, double-blind, randomized, parallel group, multicenter, outpatient study. The data published in The Lancet represent the results of the first year of treatment, in which patients were randomly assigned to receive combination ENBREL 50 mg plus methotrexate therapy, or methotrexate alone, once a week for 52 weeks. The population under study had less than two years (median seven months) of moderately to severely active disease.

At one year, there were no differences in rates of serious infections or malignancies among patients in the ENBREL plus methotrexate group compared with the methotrexate-only group. No cases of tuberculosis or demyelinating disease were reported. No new safety signals were identified.

In other RA clinical trials of ENBREL, the most common adverse events were injection site reaction, infection, and headache. Rare cases of tuberculosis and demyelinating diseases have been reported in post-marketing surveillance.

To view the abstract of this manuscript, please visit the following Web site: [www.thelancet.com/journals/lancet](http://www.thelancet.com/journals/lancet).

### **ABOUT ENBREL**

ENBREL is a soluble form of a fully human tumor necrosis factor (TNF) receptor and has 16 years of collective clinical experience with an established safety profile. ENBREL was first approved in 1998 for moderate to severe rheumatoid arthritis and was later approved to treat children and adolescents with juvenile rheumatoid arthritis (now called juvenile idiopathic arthritis) in 1999. ENBREL was approved in 2004 to treat moderate to severe plaque psoriasis in adults.

ENBREL indications in the U.S.:

-- ENBREL is indicated for reducing signs and symptoms, keeping joint damage from getting worse, and improving physical function in patients with moderate to severe rheumatoid arthritis. ENBREL can be taken with methotrexate or used alone.

-- ENBREL is indicated for reducing the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients ages 2 and older.

-- ENBREL is indicated for reducing signs and symptoms, keeping joint damage from getting worse, and improving physical function in patients with psoriatic arthritis. ENBREL can be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.

-- 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

What important safety information do I need to know about taking prescription ENBREL?

ENBREL is a type of protein called a tumor necrosis factor (TNF) blocker that blocks the action of a substance your body's immune system makes called TNF. People with an immune disease, such as rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, or psoriasis, have too much TNF in their bodies. ENBREL can reduce the amount of active TNF in the body to normal levels, helping to treat your disease. But, in doing so, ENBREL can also lower the ability of your immune system to fight infections.

Serious infections, including tuberculosis (TB), have happened in patients taking ENBREL. Some of these serious infections have been fatal. Many serious infections occurred in people prone to infection. Serious infections have also occurred in patients with advanced or poorly controlled diabetes. Do not start ENBREL if you have an infection or are allergic to ENBREL or its components. Once on ENBREL, if you get an infection or have any sign of an infection, including fever, cough, or flu-like symptoms, or have open sores, tell your doctor. Your doctor should test you for TB before starting ENBREL and should monitor you closely for signs and symptoms of TB.

Serious nervous system disorders, such as multiple sclerosis, seizures, or inflammation of the nerves of the eyes have been reported. There have been rare reports of serious blood disorders (some fatal).

In medical studies, more cases of lymphoma (a type of cancer) were seen in patients taking TNF blockers compared to similar patients who were not taking TNF blockers. The risk of lymphoma may be several-fold higher in people with rheumatoid arthritis and psoriasis; the role of TNF blockers in the development of malignancies is unknown.

Tell your doctor if you:

- Think you have, are being treated for, have signs of, or are prone to infection
- Have any open sores
- Have or have had TB or hepatitis B
- Have ever been treated for heart failure
- Have ever had or develop a serious nervous system disorder
- Develop symptoms such as persistent fever, bruising, bleeding, or paleness while taking ENBREL

Common side effects in adult clinical trials were injection site reaction, infection and headache.

In a medical study of patients with JIA, infection, headache, 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, including serious infection and depression/personality disorder.

If you have any questions about this information, be sure to discuss them with your doctor. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.

Please visit [www.enbrel.com](http://www.enbrel.com) or call 1-888-4ENBREL to request additional information, including the full U.S. Prescribing Information and Medication Guide.

#### About Amgen and Wyeth

Amgen 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.

Amgen discovers, develops, manufactures and delivers innovative human therapeutics. A biotechnology pioneer since 1980, Amgen was one of the first companies to realize the new science's promise by bringing safe and effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, and other serious illnesses. With a deep and broad pipeline of potential new medicines, Amgen remains committed to advancing science to dramatically improve people's lives. To learn more about our pioneering science and our vital medicines, visit [www.amgen.com](http://www.amgen.com).

Wyeth Pharmaceuticals, a division of Wyeth, has leading products in the areas of women's health care, infectious disease, gastrointestinal health, 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 non-prescription 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. To

learn more, visit [www.wyeth.com](http://www.wyeth.com).

#### Amgen Forward-Looking Statement

This news release contains forward-looking statements that are based on Amgen's current expectations and beliefs 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, 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 (SEC) reports filed by Amgen, including Amgen's most recent annual report on Form 10-K and most recent periodic reports on Form 10-Q and Form 8-K. Please refer to Amgen's most recent Forms 10-K, 10-Q and 8-K for additional information on the uncertainties and risk factors related to Amgen's business. Unless otherwise noted, Amgen is providing this information as of July 15, 2008, 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 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 safety, side effects or manufacturing problems with Amgen's products after they are on the market. Amgen's business may be impacted by government investigations, litigation and products liability claims. Amgen depends on third parties for a significant portion of its manufacturing capacity for the supply of certain of its current and future products and limits on supply may constrain sales of certain of its current products and product candidate development.

In addition, sales of Amgen's products are affected by the reimbursement policies imposed by third-party payors, 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 health care cost containment as well as U.S. legislation affecting pharmaceutical pricing and reimbursement. Government and others' regulations and reimbursement policies may affect the development, usage and pricing of Amgen's products. In addition, Amgen competes with other companies with respect to some of its 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 administer, or that are otherwise competitive with its products. In addition, while Amgen routinely obtain patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors and there can be no guarantee of Amgen's ability to obtain or maintain patent protection for its products or product candidates. Amgen cannot guarantee that it will be able to produce commercially successful products or maintain the commercial success of its existing products. Amgen's stock price may be affected by actual or perceived market opportunity, competitive position, and success or failure of its products or product candidates. Further, the discovery of significant problems with a product similar to one of Amgen's products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on Amgen's business and results of operations.

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 Amgen's products is preliminary and investigative and is not part of the labeling approved by the 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.

#### Wyeth Forward-Looking Statement

The statements in this press release that are not historical facts are forward-looking statements based on current expectations of future events and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. These risks and uncertainties include the inherent uncertainty of the timing and success of, and expense associated with, research, development, regulatory approval and commercialization of our products, including with respect to our pipeline products; government cost-containment initiatives; restrictions on third-party payments for our products; substantial competition in our industry, including from branded and generic products; data generated on our products; the importance of strong performance from our principal products and our anticipated new product introductions; the highly regulated nature of our business; product liability, intellectual property and other litigation risks and environmental liabilities; uncertainty regarding our intellectual property rights and those of others; difficulties associated with, and regulatory compliance with respect to, manufacturing of our products; risks associated with our strategic relationships; economic conditions including interest and currency exchange rate fluctuations; changes in generally accepted accounting principles; trade buying patterns; the impact of legislation and regulatory compliance; risks and uncertainties associated with global operations and sales; and other risks and uncertainties, including those detailed from time to time in our periodic reports filed with the Securities and Exchange Commission, including our current reports on Form 8-K, quarterly reports on Form 10-Q and annual report on Form 10-K, particularly the discussion under the caption "Item 1A, RISK FACTORS." The forward-looking statements in this press release are qualified by these risk factors. We assume no obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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SOURCE: Amgen