



## Enbrel is First Biologic to Receive FDA Approval for the Treatment of Ankylosing Spondylitis

July 24, 2003

### FOR IMMEDIATE RELEASE

**THOUSAND OAKS, Calif., and COLLEGEVILLE, Pa.**, July 24, 2003 - Amgen (NASDAQ: AMGN) and Wyeth Pharmaceuticals, a division of Wyeth (NYSE: WYE), today announced that ENBREL <sup>®</sup> (etanercept) (25 mg twice weekly) is the first biologic to be approved by the U.S. Food and Drug Administration (FDA) to reduce the signs and symptoms in patients with active ankylosing spondylitis (AS). Ankylosing spondylitis marks the fourth indication for ENBREL. The FDA's decision follows an expedited review.

"The approval of ENBREL for the treatment of AS is truly exciting, offering many patients significant relief of symptoms such as back pain, morning stiffness and fatigue as rapidly as two weeks after initiation of therapy. Also, for the first time, we see improvement in spinal mobility which is a debilitating symptom of the disease," said Kevin Young, vice president of Amgen's Inflammation Business Unit.

Ankylosing spondylitis, which affects approximately 350,000 people in the United States, is a painful, and potentially progressive inflammatory disease affecting joints and ligaments that normally allow a person's back to move and flex. The disease most often occurs in the lower back but can affect the upper spine, chest, and neck. The spine can fuse, causing loss of motion and a permanent stooped-over posture. Ankylosing spondylitis may also involve other joints, such as the hips, shoulders, knees, and ankles. Unlike some other forms of arthritis, AS frequently strikes between the ages of 16 and 30. It tends to affect more men than women.

"Ankylosing spondylitis is widely underdiagnosed and in its most severe forms, can be devastating to a person's ability to function at home or work," said Jane Bruckel, RN, executive director of the Spondylitis Association of America.

"We are pleased to now be able to offer ENBREL to physicians and patients battling ankylosing spondylitis," said Dr. Victoria Kusiak, vice president of global medical affairs and North American medical director of Wyeth Pharmaceuticals. "ENBREL has a history of proven efficacy and tolerability which will be important to physicians introducing the therapy to a new group of patients."

In a pivotal Phase 3 study (n=277), 60 percent of patients treated with ENBREL (n=138) achieved a 20 percent improvement in the Assessment in Ankylosing Spondylitis Response Criteria (ASAS 20), a composite measure that includes back pain, morning stiffness, inflammation and physical function, compared with 27 percent of patients receiving placebo after 12 weeks. At 24 weeks, 58 percent of patients treated with ENBREL achieved this significant reduction compared with 23 percent of the placebo patients.

Adverse events were similar to those reported in previous clinical trials of ENBREL, with injection site reactions occurring more frequently than in the placebo group. The most frequent adverse events in placebo-controlled rheumatoid arthritis (RA) clinical trials (n=349) were injection site reactions (ISR) (37%), infections (35%), and headache (17%). Only the rate of ISR was higher than that of placebo. The most frequent adverse events in a methotrexate-controlled trial (n=415) were infections (64%), ISR (34%), and headache (24%). Only the rate of ISR was higher than that of methotrexate.

### ABOUT ENBREL

ENBREL is the only fully human anti-TNF receptor approved to reduce the signs and symptoms and inhibit the structural damage in patients with moderately to severely active RA, and to reduce the signs and symptoms of active arthritis in patients with psoriatic arthritis. ENBREL can be used in combination or alone. It is also 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 disease-modifying medicines.

Physicians have become familiar with the benefits and proven long-term tolerability profile of ENBREL. It has been used to treat over 180,000 patients worldwide across all indications since becoming commercially available nearly five years ago.

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 that causes the inflammatory process of psoriatic arthritis, RA 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 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
- 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
- The incidence of cancer 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%) and depression/personality disorder (1%)

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 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 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, hemophilia, oncology and vaccines. 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.

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, 2002, 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 we project. Amgen's results may be affected by its ability to successfully market both new and existing products domestically and internationally, sales growth of recently launched products, difficulties or delays in manufacturing its products, and regulatory developments (domestic or foreign) involving current and future products and manufacturing facilities. In addition, sales of Amgen's products are affected by 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 Amgen's products. Furthermore, Amgen's research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. Amgen or others could identify side effects or manufacturing problems with its products after they are on the market. 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. Discovery or identification of new product

candidates cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate will be successful and become a commercial product. In addition, while Amgen routinely obtains patents for its products and technology, the protection offered by its patents and patent applications may be challenged, invalidated or circumvented by its competitors. Further, some raw materials, medical devices and component parts for Amgen's products are supplied by sole third party suppliers.

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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For further information, please contact:

Amgen Wyeth Pharmaceuticals Media: 805/447-4587 Douglas Petkus (media) Investors: 805/447-1060 484/865-5140 Justin Victoria (investors) 973/660-5340