



## Long-Term Data Support Sustained Efficacy, Tolerability and Increased Vitality For Psoriatic Arthritis Patients Treated With ENBREL and Landmark Phase 3 Data Show Ankylosing Spondylitis Patients Experienced Partial Clinical Remission, Improved Pain Relief

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THOUSAND OAKS, Calif. and COLLEGEVILLE, Pa., Oct 24, 2003 -- Data on Enbrel(R) (etanercept) demonstrate improvements that were sustained for more than one year in many patients in both the joint symptoms and skin lesions associated with psoriatic arthritis, according to reports presented this week at the American College of Rheumatology's (ACR) Annual Scientific Meeting in Orlando, Fla. Additional ENBREL data showed that patients with ankylosing spondylitis (AS) experienced statistically significant improvements in patient-reported outcomes, including pain, fatigue and functional status.

Psoriatic arthritis and AS belong to a group of diseases referred to as the spondylarthropathies. Spondylarthropathies are arthritic in nature, can affect the spine and joints and can occur in young adults, commonly beginning before the age of 35. ENBREL is the only therapy approved to reduce signs and symptoms and inhibit the progression of structural damage of active arthritis in patients with psoriatic arthritis and is the only anti-TNF receptor approved to reduce signs and symptoms in patients with active AS.

### Sustained Efficacy, Tolerability and Improved Function in Psoriatic Arthritis Patients

In an open-label extension study of 169 patients, ENBREL was generally well-tolerated and demonstrated sustained efficacy, reducing clinical signs and symptoms of psoriatic arthritis for up to 106 weeks in many patients. These patients experienced less joint pain, fewer swollen joints and exhibited clearer skin.

At 48 weeks (n=145), 66 percent of patients treated with ENBREL achieved an ACR 20, and 47 percent achieved an ACR 50 (improvement in ACR score of 20 or 50 percent, respectively). Fifty-seven percent of patients also had substantial clearing of their psoriasis plaques.

Patients also completed a Health Assessment Questionnaire (HAQ), which included measures of vitality and questions regarding activities of daily living. Thirty-nine percent of patients achieved a HAQ score of zero, indicating no functional disability, at 48 weeks. In another analysis of these psoriatic arthritis patients (n=69), many of those treated with ENBREL experienced a significant, rapid and sustained increase in their ability to perform daily activities such as walking, dressing, grooming and gripping, for up to 72 weeks as assessed by HAQ scores.

"Patients with psoriatic arthritis experience painful and debilitating symptoms that affect many basic activities, such as dressing, that most of us take for granted," said Philip Mease, M.D., lead study investigator and chief of rheumatology clinical research at Swedish Hospital Medical Center in Seattle. "It is gratifying as a physician to see patients on ENBREL experiencing long-term improvement of painful joints and unsightly skin lesions, allowing them to resume normal activities of daily living and participate confidently in family, social and work life."

### Ankylosing Spondylitis Patients Feel Improvements With ENBREL Treatment

In a landmark Phase 3 study, patients taking ENBREL experienced rapid and statistically significant improvements in patient-reported outcomes, including pain, overall disease activity, function and fatigue in as early as two weeks, compared with patients receiving placebo.

After six months, 57 percent of patients achieved a 20 percent improvement in the Assessment on Ankylosing Spondylitis Response Criteria (ASAS 20) compared to 22 percent for those taking placebo. ASAS is a composite measure that includes back pain, morning stiffness, inflammation and physical function. Approximately 17 percent of patients achieved partial remission, compared to four percent taking placebo. Partial remission, as defined by ASAS is a low disease activity level (absolute score less than or equal to 20 for the four ASAS criteria).

"ENBREL actually induced partial remission in some patients in a very short time after initiation of treatment," said John C. Davis, M.D., University of California, San Francisco. "This was a significant improvement for these patients."

### About Psoriatic Arthritis

Psoriatic arthritis is a chronic inflammatory disease of the joints and connective tissue. The disease involves joint pain and swelling that can lead to debilitation with inflamed and irritated scaly red patches of skin. The disease can be difficult to diagnose, particularly in its milder forms and earlier stages. Up to one million people in the U.S. population have psoriatic arthritis. ENBREL is the first and only biologic approved to reduce the signs and symptoms and to inhibit the progression of structural damage of active arthritis in patients with psoriatic arthritis.

### About AS

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 spine can fuse, causing loss of motion and a permanent stooped-over posture. AS frequently strikes between the ages of 16 and 30 and tends to affect more men than women.

### About ENBREL

ENBREL is the only fully human TNF receptor approved to reduce signs and symptoms, improve physical function, and inhibit the progression of structural damage in patients with moderately to severely active rheumatoid arthritis (RA), and to reduce the signs and symptoms and inhibit the progression of structural damage of active arthritis in patients with psoriatic arthritis. ENBREL is the only biologic therapy approved for first-line treatment of RA patients, and can be used alone or in combination with methotrexate. 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 has been used by more than 200,000 patients worldwide across 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 RA, JRA, psoriatic arthritis and AS. The binding of ENBREL to TNF renders the bound TNF biologically inactive, resulting in significant reduction in inflammatory activity.

Adverse events in psoriatic arthritis and AS clinical trials were similar to those reported in previous clinical trials of ENBREL in patients with rheumatoid arthritis. There was no increase in the number of serious adverse events occurring in patients treated with ENBREL compared to those receiving placebo. Only the rate of injection site reactions (ISRs) in patients receiving ENBREL was statistically different compared to those receiving placebo (36 percent with ENBREL versus 9 percent in placebo-treated patients).

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
- \* 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 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 (two percent) and depression/personality disorder (one percent)

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. 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.

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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.

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