Pfizer Logo

Treatment with Enbrel® (etanercept) Shows Significant and Sustained Clinical Benefits in Rheumatoid Arthritis (RA) Patients with Moderately Active Disease

Saturday, November 05, 2011 - 07:50am

Amgen and Pfizer Announce Results From the Largest Completed Clinical Trial of a Biologic Therapy in Adults with Moderately Active RA

"These data show that patients with moderately active disease who achieve LDA or clinical remission with ENBREL treatment may lose these clinical benefits if ENBREL is discontinued."

(BUSINESS WIRE)--Amgen (NASDAQ: AMGN) and Pfizer Inc. (NYSE: PFE) today announced results of the second and final period of the PRESERVE trial. PRESERVE is a two-period multi-center trial in patients with moderately active rheumatoid arthritis (RA) who achieved Disease Activity Score (DAS) 28 low disease activity (LDA) or clinical remission on combination Enbrel® (etanercept) plus methotrexate (MTX) in Period one and were randomized to continue on ENBREL plus MTX or MTX alone in Period two. Results of Period two showed that the percentage of patients who maintained LDA or achieved clinical remission at week 88 was significantly higher in patients receiving ENBREL plus MTX than those on MTX alone. These results have been accepted in the late-breaker poster presentation at the 2011 American College of Rheumatology Annual Scientific Meeting in Chicago, from Nov. 5-9, 2011.

Patients with moderately active RA represent the largest RA population, yet they have not been widely studied as a distinct group in prospective clinical studies. The PRESERVE (A Prospective, Randomized Etanercept S tudy to Evaluate Reduced dose Etanercept + MTX v. full dose Etanercept + MTX v. MTX alone for efficacy and radiographic endpoints in a moderate RA population) study is the largest completed clinical trial of a biologic therapy in adults with moderately active RA, despite MTX treatment.

The PRESERVE trial met both its primary and conditional primary endpoints by demonstrating a statistically superior response in moderately active RA patients taking ENBREL 50mg weekly (QW) plus MTX or ENBREL 25mg QW plus MTX compared with those taking MTX monotherapy at 88 weeks. Specifically, after achieving LDA ([DAS] 28 ?3.2) at 36 weeks on ENBREL 50mg QW plus MTX, the percentage of patients maintaining LDA at week 88 was significantly higher in the ENBREL 50mg QW (82.6 percent, primary endpoint) and ENBREL 25mg QW (79.1 percent, conditional primary endpoint) treatment groups than the MTX- alone group (42.6 percent, P<0.0001 versus either ENBREL group). The U.S. Food and Drug Administration (FDA)- and the European Medicines Agency (EMA)- recommended dose for ENBREL for the treatment of moderate to severe RA is 50mg QW.

Additionally, for DAS 28 clinical remission (DAS28<2.6) HAQ ? 0.5,ACR20/50/70, and European League Against Rheumatism (EULAR) good response, the percentage of patients who achieved these secondary endpoints was significantly higher in the ENBREL treatment groups than the MTX-alone group (P<0.05).

“The medical community has recently questioned whether clinical remission or LDA could be sustained if a biologic agent is discontinued,” said Josef S. Smolen, M.D., lead PRESERVE trial investigator and chairman of the Department of Rheumatology, Medical University of Vienna, Austria. “These data show that patients with moderately active disease who achieve LDA or clinical remission with ENBREL treatment may lose these clinical benefits if ENBREL is discontinued.”

There were no new safety signals, and the safety profile from PRESERVE was consistent with that seen in previous ENBREL studies. Thirty-five subjects (5.8 percent) reported at least one serious adverse event (SAE) during Period two. The proportion of subjects with at least one SAE was similar among treatment groups (13 [6.4 percent], 7 [3.5 percent], and 15 [7.5 percent] in the full-dose, dose reduction, and MTX-only groups, respectively). No specific SAE was observed in more than two subjects. Two deaths, which were considered to be unrelated to the study medication, occurred in the ENBREL 50mg QW plus MTX group.

About PRESERVE

The 88-week PRESERVE study, the largest completed clinical trial of biologic therapy conducted in patients with moderately active RA (DAS28 >3.2 and ? 5.1), consisted of two study periods. During Period one, patients received open-label ENBREL 50mg QW plus MTX for 36 weeks. Those who responded to treatment (n=604; DAS28 ?3.2 at week 36 and an average DAS28 ?3.2 from week 12 through 36) were randomized to one of three treatment arms (ENBREL 50mg QW, ENBREL 25mg QW, or placebo) plus MTX, and followed for an additional 52 weeks. The FDA- and EMA- recommended dose for ENBREL for the treatment of moderate to severe RA is 50mg QW.

About ENBREL Data at the American College of Rheumatology Annual Scientific Meeting

Amgen and Pfizer will also be presenting new analyses of data from several studies of ENBREL at the American College of Rheumatology Annual Scientific Meeting. Selected abstracts and presentations include:

- **Treatment Outcomes Based on Methotrexate Dose Range in Patients with Rheumatoid Arthritis Receiving Etanercept Plus Methotrexate Versus Methotrexate Alone**
  Sunday, Nov. 6, PRESENTATION #: 441

- **Baseline Predictors of Remission with Combination Etanercept-Methotrexate Therapy in Moderately Active Rheumatoid Arthritis: Interim Results of the PRESERVE Trial**
  Monday, Nov. 7, PRESENTATION #: 1216

- **Discordance Between Patients and Physicians in Assessments of Global Disease Activity in Rheumatoid Arthritis: Agreeing to Disagree**
  Tuesday, Nov. 8, PRESENTATION #: 2512

- **Higher Proportion of Rheumatoid Arthritis Patients Achieve Low Swollen and Tender Joint Counts and No Radiographic Progression with Etanercept Plus Methotrexate Versus Methotrexate Alone**
  Tuesday, Nov. 8, PRESENTATION #: 2239

About Rheumatoid Arthritis

RA is a chronic inflammatory disease that affects approximately one percent of the adult population worldwide and can start at any age, but usually occurs between 40 and 70 years. RA can cause pain, stiffness, swelling and limitations in the motion and function of multiple joints. In RA, joint damage can significantly worsen over time, especially if left untreated. Joint damage may impair function, and potentially disable some patients.

About ENBREL

ENBREL is a soluble form of a fully human tumor necrosis factor (TNF) receptor with a clinical efficacy and safety profile established over 18 years of collective clinical experience. ENBREL was first approved in the U.S. in 1998 for moderate to severe rheumatoid arthritis and was later approved to treat children and adolescents with moderate to severe juvenile rheumatoid arthritis (now called juvenile idiopathic arthritis) in 1999. In 2004, ENBREL was approved in the U.S. to treat adult chronic moderate to severe plaque psoriasis. Prescription ENBREL is given by injection.

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 signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in children ages 2 years 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 is the most important information I should know about ENBREL?

ENBREL is a medicine that affects your immune system. ENBREL can lower the ability of your immune system to fight infections. Serious infections have happened in patients taking ENBREL. These infections include tuberculosis (TB) and infections caused by viruses, fungi, or bacteria that have spread throughout the body. Some patients have died from these infections. Your doctor should test you for TB before you take ENBREL and monitor you closely for TB before, during, and after ENBREL treatment, even if you have tested negative for TB.

There have been some cases of unusual cancers reported in children and teenage patients who started using tumor necrosis factor (TNF) blockers before 18 years of age. Also, for children, teenagers, and adults taking TNF blockers, including ENBREL, the chances of getting lymphoma or other cancers may increase. Patients with RA or psoriasis may be more likely to get lymphoma.

Before starting ENBREL, tell your doctor if you:

- Have any existing medical conditions
- Are taking any medicines, including herbals
- Think you have, are being treated for, have signs of, or are prone to infection. You should not start taking ENBREL if you have any kind of infection, unless your doctor says it is okay
- Have any open cuts or sores
- Have diabetes, HIV, or a weak immune system
- Have TB or have been in close contact with someone who has had TB
- Were born in, lived in, or traveled to countries where there is more risk for getting TB. Ask your doctor if you are not sure

- Live, have lived in, or traveled to certain parts of the country (such as, the Ohio and Mississippi River valleys, or the Southwest) where there is a greater risk for certain kinds of fungal infections, such as histoplasmosis. These infections may develop or become more severe if you take ENBREL. If you don't know if these infections are common in the areas you've been to, ask your doctor
- Have or have had hepatitis B
- Have or have had heart failure
- Develop symptoms such as persistent fever, bruising, bleeding, or paleness while taking ENBREL
- Use the medicine Kineret® (anakinra), Orencia® (abatacept), or Cytoxan® (cyclophosphamide)
- Are taking anti-diabetic medicines
- Have, have had, or develop a serious nervous disorder, seizures, any numbness or tingling, or a disease that affects your nervous system such as multiple sclerosis or Guillain-Barré syndrome
- Are scheduled to have surgery
- Have recently received or are scheduled for any vaccines. All vaccines should be brought up-to-date before starting ENBREL. Patients taking ENBREL should not receive live vaccines.
- Are allergic to rubber or latex
- Are pregnant, planning to become pregnant, or breastfeeding
- Have been around someone with chicken pox

What are the possible side effects of ENBREL?

ENBREL can cause serious side effects including: New **infections** or worsening of infections you already have**; hepatitis B** can become active if you already have had it**; nervous system problems,** such as multiple sclerosis, seizures, or inflammation of the nerves of the eyes; **blood problems** (some fatal); new or worsening **heart failure**; new or worsening **psoriasis**; **allergic reactions**; **autoimmune reactions**, including a lupus-like syndrome and autoimmune hepatitis.

Common side effects include: Injection site reactions, upper respiratory infections (sinus infections), and headache.

These are not all the side effects with ENBREL. Tell your doctor about any side effect that bothers you or does not go away.

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, or call 1-800-FDA-1088.

Please see Prescribing Information and Medication Guide at www.ENBREL.com

About Amgen and Pfizer

About Amgen

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, bone disease 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. Follow us on www.twitter.com/amgen.

About Pfizer

At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines for people and animals. Our diversified global health care portfolio includes human and animal biologic and small molecule medicines and vaccines, as well as nutritional products and many of the world's best-known consumer products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as the world's leading biopharmaceutical company, we also collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. To learn more about our commitments, please visit us at www.pfizer.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 Nov. 5, 2011 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 healthcare 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 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 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 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.

MC62777-R1-V1

Amgen Christine Regan (media) Office: 805-447-5476 Cell: 617-359-1324 or Arvind Sood (investors) Office: 805-447-1060 or Pfizer Victoria Davis (media) Office: 212-733-3227 Cell: 347-558-3455 or Suzanne Harnett (investors) Office: 212-733-8009