

Friday, Jan 8, 2010

FDA Approves ACTEMRA® (tocilizumab) for the Treatment of Moderately to Severely Active Rheumatoid Arthritis

-- First-in-class, IL-6 receptor-inhibiting monoclonal antibody approved based on largest clinical development program in rheumatoid arthritis to date --

South San Francisco, Calif. -- January 8, 2010 -- Genentech, Inc. , a wholly owned member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), today announced that the U.S. Food and Drug Administration (FDA) approved ACTEMRA® (tocilizumab) for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. ACTEMRA is the first interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody approved to treat RA, and may be used alone or in combination with methotrexate or other disease modifying anti-rheumatic drugs (DMARDs).

"The FDA approval of ACTEMRA marks a major step forward in the treatment of RA, providing a new option for patients with this very serious disease," said Hal Barron, M.D., executive vice president, Global Development and chief medical officer, Roche and Genentech. "We are optimistic that working with the agency, we will be able to generate the additional data required to support approval in earlier lines of RA therapy and are committed to comprehensively characterizing both the clinical benefit and the safety of ACTEMRA in earlier lines of therapy through our large pharmacovigilance program, including the risk management program, and ongoing clinical and post-marketing studies globally."

RA is a chronic, progressive inflammatory disease of the joints and surrounding tissues that is associated with intense pain, irreversible joint destruction and systemic complications. There are several key cytokines, or proteins, involved in the inflammatory process, including IL-6. Research shows that IL-6 levels are elevated in patients with RA. ACTEMRA is the first medication designed to specifically inhibit the biological activity of IL-6.

"For many RA patients, treatment with existing therapies does not resolve the painful and debilitating symptoms of the disease," said Mark Genovese, M.D. , ACTEMRA study investigator and Professor of Medicine and Co-Chief of the Division of Immunology and Rheumatology at Stanford University Medical Center. "Data from the clinical development program clearly establish ACTEMRA and its unique mechanism of action as an important new option for RA patients who experience continued disease symptoms despite treatment with existing therapies. "

ACTEMRA has been studied in five multi-national Phase III studies, involving more than 4,000 patients, making it the largest clinical development program for an indication in RA to date. The studies showed that ACTEMRA – alone or in combination with methotrexate or other DMARDs – significantly reduced RA signs and symptoms compared with DMARDs alone. This approval is based on data from the following studies:

RADIATE (RheumAtoiD Arthritis Study in Anti-TNF Failure) Trial:

50% and 30% of patients who received ACTEMRA 8 mg/kg or 4 mg/kg plus methotrexate, respectively, achieved ACR20 at week 24, compared with 10% of patients who received placebo plus methotrexate¹

OPTION (Tocilizumab Pivotal Trial in Methotrexate Inadequate responders) Trial:

59% and 48% of patients who received ACTEMRA 8 mg/kg and 4 mg/kg plus methotrexate, respectively, achieved ACR20 at week 24, compared with 27% of patients who received placebo plus methotrexate²

TOWARD (**T**ocilizumab in **c**ombination **W**ith traditional **DMARD** therapy) Trial:

61% of patients who received ACTEMRA 8 mg/kg plus DMARDs achieved ACR20 at 24 weeks, compared with 25% of patients treated with DMARDs plus placebo³

AMBITION (**A**ctemra versus **M**ethotrexate double-**B**lind **I**nvestigative **T**rial **I**n **m**ONotherapy) Trial:

70% of patients who received ACTEMRA 8 mg/kg achieved ACR20 at week 24, compared with 53% of patients receiving methotrexate alone⁴

LITHE (Toci**L**izumab Safety and **T**HE Prevention of Structural Joint Damage) Trial:

56% and 51% of patients who received ACTEMRA 8 mg/kg or 4 mg/kg plus methotrexate, respectively, achieved ACR20 at week 24 compared with 27% of patients who received placebo plus methotrexate⁵

ACTEMRA is approved for once-a-month intravenous administration in doctors' offices, hospitals and infusion centers, and may be used alone or in combination with methotrexate or other DMARDs in the following dosage:

ACTEMRA 4 mg/kg is the recommended starting dose when used in combination with DMARDs or as a monotherapy in patients who have had an inadequate response to one or more TNF antagonists; the dose may then be increased to 8 mg/kg based on clinical response.

ACTEMRA has been approved with a Risk Evaluation and Mitigation Strategy (REMS) that includes a medication guide, communication plan and timetable for submission of assessments. This plan was developed to provide support and education to patients and healthcare providers. ACTEMRA will be available the week of January 18, 2010.

About ACTEMRA® (tocilizumab)

ACTEMRA is the first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. Studies demonstrate that reducing the activity of IL-6, one of several key cytokines involved in the inflammatory process, relieves both inflammation of the joints and certain systemic symptoms of RA. The extensive ACTEMRA clinical development program included five Phase III clinical studies and enrolled more than 4,000 people with RA in 41 countries, including the United States.

Serious side effects associated with ACTEMRA include serious infections that may lead to hospitalization or death, gastrointestinal perforations (a hole in the stomach or intestines), and hypersensitivity reactions including anaphylaxis. The most common AEs reported in clinical studies were upper respiratory tract infection, nasopharyngitis (inflammation of the nose and throat), headache, high blood pressure and increased liver enzymes. The increases in liver enzymes that were seen in patients were generally mild and reversible and did not result in apparent permanent

or clinically evident hepatic injury. Laboratory changes, including increases in total cholesterol, the amount of fat circulating in the blood, and decreases in neutrophils (one of the cell types that helps fight infections) and platelets, were seen. Treatments that suppress the immune system, such as ACTEMRA, may cause an increase in the risk of cancer. For additional important safety information, including Boxed WARNINGS and Medication Guide, please visit <http://www.actemra.com> or call 1-800-ACTEMRA (228-3672).

ACTEMRA is part of a co-development agreement with Chugai Pharmaceutical Co. and has been approved in Japan since June 2005. ACTEMRA is approved in the European Union, where it is known as RoACTEMRA, and several other countries, including India, Brazil, Switzerland and Australia.

About Rheumatoid Arthritis

Rheumatoid arthritis is a progressive, systemic autoimmune disease characterized by inflammation of the membrane lining in the joints. This inflammation causes a loss of joint shape and function, resulting in pain, stiffness and swelling, ultimately leading to irreversible joint destruction and disability. Characteristics of RA include redness, swelling, pain and movement limitation around joints of the hands, feet, elbows, knees and neck that leads to loss of function. In addition, the systemic symptoms of RA include fatigue, decreased hemoglobin, osteoporosis and may contribute to shortening life expectancy by affecting major organ systems. After 10 years, less than 50 percent of patients can continue to work or function normally on a daily basis. According to the Arthritis Foundation, RA affects approximately 1.3 million adults in the United States.

About Genentech

Founded more than 30 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with serious or life-threatening medical conditions. The company, a wholly owned member of the Roche Group, has headquarters in South San Francisco, California. For additional information about the company, please visit <http://www.gene.com>.

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¹ Emery P. et al. IL-6 Receptor Inhibition with Tocilizumab Improves Treatment Outcomes in Patients with Rheumatoid Arthritis Refractory to Anti-TNF Biologics: The RADIATE Study. *Annals of the Rheumatic Diseases*. 2008;67:1516-1523.

²Smolen J. et al. Effect of Interleukin-6 Receptor Inhibition with Tocilizumab in Patients with Rheumatoid Arthritis (OPTION Study): a Double-Blind, Placebo-Controlled, Randomised Trial. *The Lancet*. 2008;371,9617:987-997.

³Genovese M. , et al. Interleukin-6 Receptor Inhibition with Tocilizumab Reduces Disease Activity in Rheumatoid Arthritis with Inadequate Response to Disease-Modifying Antirheumatic Drugs. *Arthritis & Rheumatism*. 2008;58(10):2968-2980.

⁴Jones. G., Abstract 1210. The AMBITION Study: Superiority of Tocilizumab (TCZ) vs Methotrexate

(MTX) Monotherapy in Patients with Rheumatoid Arthritis (RA). Data presented at the American College of Rheumatology (ACR) Annual Scientific Meeting 2008.

⁵Fleischmann R. , Abstract 637. LITHE: Tocilizumab Inhibits Radiographic Progression and Improves Physical Function in Rheumatoid Arthritis (RA) Patients (Pts) at 2 Yrs with Increasing Clinical Efficacy Over Time. Data presented at ACR 2008.