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**ACTEMRA[®],
a Humanized Anti-Human IL-6 Receptor Monoclonal Antibody,
Approved in the United States for Rheumatoid Arthritis**

January 9, 2010 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Head Office: Chuo-ku, Tokyo; President Osamu Nagayama (hereafter, "Chugai")] and F. Hoffmann-La Roche Ltd. [Head Office: Basel, Switzerland. CEO: Severin Schwan (hereafter "Roche")] today announced that the United States (US) Food and Drug Administration (FDA) approved ACTEMRA[®], the humanized anti-human IL-6 (interleukin-6) receptor monoclonal antibody (tocilizumab, RoACTEMRA[®] in the European Union) 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[®], the result of research collaboration between Chugai and Osaka University, 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).

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.

Outside of Japan, 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, regardless of previous therapy, compared with DMARDs alone. This approval is based on data from the following studies:

- RADIATE (RheumAtoiD ArthritIs Study in Anti-TNF FailurEs) 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 methotrexateⁱⁱ
- **TOWARD (TOcilizumab in cOmbination With traditional DMARD therapy) Trial:**
 - 61% of patients who received ACTEMRA 8mg/kg plus DMARD(s) achieved ACR20 at 24 weeks, compared with 25% of patients treated with DMARDs plus placeboⁱⁱⁱ
- **AMBITION (Actemra versus Methotrexate double-Blind Investigative Trial In mONotherapy) Trial:**
 - 70% of patients who received ACTEMRA 8 mg/kg achieved ACR20 at week 24, compared with 53% of patients receiving methotrexate alone^{iv}
- **LITHE (TociLIZumab Safety and THE 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 methotrexate^v

With this US approval of ACTEMRA[®] following that of EU, our innovative in-house drug will also be available in the US market, through Roche. In the US, ACTEMRA[®] will be marketed by Genentech, a wholly-owned company by Roche. Chugai will supply the final formulation of the drug to Roche and receive royalties based on the sales. ACTEMRA[®] will be available in the US the week of January 18, 2010.

Roche will work closely with the agency to understand the additional data required to support approval in earlier lines of RA therapy. We are committed to comprehensively characterizing both the clinical benefit and the safety of ACTEMRA[®] in earlier lines of therapy through our large clinical and pharmacovigilance programs including the REMS program, and ongoing development and postmarketing studies globally.

In Japan, Actemra[®] was launched in June 2005 by Chugai for Castleman's disease, following approval in April, the same year. Subsequently, it was approved for the additional indications of RA (including prevention of structural damage of joints), polyarticular-course juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis in April 2008.

In the EU, approval was granted on January 2009 for the indication of RA and it was launched under the brand name RoACTEMRA[®]. Chugai co-promotes RoACTEMRA[®] in U.K., France and Germany, where its wholly-owned subsidiary Chugai Pharma Marketing Ltd. has its marketing bases. Currently ACTEMRA[®]/RoACTEMRA[®] is approved in a growing number of other countries including Mexico, India, Brazil, Switzerland and Australia.

Chugai focuses on bone and joint diseases area as one of the strategic domains, and is committed to contribute to the treatment by providing new therapeutic options for medical professionals and patients.

The sales estimate related to the US approval of Actemra[®] is scheduled to be announced at Chugai's next full year results announcement.

[Reference]

Approved Dosage in the US

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.

About Actemra[®]

ACTEMRA[®], the first antibody drug (humanized monoclonal antibody) originating from Japan, was created by Chugai in collaboration with Osaka University, utilizing genetic recombinant technology to produce a monoclonal antibody against the anti-IL6 receptor. It was designed to inhibit the biological activity of IL-6, a cytokine known to be involved in the inflammatory process, through competitively blocking the binding of IL-6 to its receptor.

The main symptoms of RA are multiple joint inflammation and progressive joint damage, and it is reported that 1.3 million patients suffer from RA in US.

The overall safety profile of ACTEMRA[®] is consistent across all global clinical studies. 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.

i 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.

ii Smolen 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.

iii Genovese 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.

iv Jones. 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.

v Fleischmann 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.