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RoACTEMRA filed in Europe for the Inhibition of Joint Damage and Improvement in Physical Function in Rheumatoid Arthritis

Roche announced today that it has submitted a filing to the European health authorities (the European Medicines Agency) to extend the indication of RoACTEMRA to inhibit the progression of joint damage and to improve physical function in patients with rheumatoid arthritis (RA). Joint damage in RA often begins early in the disease and can lead to permanent disability, so inhibiting this structural damage to patients' joints is a critical measure of effectiveness of an RA treatment.

"A successful regulatory outcome will be an important milestone for RoACTEMRA. It will give both physicians and patients further confidence that RoACTEMRA not only helps achieve a long-lasting remission from the painful and debilitating disease symptoms, but that it inhibits the progression of structural joint damage which is the major cause of loss of normal function and permanent disability for RA patients", said Urs Schleuniger, Roche's Global Product Strategy Head, Inflammation/Immunology.

The filing follows positive two-year data from the LITHE¹ pivotal trial. Results from the trial showed that patients receiving RoACTEMRA in combination with methotrexate (MTX) had significantly less damage to their joints at two years, compared to patients who received MTX alone. The outcome was determined by x-ray evidence of the progression of bone erosions and narrowing of joint spaces.

RoACTEMRA is currently licensed in Europe for use in combination with MTX, to treat adult patients with moderate to severe RA who responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor antagonists (anti-TNFs).² In these patients, RoACTEMRA can be given as a monotherapy in cases of intolerance to MTX or where continued treatment with MTX is inappropriate.²

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About the LITHE study

The LITHE study, a randomized, double-blind, placebo-controlled trial was designed to evaluate the efficacy of TCZ plus MTX in preventing structural joint damage and improving physical function over 2 years. LITHE is an international study, including 15 countries and 1196 patients with moderate to severe RA who had an inadequate response to MTX. In this randomized study, patients received either RoACTEMRA (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with MTX or MTX alone.

Results from the 12-month analysis showed that at 52 weeks, total Genant-modified Sharp Score changes from baseline for the RoACTEMRA 8mg + MTX, 4mg +MTX, and MTX alone groups were: 0.29, 0.34 and 1.1 respectively.³ The percentage of patients achieving no progression in total Genant-modified Sharp Score was 85%, 81% and 67%.³ Results from two global measures, the HAQ-DI⁴ for physical function, and the DAS28⁵ for clinical remission, both demonstrated a benefit in the treatment groups. The HAQ-DI AUC change from baseline, adjusted mean scores were: -144.1, -128.4 and -58.1 respectively. DAS28 clinical remission (<2.6) was 47%, 30% and 8%.³

The recently announced two-year data from the LITHE study demonstrate that ACTEMRA continues to be highly effective at inhibiting joint structural damage and maintaining consistently high remission rates as seen in the one-year results. The study outcomes will be presented at the Annual Meeting of the American Society of Rheumatology (ACR) in October.

About RoACTEMRA

RoACTEMRA is the result of research collaboration by Chugai and is being co-developed globally with Chugai. RoACTEMRA is the first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development programme of five Phase III trials was designed to evaluate clinical findings of RoACTEMRA, all of which met their primary endpoints. RoACTEMRA was first approved in Japan, and launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for RA, juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan. RoACTEMRA was approved in the European Union in January 2009 for the treatment of RA in patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or TNF inhibitors. It is also approved for use in several other countries, including India, Brazil, Switzerland and Australia.

ACTEMRA is generally well tolerated. The overall safety profile of ACTEMRA is consistent across all global clinical studies. The serious adverse events reported in ACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse events reported in clinical studies were upper respiratory tract infection, nasopharyngitis, headache, hypertension and increased ALT. Increases in liver enzymes (ALT and AST) were seen in some patients; these increases were generally mild and reversible, with no evidence of hepatic injuries or any observed impact on liver function. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some patients without association with clinical outcomes. Treatments that suppress the immune system, such as ACTEMRA, may cause an increase in the risk of malignancies.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2008, Roche had over 80,000 employees worldwide and invested almost 9 billion Swiss francs in R&D.

The Group posted sales of 45.6 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: www.roche.com.

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References

- (1) LITHE refers to the Tocilizumab safety and **THE** prevention of structural joint damage trial
- (2) RoACTEMRA SmPC
- (3) Kremer, J. *et al.* Tocilizumab inhibits structural joint damage, improves physical function, and increases DAS28 remission rates in RA patients who respond inadequately to methotrexate: The LITHE Study. Presented on 12th June 2009 at EULAR
- (4) HAQ, or the Health Assessment Questionnaire Disability Index, is a patient self-report functional status (disability) measurement used to assess the patient's functional ability and discomfort during the past week. It is a commonly used instrument in many disease areas, including RA
- (5) National Rheumatoid Arthritis Society, The DAS28 score
http://www.rheumatoid.org.uk/article.php?article_id=475 Last accessed 21 September 2009