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CHUGAI
Roche Group

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Roche's RoACTEMRA Monotherapy Showed Superior Improvement in Rheumatoid Arthritis Signs and Symptoms Versus Adalimumab Monotherapy

Statistically significant greater improvement in signs and symptoms, as measured by mean change in DAS28 (primary endpoint), DAS28 remission and low disease activity, ACR20, 50 and 70 (secondary endpoints)

Roche today announced that preliminary results from the ADACTA study (ADalimumab ACTemrA) showed that patients who received RoACTEMRA (tocilizumab) as monotherapy achieved a significantly greater reduction in disease activity (assessed by the mean change of DAS28[1]) after 24 weeks than those given adalimumab monotherapy. Statistical significance was also achieved on key secondary endpoints including DAS28 remission and low disease activity, ACR20, 50 and 70[2] (standard criteria to assess effectiveness of treatments for rheumatoid arthritis). Preliminary safety analysis showed adverse event rates were similar between the two groups.

"These data add to the growing body of evidence supporting the benefit of RoACTEMRA alone when methotrexate is not appropriate," said Hal Barron, M.D., Head of Global Development and Chief Medical Officer for Roche. "Now that there are several therapies approved to treat patients with rheumatoid arthritis, trials comparing two active agents are critical as they provide important information to help healthcare professionals choose the right drug for their patients."

ADACTA is the first study that was specifically designed to determine superiority between two approved biologic therapies for the treatment of rheumatoid arthritis (RA) in the monotherapy setting. The study was designed to evaluate if RoACTEMRA was superior to adalimumab based on the mean change from baseline of DAS28 at week 24 in patients with severe active RA and intolerance or inadequate response to methotrexate (MTX). MTX is widely prescribed for people with RA, although about 1 in 3 RA patients on a biologic medicine are currently receiving their medication as monotherapy, largely due to intolerance to MTX[3,4,5,6].

Data from the study will be submitted for presentation at an upcoming medical meeting.

About ADACTA

ADACTA is a Phase IV multi-centre, randomized, double blinded, parallel group study designed to compare the reduction in signs and symptoms during monotherapy treatment with RoACTEMRA versus adalimumab in adult patients with severe active RA who either have an intolerance to methotrexate (MTX) or in whom continued MTX treatment is inappropriate. Also, patients participating in the trial had not previously received a biologic medicine for RA.

326 patients were randomised (1:1) to receive RoACTEMRA 8 mg/kg IV every 4 weeks (plus placebo adalimumab) or adalimumab 40 mg subcutaneously (SC) every 2 weeks (plus placebo RoACTEMRA) for 24 weeks. The study met its primary endpoint of a significantly greater reduction in the mean change from baseline in the DAS28 score at 24 weeks in patients receiving RoACTEMRA as a monotherapy compared to those receiving adalimumab as a monotherapy. The safety profile of RoACTEMRA in the ADACTA study is consistent with previous findings in the RoACTEMRA clinical trials.

About RoACTEMRA / ACTEMRA

RoACTEMRA (tocilizumab, known as ACTEMRA outside Europe) is the result of research collaboration by Chugai and is also being co-developed globally with Chugai. RoACTEMRA is the first humanised interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. ACTEMRA 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 rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA) and systemic-onset juvenile idiopathic arthritis (sJIA) 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 tumour necrosis factor (TNF) inhibitors. It is also approved for use in over 90 other countries, including India, Brazil, Switzerland, and Australia. ACTEMRA was approved in the United States in January 2010 for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF inhibitors. In addition, ACTEMRA is now approved in the EU, United States and Mexico for the treatment of active SJIA in patients two years of age and older.

The safety and efficacy of RoACTEMRA in RA has been characterized in an extensive clinical development program including five Phase III clinical studies that enrolled more than 4,000 people with RA in 41 countries, including the United States. The overall safety profile of RoACTEMRA is consistent across all global clinical studies. The serious adverse events reported in RoACTEMRA clinical studies include serious infections, gastrointestinal perforations and serious 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. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some patients. Treatments that suppress the immune system, such as RoACTEMRA, 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 personalized healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2011, Roche had over 80,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 42.5 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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1 The Disease Activity Score (DAS)28 is a combined index that measures disease activity in patients with RA. It combines information from 28 tender and swollen joints (range0-28), erythrocyte sedimentation rate, and a general health assessment on a visual analog scale. The level of disease activity is interpreted as low (DAS28≤3.2), moderate (3.2<DAS28≤5.1) or high (DAS28>5.1). DAS28<2.6 corresponds to being in remission according to the criteria of the American College of Rheumatology.

2 ACR20, ACR50, ACR70 represent the percentage of reduction (20%, 50%, 70%) in certain RA symptoms and measures the number of tender and swollen joints, pain, patient's and physician's global assessments and certain laboratory markers.

3 Yazici Y, *et al. Bulletin of the NYU Hospital for Joint Diseases* 2008;**66**(2):77-85

4 Soliman M, *et al. Ann Rheum Dis* 2011;**70**:583–589

5 Listing J, *et al. Arthritis Research & Therapy* 2006, **8**:R66

6 Askling J, *et al. Ann Rheum Dis* 2007;**66**:1339–1344