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Roche Roche Group

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Roche Reports Second Positive Study of RoACTEMRA Given by Subcutaneous Injection to Patients with Rheumatoid Arthritis

Data will be submitted to health authorities globally for RoACTEMRA subcutaneous formulation

Roche today announced that the BREVACTA study of RoACTEMRA (tocilizumab, known as ACTEMRA outside Europe) given as a subcutaneous (SC) injection to patients with rheumatoid arthritis (RA) met its primary endpoint. After 24 weeks of treatment, RA patients who received RoACTEMRA every two weeks were significantly more likely to have experienced at least a 20% improvement in tender and swollen joint counts than those given placebo injections(ACR20). Preliminary safety analysis showed that the adverse event profile of RoACTEMRA SC was consistent with previous findings.

BREVACTA is the second positive study of an SC formulation of RoACTEMRA and follows results reported in May from the SUMMACTA study. Roche intends to submit these data with health authorities globally to gain approval for the SC formulation of RoACTEMRA.

“These two studies mark a significant milestone for RoACTEMRA consistently demonstrating that a subcutaneous formulation provides clinically meaningful results for patients with rheumatoid arthritis,” said Hal Barron, M.D., Head of Global Product Development and Chief Medical Officer for Roche. “If approved, doctors and patients will have an important alternative treatment option to choose from”.

RA is an autoimmune disease estimated to affect up to 70 million people worldwide, including children. Joints become chronically inflamed, painful and swollen, and patients can become increasingly disabled as cartilage and bone is damaged. Preventing or slowing the progression of damage to RA patients’ joints is an important aim of treatment, preserving functionality and mobility.

Analysis of X-ray results, a secondary endpoint in BREVACTA, also showed patients who received RoACTEMRA SC every two weeks were significantly less likely to have experienced worsening joint damage at week 24 than those given a placebo SC injection in combination with DMARDs. Statistical significance was also achieved on other key secondary endpoints including ACR50 and 70, DAS28 low disease activity and DAS28 remission.

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

About BREVACTA

BREVACTA is a randomised, double-blind, parallel-group study of RoACTEMRA SC versus placebo SC in combination with traditional DMARDs in patients with moderate to severe, active RA who had an inadequate response to DMARD therapy. BREVACTA was designed to assess the efficacy of treatment with RoACTEMRA 162 mg SC given every 2 weeks versus placebo given every 2 weeks, both in combination with DMARDs, based on ACR20 response at Week 24. Safety profile was assessed with regard to adverse events and laboratory assessments.

656 patients were randomly assigned in a 2:1 ratio to two treatment groups at baseline. 437 patients received RoACTEMRA SC (Group A) every two weeks administered with a prefilled syringe (PFS) and 219 received placebo SC (Group B) every two weeks with a PFS. All patients continued their background DMARD therapy. At Week 24 patients were re-randomised to continue receiving administration with the PFS or to change to administration with an autoinjector (AI). Furthermore all patients on placebo were switched to receive RoACTEMRA SC 162mg every two weeks. Secondary endpoints included assessment of prevention of progression of structural joint damage at week 24 between the two groups, ACR50 and 70, DAS28 response, DAS28 low disease activity and DAS28 remission.

About ACR 20, 50, 70

American College of Rheumatology (ACR) scores represent the percentage of reduction (20%, 50%, 70%) in tender and swollen joint counts, in addition to a corresponding improvement in three of the following five parameters:

- acute phase reactant (such as erythrocyte sedimentation rate)
- Patients Global Assessment of Disease Activity
- Physicians Global Assessment of Disease Activity
- pain scale
- Health Assessment Questionnaire (HAQ)

About DAS28

DAS28 is a measure of disease activity in RA. The score is calculated by a complex mathematical formula, which includes the number of tender and swollen joints (out of a total of 28), the erythrocyte sedimentation rate (a marker of systemic inflammation), and the patient's 'global assessment of global health' (indicated by marking a 10 cm line between 'very good' and 'very bad'). A DAS28 score greater than 5.1 indicates severe active disease, less than 3.2 low disease activity, and less than 2.6 is termed DAS28 remission.

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 humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. 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 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. RoACTEMRA 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, RoACTEMRA 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 have 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.