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New data shows ACTEMRA inhibits progression of joint destruction and improves physical function of patients with Rheumatoid Arthritis

Fifth phase III study also confirms significant rate of disease remission in patients treated with ACTEMRA

Roche announced today that the innovative new therapy ACTEMRA (tocilizumab) can significantly inhibit structural damage to joints in patients with rheumatoid arthritis (RA) – this is a critical measure of effectiveness of an RA treatment. ACTEMRA was also found to improve the patients' physical function after one year of therapy and to significantly increase the disease remission rate.

The results from the LITHE¹ trial, being presented at the American College of Rheumatology (ACR) Annual Scientific Meeting in San Francisco, showed that:

- A greater proportion of patients treated with ACTEMRA in combination with a commonly used RA drug called methotrexate (MTX) benefited from a significant inhibition of structural damage during 12 months of therapy compared to patients treated with MTX alone. The outcome was determined by x-ray evidence of the progression of bone erosions and narrowing of joint spaces. This benefit is important to patients as damage to the joints caused by the disease leads to the disability and pain associated with RA.
- ACTEMRA improved the patients' ability to perform normal daily activities, as assessed by the Health Assessment Questionnaire (HAQ)², leading to a better quality of life.
- Significantly more patients treated with ACTEMRA achieved remission* than those treated with MTX alone (47% vs. 8%). The improvement in remission at one year reinforces the strong remission data seen at 6 months in four additional ACTEMRA phase III trials across multiple RA patient populations.

“The outcome of this study is good news for RA patients as presently many either fail to achieve an adequate response or cannot tolerate therapies currently available,” said William M. Burns, Head of the Roche Pharma Division. “New treatment options are needed, particularly those that can target different pathways to bring relief and inhibit joint damage in patients suffering from RA.”

“The LITHE study demonstrated that treatment with ACTEMRA inhibited structural joint damage, which is a major cause of disability and loss of physical function for RA patients,” said

Joel Kremer, M.D., investigator in the LITHE study and Director of Research at The Center for Rheumatology in Albany, New York. “It is critical to stop joint damage as quickly as possible to avoid joint deformity and to help patients maintain their quality of life.”

In the LITHE study, ACTEMRA was generally well tolerated and the overall safety profile after 12 months of treatment was consistent with previously reported 6 month trial data.

ACTEMRA is the first of a new class of drug with a novel mechanism of action that brings new hope to RA patients. It is a humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody which works by suppressing the activity of IL-6, an important trigger of the inflammatory process. This novel mode of action reduces inflammation of the joints and relieves the systemic effects of RA.

*defined by the recognised measure DAS28<2.6

Rheumatoid Arthritis - A High Unmet Medical Need

Rheumatoid arthritis is thought to affect over 21 million people worldwide. It is a progressive autoimmune disease characterized by inflammation of the membrane lining in the joints throughout the body. This inflammation causes distortion of the joint and impaired function accompanied by pain, stiffness and swelling and ultimately leading to irreversible joint destruction and disability. In addition, the systemic symptoms of RA include fatigue, anaemia, osteoporosis and may contribute to shortening life expectancy by affecting major organ systems. After 10 years, less than 50% of patients can continue to work or function normally on a daily basis.

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. 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 ACTEMRA (4 mg/kg or 8 mg/kg, one infusion every four weeks) in combination with methotrexate or methotrexate alone. The results presented are from a planned 12-month analysis of a 2-year study. At 52 weeks, total Genant-modified Sharp Score change from baseline for the ACTEMRA 8mg + MTX, 4mg +MTX, and MTX alone groups were: 0.29,

0.34 and 1.1 respectively. The percentage of patients achieving no progression in total Genant-modified Sharp Score were 85%, 81% and 67%. 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%.

About ACTEMRA

ACTEMRA is the result of research collaboration by Chugai and is being co-developed globally with Chugai. ACTEMRA is the first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development program of five Phase III trials was designed to evaluate clinical findings of ACTEMRA. The five studies have reported meeting their primary endpoints. In Japan, ACTEMRA was launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for rheumatoid arthritis, polyarticular-course juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan.

ACTEMRA is generally well tolerated. The overall safety profile of ACTEMRA is consistent across all global clinical studies. The serious adverse reactions reported in ACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse reactions 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 patients; these increases were generally mild and reversible, with no evidence of hepatic injuries. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in 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 in rheumatoid arthritis

One of the most important drivers for growth at Roche over the next few years is expected to be the company's emerging franchise in autoimmune diseases with rheumatoid arthritis as the first indication. Following the launch of MabThera (rituximab) there are a number of projects in development, potentially allowing Roche to build on further opportunities. MabThera is the first and only selective B-cell therapy for RA, providing a fundamentally different treatment approach by targeting B cells, one of the key players in the pathogenesis of RA. ACTEMRA is Roche's second novel medicine and is a humanised monoclonal antibody to the interleukin-6 (IL-6) receptor, inhibiting the activity of IL-6, a protein that plays a major role in the RA inflammation process. Additional projects creating a rich pipeline include compounds in Phase I, II and III clinical trials. Notably, ocrelizumab, a humanised anti-CD20 antibody, has entered phase III development for

RA.

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As the world's biggest biotech company and an innovator of products and services for the early detection, prevention, diagnosis and treatment of diseases, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is the world leader in in-vitro diagnostics and drugs for cancer and transplantation, and is a market leader in virology. It is also active in other major therapeutic areas such as autoimmune diseases, inflammatory and metabolic disorders and diseases of the central nervous system. In 2007 sales by the Pharmaceuticals Division totalled 36.8 billion Swiss francs, and the Diagnostics Division posted sales of 9.3 billion francs. Roche has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai, and invested over 8 billion Swiss francs in R&D in 2007. Worldwide, the Group employs about 79,000 people. Additional information is available on the Internet at www.roche.com.

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References:

¹LITHE refers to the Tocilizumab safety and THE prevention of structural joint damage trial

²HAQ, 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

