

Basel, 11 Dezember 2009

## **First Phase III study evaluating Roche's ocrelizumab in patients with rheumatoid arthritis meets primary endpoint**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that STAGE, a Phase III trial evaluating ocrelizumab as a treatment for seropositive\* rheumatoid arthritis (RA) patients with a previous inadequate response to methotrexate (MTX), met its primary efficacy endpoint.

The study shows that patients treated with ocrelizumab in combination with MTX achieved the primary efficacy endpoint, which was a co-primary endpoint measured by an improvement in the signs and symptoms of their disease (ACR20 response\*\*) both at week 24 and week 48, compared to those treated with MTX alone.

While overall adverse events were comparable between ocrelizumab and placebo treatment groups, a higher percentage of serious infections was observed in the pooled ocrelizumab groups when compared to the placebo group. Safety analyses from the study are ongoing and will be presented at an upcoming medical meeting.

“RA is a severe, chronic disease which causes painful inflammation of the joints and can lead to deformity and disability. We believe ocrelizumab has the potential to offer a differentiated treatment option for these patients.” said William M. Burns, CEO Pharmaceuticals Division of Roche.

The results from this first Phase III trial in RA build on findings from previous Phase II studies and confirm that targeting seropositive RA patients with ocrelizumab, a humanized anti-CD20 therapy, can lead to an improvement in RA symptoms.

The full results from the study will be shared at a forthcoming scientific conference.

Results from three additional Phase III trials on the use of ocrelizumab in patients with RA will become

known in the first half of 2010. Results from these trials should further determine the potential benefit of ocrelizumab in patients with seropositive RA and further assess the safety profile across the programme.

### **About the STAGE Study**

STAGE is a Phase III international randomized, placebo controlled, double blind parallel group study, consisting of a 48-week double-blind treatment period and study extension period of at least 48 weeks. It involved 1015 seropositive patients with active RA who have had an inadequate response to MTX. Approximately 80% of the RA population are seropositive, which means that they have tested positive for the presence of specific antibodies (rheumatoid factor and/or anti-cyclic citrullinated peptide).

During the double-blind treatment period, patients received 2 courses at 6 month intervals of either ocrelizumab (at a dose of either 2 infusions of 200mg or 2 infusions of 500mg) or placebo by intravenous infusion on days 1 and 15, with weekly MTX as a background therapy. Eligible patients in the study extension period received open label treatment with ocrelizumab.

The co-primary endpoint of the study was to determine the proportion of patients with an ACR 20 response both at week 24 and week 48.

The study was conducted at 209 study sites around the world.

### **About Ocrelizumab**

Ocrelizumab is the first humanized treatment which selectively targets CD20 positive B cells and has been developed specifically for use in autoimmune diseases such as RA. It builds on the heritage of rituximab, which is the first B cell targeted therapy approved for use in RA, and which exhibits evidence for the role of B cells in the pathophysiology of RA. Ocrelizumab interferes with the inflammatory cascade in RA, inhibiting the series of reactions which lead to the symptoms and irreversible joint damage experienced by people with RA.

Results from two ocrelizumab phase I/II studies have been previously communicated:

### **Previous Phase I/II Studies**

Results from the combined Phase I/II ACTION<sup>1</sup> trial conducted in 237 patients with inadequate response to traditional or biological DMARDs, showed that patients treated with a dual infusion of ocrelizumab (10, 50,

200, 500, 1000mg) achieved significantly greater improvements in the signs and symptoms of their disease (measured by ACR20, ACR50 and ACR70) compared to those treated with MTX alone at 24 weeks, with the best response rates reported in ocrelizumab doses above 200mg. On completion of the study at 72 weeks, ocrelizumab appeared to be safe and well tolerated.

In another phase I/II study,<sup>ii</sup> ocrelizumab was administered as a single infusion regimen of 400, 1000, 1500, 2000 mg or placebo with methotrexate as a background therapy in RA patients who had previously failed on DMARD therapy. The study showed that ocrelizumab administered as a single infusion was well tolerated at 24 weeks and associated with an increase in ACR 20, 50 and 70 responses versus methotrexate alone.

### **About RA**

Rheumatoid arthritis (RA) is an autoimmune disease characterized by inflammation that leads to stiff, swollen and painful joints. This ultimately results in irreversible joint damage and disability. More than 20 million people worldwide and twice as many women as men suffer from RA.<sup>iii</sup> In addition to inflammation of the joints, such as the hands, feet and wrists, RA can cause fatigue, heart disease and increase the likelihood of developing other complications such as osteoporosis, anaemia, and problems with the lungs and eyes.<sup>iv</sup> It can shorten life expectancy by around 6-10 years.<sup>v</sup>

### **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](http://www.roche.com).

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\* Seropositive patients are those who have tested positive for the presence of specific antibodies (rheumatoid factor and/or anti-cyclic citrullinated peptide). This is approximately 80% of the RA population

\*\* An ACR 20 response requires at least a 20% improvement compared with baseline in both Tender Joint Counts (TJC) and Swollen Joint Counts (SJC), as well as a 20% improvement in three of the five additional measurements from physician's global assessment of disease activity, patient's global assessment of disease activity, patient's assessment of pain, Disability Index (HAQ-DI), and acute phase reactant (CRP or ESR)

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<sup>i</sup> Genovese MC, Kaine JL, Lowenstein MB, et al. Ocrelizumab, a humanized anti-CD20 monoclonal antibody, in the treatment of patients with rheumatoid arthritis. *Arthritis Rheum* 2008;58(9):2652-61

<sup>ii</sup> Chirinos-Rojas C, Ilivanova E, Boyd P, et al. The safety and efficacy of ocrelizumab; a humanized anti CD20 antibody administered as a single infusion regimen to patients with active rheumatoid arthritis [abstract OP-0250]. EULAR 2008 Available from: <http://www.hopkins-arthritis.org/physician-corner/education/eular2008/RA-Anti-B-Cell-Therapy/abstract-op-0250.html> [Last accessed 11 May 2009]

<sup>iii</sup> WHO report: The global burden of rheumatoid arthritis in the year 2000  
[http://www.who.int/healthinfo/statistics/bod\\_rheumatoidarthritis.pdf](http://www.who.int/healthinfo/statistics/bod_rheumatoidarthritis.pdf) Last accessed 21<sup>st</sup> May 2009

<sup>iv</sup> National Rheumatoid Arthritis Society Website: What is RA? [http://www.rheumatoid.org.uk/article.php?article\\_id=224](http://www.rheumatoid.org.uk/article.php?article_id=224) Last accessed 8<sup>th</sup> January 2009

<sup>v</sup> Firestein GS. Evolving concepts of rheumatoid arthritis. *Nature* 2003;423:356-361