

Basel, 19 December 2008

## **MabThera inhibits the destruction of joints in patients with early rheumatoid arthritis**

**Phase III study in patients not previously treated with methotrexate meets primary endpoint**

Roche announced today that MabThera (rituximab) can significantly inhibit structural damage to joints in patients with early rheumatoid arthritis (RA) who have not been treated with methotrexate (MTX), the current standard of care for RA treatment.

Results from the IMAGE<sup>1</sup> study showed that at one year initiating treatment with MabThera in combination with MTX exhibited a significant reduction in the rate of progressive joint damage<sup>2</sup>, compared to initiating treatment with MTX alone. The trial was conducted in patients not previously treated with MTX and studied MabThera infusions of either the currently approved 1000mg dose or low dose 500mg in combination with MTX. Patients in each MabThera dosing group were compared to patients receiving MTX alone. Only the standard, currently approved 1000mg MabThera dose showed ability to significantly inhibit structural joint damage.

Damage to the structure of joints ultimately contributes to joint deformity and loss of mobility. As a result, prevention of structural joint damage, particularly in early disease, is a major goal of treatment in RA.

The study also showed that both doses of MabThera in combination with MTX were superior to MTX alone in relieving the signs and symptoms of RA (ACR scores<sup>3</sup>). Relieving the debilitating symptoms of the disease is another very important objective of RA therapy.

“The results of IMAGE show that MabThera has the potential to alter the course of rheumatoid arthritis by preventing the early damage to joints which ultimately causes deformity and disability. These pivotal findings add support for the early use of MabThera in the treatment of rheumatoid arthritis to allow patients to maintain a life as normal as possible,” said William M. Burns, CEO Pharmaceuticals Division of Roche.

MabThera is the first and only selective B cell therapy available for the treatment of RA. It has already

demonstrated significant clinical and radiographic benefits when used later in the RA treatment pathway. It is currently licensed for patients with severe disease who have had an inadequate response or intolerance to one or more tumour necrosis factor (TNF) inhibitors.

Data from the IMAGE study will be submitted for presentation at upcoming international scientific meetings. Roche plans to file the IMAGE data together with data from two other studies with the European health authorities in 2009 to extend the current label for MabThera.

RA is one of the most common autoimmune diseases, affecting more than 21 million people worldwide, with as many as three million sufferers in Europe alone. It is twice as common in women as in men and also impacts on the average life expectancy, shortening it by three to seven years. Seventy per cent of people with rheumatoid arthritis have signs of permanent joint damage within two years of the start of their disease.<sup>4</sup>

#### **About the IMAGE study**

IMAGE is a phase III international study involving 755 MTX-naïve patients with active RA. The study was conducted at 168 study sites across 27 countries. In this Phase III, randomised, controlled, double-blind, parallel-group multicenter study, patients received either MabThera (500mg or the currently approved 1000mg dose) or placebo by intravenous infusion on days 1 and 15, in combination with newly initiated MTX. The eligible patients who were not in DAS28<sup>5</sup> remission at week 24 received a second course of MabThera at the same dose as the first course. The study aimed to determine the efficacy of MabThera in reducing the progression of structural joint damage, as demonstrated by changes in validated radiographic parameters. The study also assessed the efficacy of MabThera in improving the signs and symptoms of RA and patients' physical function. A preliminary analysis of the data did not reveal any unexpected safety signals and the overall safety profile was consistent with that reported in previous studies.

#### **About rheumatoid arthritis and MabThera**

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. MabThera selectively targets B cells and represents a new highly effective therapeutic approach for RA in addition to existing treatments such as DMARDs and TNF inhibitors.

B cells are known to play a key role in the inflammation associated with RA. As the first and only selective B cell therapy available for the treatment of RA, MabThera represents a proven and truly different alternative

for RA patients. MabThera is the only RA treatment that has demonstrated the ability to preserve joint structure in patients who have inadequate response or are not able to tolerate TNF inhibitor therapy and offers an unprecedented duration of response of at least six months with each course. Each course of MabThera also provides the opportunity of sustained or improved relief for patients from the signs and symptoms of their disease.

MabThera is marketed in the US by Genentech and Biogen Idec under the brand name Rituxan®.

For a selection of broadcast footage clips relating to MabThera and rheumatoid arthritis please visit [www.thenewsmarket.com/roche](http://www.thenewsmarket.com/roche).

To view and download high resolution stills and media materials please visit the MabThera Virtual Press Office at [www.mabthera-ra.com](http://www.mabthera-ra.com)

#### **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 80,000 people. Additional information is available on the Internet at [www.roche.com](http://www.roche.com).

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### References

<sup>1</sup>IMAGE refers to International study in Methotrexate-nAive subjects investiGating Rituximabs Efficacy

<sup>2</sup>As measured by the change from baseline in total Genant modified Sharp score at week 52

<sup>3</sup>The ACR response is a standard assessment used to measure patients' responses to anti-rheumatic therapies, devised by the American College of Rheumatology (ACR). It requires a patient to have a defined percentage reduction in a number of symptoms and measures of their disease. For example, a 20%, 50% or 70% level of reduction (the percentage of reduction of RA symptoms) is represented as ACR20, ACR50 or ACR70. An ACR70 response is exceptional for existing treatments and represents a significant improvement in a patient's condition.

<sup>4</sup>O'Dell JR. *N Engl J Med* 2004; 350: 2591-2602

<sup>5</sup>The Disease Activity Score (DAS28) is a combined index that measures disease activity in patients with RA. It combines information from 28 tender and swollen joints (range 0-28), 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 Rheumatism Association (ARA).