

## **PRESS RELEASE**

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### **MabThera – a Unique Approach Providing Lasting Benefits for Patients with Rheumatoid Arthritis**

*Comprehensive long-term clinical success achieved in difficult-to-treat patients following just two administrations, two weeks apart*

San Diego, U.S.A.: Roche today announced positive results of the Phase III REFLEX study, evaluating the efficacy and safety of MabThera in patients with rheumatoid arthritis (RA), who have had an inadequate response to anti-TNF biologic therapy. The data were presented today at the American College of Rheumatology meeting in San Diego, California and demonstrate that MabThera (rituximab) significantly improved all efficacy measures of rheumatoid arthritis (RA) for six months following a single course of just two administrations. MabThera provided relief to almost three times as many patients compared to placebo. Currently these difficult-to-treat patients, who represent at least 30% of all those treated with existing biologic therapy, are left with few treatment alternatives.

These data herald the start of a unique way to treat RA, a common condition affecting over 21 million people worldwide, in which the immune system attacks the joints, often causing severe swelling, pain, fatigue and disability. Traditionally, biologic therapy is focussed on blocking the action of an immune system molecule called TNF while MabThera is the first and only RA treatment to target specific types of immune cells, called B cells. B cells play a key role in the chain of inflammatory events that ultimately lead to the damage of bone and cartilage in the joints, characteristic of RA. Moreover, MabThera's long-term treatment success was achieved following just 2 administrations, 2 weeks apart, providing a highly convenient regimen.

Presenting the results, Dr Stanley Cohen, M.D. Lead REFLEX investigator and Clinical Professor, Department of Internal Medicine at the University of Texas Southwestern Medical School, Dallas, commented, “These data will be of great interest to both physicians and patients, since they suggest that MabThera may offer patients the opportunity of at least six months relief of their symptoms with just two infusions. We observed MabThera responses as being consistently greater across the broad range of measures we looked at, in particular tender and swollen joint counts and fatigue.”

### **Significant improvements across all symptom parameters**

The results of the six-month analysis show that MabThera in combination with methotrexate (MTX), a standard RA treatment, was highly effective, producing statistically significantly higher response rates compared to MTX plus placebo: 51% of patients achieved 20% improvement in signs and symptoms (ACR20<sup>1</sup>), compared to 18% with MTX alone. The difference in the two groups was apparent after 8 weeks and sustained for the duration of the study after only 2 infusions of MabThera, two weeks apart. Over the six-month period, more than five times as many patients in the MabThera group achieved a 50% improvement in signs and symptoms compared to MTX alone (ACR50: 27% vs 5%), and twelve times more MabThera patients achieved a 70% improvement (ACR70: 12% vs 1%).

### **Safety Consistent with Earlier Studies**

Overall the MabThera regimens were well tolerated. Adverse events experienced were consistent with those noted in earlier studies of MabThera in RA. The most frequently reported adverse events in the study were primarily infusion-related, comparable to placebo and mild-to-moderate in intensity. Serious adverse events were similar in both treatment groups (7% in the MabThera group and 10% in the placebo group).

**-ENDS-**

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1. 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 or 50% 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.

## **Editor's Notes**

### **About Rheumatoid Arthritis and MabThera**

Rheumatoid arthritis is an autoimmune disease characterised by inflammation that leads to stiff, swollen and painful joints. Current treatments include disease-modifying drugs (DMARDs) and biologic therapy such as the anti-TNF drugs.

MabThera is a first-in-class therapy that selectively targets B cells early in the inflammatory cascade of rheumatoid arthritis. B cells are known to play a key role in the inflammation associated with rheumatoid arthritis and MabThera breaks the inflammatory cascade of RA – a series of reactions inflaming the synovia and leading to the cartilage loss and bone erosion that is characteristic of the disease, and may provide an innovative new treatment even in the most difficult-to-treat patients. MabThera has a strong heritage in the treatment of a form of lymphatic cancer called non-Hodgkin's lymphoma (NHL) where over 730,000 patients have been treated worldwide with MabThera over the last 8 years.

### **About the Study**

REFLEX (**R**andomised **E**valuation **o**f **L**ong-term **E**fficacy of **R**itu**X**imab in RA) is a pivotal Phase III study evaluating the efficacy and safety of rituximab in combination with methotrexate (MTX) in patients with the most difficult-to-treat RA – those with long-standing, severe disease who have failed to respond or are intolerant to anti-TNF therapy (based on lack of response or toxicity in accordance with the FDA approved dosage and administration guidelines for the use of anti-TNF therapy). A total of 520 patients were randomised in this multi-centre, double-blind, placebo-controlled trial. Patients received either a single treatment course of just two infusions of MabThera two weeks apart (1000mg i.v. on days 1 and 15), or placebo infusions, in combination with continuing MTX and a two-week course of glucocorticoids. The study was conducted as part of the overall development programme in 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 a supplier of innovative 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 a world leader in diagnostics, the leading supplier of drugs for cancer and transplantation and a market leader in virology. In 2004 sales by the Pharmaceuticals Division totalled 21.7 billion Swiss francs, while the Diagnostics Division posted sales of 7.8 billion Swiss francs. Roche employs roughly 65,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet ([www.roche.com](http://www.roche.com)).

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