

Basel, 18 September 2008

## **FDA issues complete response letter to Roche for Actemra Biologics License Application**

**No new clinical studies requested**

Roche today announced that the U.S. Food and Drug Administration (FDA) has issued a complete response letter for the Biologics License Application (BLA) for Actemra (tocilizumab), the first interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody studied for the treatment of adult patients with moderate to severe rheumatoid arthritis (RA).

Additional information requested by the FDA for approval does not involve safety or efficacy issues, nor do any additional studies need to be conducted as a pre-requisite for approval of Actemra. The FDA has requested additional documentation related to the manufacturing of Actemra and certain other outstanding components such as final labelling. Roche is committed to working with the FDA to promptly address these outstanding matters. Upon satisfactory completion of the FDA's requests and an approved label, Roche does not foresee any issues that would impact the quality, availability and supply of Actemra in the U.S.

“Roche is committed to making this important new therapy available to RA patients,” said William M. Burns, CEO of Roche's Pharmaceutical Division. “We will continue to work closely with the FDA to address its questions and define the path forward for Actemra. We are confident that we will be able to resolve these matters with the agency in the near future.”

Roche submitted the BLA for Actemra to the agency on November 26, 2007. The BLA for Actemra included results from five multi-national Phase III studies, which demonstrated that treatment with Actemra - alone or in combination with methotrexate or other disease modifying anti-rheumatic drugs (DMARDs) - significantly reduced RA signs and symptoms, regardless of previous therapy or disease severity, compared with current DMARDs alone. On July 29, 2008, the Arthritis Advisory Committee of the FDA voted 10-1 to recommend approval of Actemra. Actemra has also been filed with the European authorities and other world authorities.

### **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 some patients; these increases were generally mild and reversible, with no evidence of hepatic injuries or any observed impact on liver function. Laboratory changes, including increases in lipids (total cholesterol, LDL, HDL, triglycerides) and decreases in neutrophils and platelets, were seen in some 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 totaled 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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