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Roche Roche Group

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ACTEMRA/RoACTEMRA (tocilizumab) supplemental marketing authorizations submitted in the US and Europe for the treatment of systemic Juvenile Idiopathic Arthritis

- New hope for children suffering from debilitating arthritis -

Roche today announced that it has submitted a supplemental Biologics License Application (sBLA) to the United States (US) Food and Drug Administration (FDA) and an Accelerated Assessment[1] application to the European Medicines Agency (EMA) to extend the license indication of ACTEMRA (known as RoACTEMRA in Europe) for the treatment of systemic Juvenile Idiopathic Arthritis (sJIA).

There are currently no approved therapies for sJIA in the EU or US, which is characterised by inflammatory arthritis accompanied by intermittent fever, skin rash, anaemia, enlargement of the liver and/or spleen and inflammation of the lining of the heart and/or lungs.[i] The peak age of onset of sJIA is between 18 months and two years[ii,iii] although persistence of the disease into adulthood occurs. It has the worst long-term prognosis of all childhood arthritis subtypes, accounting for almost two-thirds of all deaths among children with arthritis, with an overall mortality rate estimated to be between two to four percent.[iv] Current treatment consists of high dose corticosteroids which do not improve the long-term prognosis and are often accompanied by severe side effects.[1]

The applications follow positive data from the global phase III TENDER study[v] that demonstrated ACTEMRA was effective in improving the signs and symptoms of sJIA. The study, presented at the European League Against Rheumatism (EULAR) congress, showed that, following three months' treatment with ACTEMRA, 85 percent of patients had a 30 percent improvement (JIA ACR30[2]) in the signs and symptoms of sJIA and absence of fever,

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[1] Accelerated Assessment Procedure Type II (Day 90) Variation. Accelerated Assessment Procedures are designed to meet the legitimate expectations of patients and to take account of the increasingly rapid progress of science and therapies. The process is reserved for medicinal products of major therapeutic interest, and procedures for obtaining temporary authorisations subject to certain annually reviewable conditions

[2] JIA ACR 30/70/90 response is defined as 3 of the 6 core components improving (from the Baseline assessments) by ≥ 30%, 70%, 90% respectively with no more than 1 of the remaining components worsening by > 30%. Core components include Physician global assessment of disease activity VAS; Parent/patient global assessment of overall well-being VAS; Number of joints with active arthritis; Number of joints with limitation of movement; Erythrocyte Sedimentation Rate (ESR); Functional ability – Childhood Health Assessment Questionnaire (CHAQ)

a primary characteristic of sJIA, compared to 24 percent of patients who received placebo. Further data showed 70 percent of patients on ACTEMRA achieved JIA ACR70† and 37 percent achieved JIA ACR90†, compared to eight percent and five percent of patients who received placebo, respectively. In addition to the significant improvement in JIA ACR response, nearly two-thirds of patients in the study were free of rash after three months.[5] In the study, ACTEMRA was well tolerated in children with sJIA with a safety profile similar to adults treated with ACTEMRA for rheumatoid arthritis (RA).

"sJIA is an extremely debilitating disease that can be life-threatening for young children, for which there are no currently approved medicines", commented Hal Barron, M.D, Head of Global Development and Chief Medical Officer for Roche. "With these striking data we hope ACTEMRA may become a treatment option that benefits children and their families living with this condition every day."

ACTEMRA inhibits the activity of interleukin-6 (IL-6), a contributor to the major features of sJIA including chronic synovial inflammation, articular cartilage damage, fever, anaemia, growth impairment and osteoporosis.[vi] It is already approved in the EU, US and other countries for adult RA, a disease also associated with elevated levels of IL-6. Studies in RA have demonstrated ACTEMRA's strong efficacy and safety, with consistently high remission rates across all patient types[vii] and inhibition of structural joint damage.[viii] In addition it is the only product to have proven superiority to methotrexate in monotherapy in ACR20, ACR50 and ACR70 responses at six months, in adult RA.[ix]

- ENDS -

About the TENDER Study

The TENDER study is an international study, including approximately 70 centres in 20 countries. The study aimed to assess efficacy for signs and symptoms and short term safety of ACTEMRA versus placebo in 112 patients with active sJIA. Additional aims were efficacy for the common systemic features of sJIA, steroid reduction, other concomitant drug reductions, safety with chronic administration and biomarkers. In this randomised study, patients received ACTEMRA 8 mg/kg (if weight ≥ 30 kg) and 12 mg/kg (if weight < 30 kg), every 2 weeks versus placebo infusions for 12 weeks. Patients were also given the option to enroll for long-term, open label follow-up. The study was performed in close collaboration with the PRINTO (Paediatric Rheumatology International Trials Organisation) and PRCSG (Paediatric Rheumatology Collaborative Study) groups.

About ACTEMRA/RoACTEMRA

ACTEMRA/RoACTEMRA is the result of research collaboration by Chugai and is also being co-developed globally with Chugai. ACTEMRA/RoACTEMRA is the first humanised interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody. An extensive clinical development programme of five Phase III trials was designed to evaluate clinical findings of ACTEMRA/RoACTEMRA, all of which met their primary endpoints. ACTEMRA/RoACTEMRA was first approved in Japan, and launched by Chugai in June 2005 as a therapy for Castleman's disease; in April 2008, additional indications for rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis and systemic-onset juvenile idiopathic arthritis were also approved in Japan. ACTEMRA/RoACTEMRA was approved in the European Union in January 2009 for the treatment of RA in patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) inhibitors. It is also approved for use in over 90 other countries, including India, Brazil, Switzerland, and Australia. ACTEMRA/RoACTEMRA was most recently (January 2010) approved in the United States for the treatment of adult patients with moderately to severely active RA who have had an inadequate response to one or more TNF inhibitors.

The overall safety profile of ACTEMRA/RoACTEMRA is consistent across all global clinical studies. The serious adverse events reported in ACTEMRA/RoACTEMRA clinical studies include serious infections, gastrointestinal perforations and hypersensitivity reactions including anaphylaxis. The most common adverse events 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/RoACTEMRA, may cause an increase in the risk of malignancies.

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 2009, Roche had over 80,000 employees worldwide and invested almost 10 billion Swiss francs in R&D. The Group posted sales of 49.1 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.

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[viii] LITHE: Tocilizumab inhibits radiographic progression and improves physical function in rheumatoid arthritis (RA) patients (Pts) at 2 years with increasing clinical efficacy over time. Fleischmann, R et al. Oral presentation at ACR, 18th October 2009

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