CHUGAI PHARMACEUTICAL CO., LTD.
Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome,
Chuo-ku Tokyo, 103-8324 Japan
TEL:+81-(0)3-3273-0881
FAX:+81-(0)3-3281-6607
E-mail:pr@chugai-pharm.co.jp
URL:http://www.chugai-pharm.co.jp

CHUGAI
Roche Roche Group

Roche Release, Basel, 20th December 2013

Roche's New Subcutaneous Formulation of RoACTEMRA Gains CHMP Positive Opinion in Europe for Moderate to Severe Rheumatoid Arthritis

- Upon approval, RoACTEMRA would be the first IL-6 biologic available in subcutaneous and intravenous administration for both monotherapy and combination therapy
- New subcutaneous formulation would offer greater flexibility for rheumatoid arthritis patients

Roche announced today that the subcutaneous formulation of RoACTEMRA (tocilizumab) has received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) for the treatment of moderate to severe active rheumatoid arthritis (RA) in patients who have either responded inadequately to, or who are intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) inhibitors.

As with the intravenous (IV) formulation indication, the CHMP has recommended approval of the subcutaneous formulation for use both as monotherapy and in combination with methotrexate (MTX).

"This positive opinion from the CHMP is an important step toward providing physicians and patients the flexibility to choose whether intravenous or subcutaneous RoACTEMRA treatment is most appropriate for them," said Hal Barron, M.D, Head of Global Product Development and Chief Medical Officer at Roche. "With the new RoACTEMRA subcutaneous formulation adult patients or their caregiver will be able to administer the medicine at home after appropriate training."

The CHMP's positive opinion is based on data from the phase III SUMMACTA and BREVACTA studies. SUMMACTA showed that the efficacy and tolerability of subcutaneous RoACTEMRA was comparable with IV RoACTEMRA.[1,2] The European Commission will now consider the CHMP positive opinion for its decision on the marketing authorisation for the subcutaneous formulation in the European Union. Upon approval, RoACTEMRA would be the first humanized interleukin-6 (IL-6) receptor-antagonist biologic in subcutaneous and intravenous formulation for both monotherapy and combination therapy.

The subcutaneous formulation is administered under the skin and would be available via a prefilled syringe and a prefilled pen, a medical device designed for self-administration of a single dose of drug. The subcutaneous formulation was authorized in Japan and the United States earlier this year, where it is known as ACTEMRA.

About Rheumatoid Arthritis

RA is an autoimmune disease estimated to affect up to 70 million people worldwide.[3] RA causes joints to become chronically inflamed, painful and swollen, and patients can become increasingly disabled as cartilage and bone is damaged.[4] RA patients are often treated with a number of medicines, combining protein-based biologic therapies with MTX, the most common DMARD.[5,6]

About RoACTEMRA (tocilizumab)

RoACTEMRA is the first humanized interleukin 6 receptor-antagonist monoclonal antibody approved for use in combination with or without methotrexate, for the treatment of moderate to severe RA in adult patients who have either responded inadequately to, or who are intolerant to, previous therapy with one or more DMARDs or TNF antagonists.[7]

The extensive RoACTEMRA clinical development program included five phase III clinical studies and enrolled more than 4,000 people with RA in 41 countries. In addition, the phase IV ADACTA study showed that monotherapy with RoACTEMRA IV was superior to monotherapy with adalimumab in reducing signs and symptoms of RA in MTX-intolerant patients or patients for whom MTX treatment was considered ineffective or inappropriate.[8] The overall safety profile of both medications was consistent with previously reported data.[8] This data was recognised in the recent European League Against Rheumatism recommendations for the management of RA, where RoACTEMRA was recommended as a first-line biologic and was highlighted for use as monotherapy.[5]

RoACTEMRA IV formulation is also approved for the treatment of active systemic juvenile idiopathic arthritis (SJIA) and polyarticular juvenile idiopathic arthritis (PJIA) in patients two years of age and older.[7]

RoACTEMRA is part of a co-development agreement with Chugai Pharmaceutical. It has been approved in Japan since April 2005 for Castleman's disease, followed by approvals for RA, SJIA and PJIA in 2008. More than 275,000 patients have been treated with RoActemra since it first launched. RoACTEMRA is approved in the European Union, and several other countries, including the United States, China, India, Brazil, Switzerland and Australia.

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, infectious diseases, inflammation, metabolism and neuroscience. Roche is also the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics, and a frontrunner 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 2012 Roche had over 82,000 employees worldwide and invested over 8 billion Swiss francs in R&D. The Group posted sales of 45.5 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

All trademarks used or mentioned in this release are protected by law.

References

1. Burmester G et al. A randomised, double-blind, parallel-group study of the safety and efficacy of subcutaneous tocilizumab versus intravenous tocilizumab in combination with traditional disease-modifying antirheumatic drugs in patients with moderate to severe rheumatoid arthritis (SUMMACTA study). Ann Rheum Dis 2013; 0:1–6. doi:10.1136/annrheumdis-2013-203523.
2. Kivitz A et al. A Randomized, Double-Blind, Parallel-Group Study of the Safety and Efficacy of Tocilizumab Subcutaneous Versus Placebo in Combination With Traditional DMARDs in Patients With Moderate to Severe Rheumatoid Arthritis (BREVACTA). ACR, November 2012.
3. World Health Organization. Chronic rheumatic conditions. http://www.who.int/chp/topics/rheumatic/en/ (Last accessed December2013).
4. Patient UK.Rheumatoid arthritis. http://www.patient.co.uk/health/rheumatoid-arthritis (Last accessed December 2013).
5. Smolen J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 0:1–18. doi:10.1136/annrheumdis-2013-20457.
6. Singh J. 2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis. Arthritis Care & Research. Vol. 64, No. 5, May 2012, pp 625–639.
7. RoACTEMRA Summary of Product Characteristics. Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000955/WC500054890.pdf (Last accessed December 2013).
8. Gabay C, et al. The Lancet 2013. 381;9877:1541-1550.