Media Release

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FDA approves Roche's Actemra/RoActemra (tocilizumab) for the treatment of CAR T cell-induced cytokine release syndrome

- **Actemra/RoActemra is the first FDA-approved treatment for severe or life-threatening cytokine release syndrome induced by CAR T cell therapy**
- **CAR T cell therapy is an immunotherapy designed for the treatment of certain cancers**
- **This is the seventh FDA approval for Actemra/RoActemra since its US launch in 2010**

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the US Food and Drug Administration (FDA) has approved Actemra/RoActemra® (tocilizumab) intravenous injection for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in patients two years of age and older. CRS, which is caused by an overactive immune response, has been identified as a potentially severe and life-threatening side effect of CAR T cell therapy for certain cancers.[1]

"Until today, there has never been an FDA-approved treatment to manage severe cytokine release syndrome associated with CAR T cell therapy, which is marked by a rapid onset and can cause life-threatening complications," said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development. "Today's approval of Actemra/RoActemra for CRS provides physicians with an important tool to help manage this potentially life-threatening side effect."

The approval is based on a retrospective analysis of pooled outcome data from clinical trials of CAR T cell therapies for blood cancers, which assessed the efficacy of Actemra/RoActemra in the treatment of CRS.[2] The study population included 45 pediatric and adult patients treated with Actemra/RoActemra, with or without additional high-dose corticosteroids, for severe or life-threatening CRS. Thirty-one patients (69%; 95% CI: 53%–82%) achieved a response, defined as resolution of CRS within 14 days of the first dose of Actemra/RoActemra, no more than two doses of Actemra/RoActemra were needed, and no drugs other than Actemra/RoActemra and corticosteroids were used for treatment. No adverse reactions related to Actemra/RoActemra were reported.[2] A second study confirmed resolution of CRS within 14 days using an independent cohort that included 15 patients with CAR T cell-induced CRS.

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The FDA granted Priority Review and Orphan Drug Designation to Actemra/RoActemra for the treatment of CAR T cell-induced CRS based on the rare, severe and life-threatening nature of CRS and available data on the safety and efficacy of Actemra/RoActemra. Priority Review Designation is granted to medicines that the FDA has determined to have the potential to provide significant improvements in the safety and effectiveness of the treatment of a serious condition. Orphan Drug Designation may be granted to medicines intended for the treatment of conditions that affect fewer than 200,000 people in the United States.

About CAR T Cell Therapy-Induced Cytokine Release Syndrome

CAR T cell therapies are designed for the treatment of certain blood cancers by modifying an individual patient's own cells to specifically target the cancer cells. CRS, which is caused by an overactive immune response, has been identified as a potentially severe and life-threatening side effect of CAR T cell therapies. Most people with CRS experience mild or moderate flu-like symptoms which are easily managed. However, some patients experience more severe symptoms that may lead to potentially life-threatening complications such as cardiac dysfunction, acute respiratory distress syndrome or multi-organ failure.[1]

About Actemra/RoActemra (tocilizumab)

Actemra/RoActemra/RoActemra is the first approved anti-IL-6 receptor biologic available in both intravenous (IV) and subcutaneous (SC) formulations for the treatment of adult patients with moderate to severe active rheumatoid arthritis (RA). Actemra/RoActemra can be used alone or with methotrexate (MTX) in adult RA patients who are intolerant to, or have failed to respond to, other anti-rheumatic medications. The extensive Actemra/RoActemra RA IV clinical development programme included five phase III clinical studies and enrolled more than 4,000 people with RA in 41 countries. The Actemra/RoActemra RA SC clinical development programme included two phase III clinical studies and enrolled more than 1,800 people with RA in 33 countries. In Europe, Actemra/RoActemra IV and SC is also approved for use in adult patients with severe, active and progressive RA who previously have not been treated with MTX. Actemra/RoActemra IV formulation is approved in most major countries for polyarticular juvenile idiopathic arthritis (pJIA) and systemic juvenile idiopathic arthritis (sJIA) in children two years of age and older. In the United States and New Zealand, Actemra/RoActemra subcutaneous injection is approved for the treatment of giant cell arteritis (GCA). Actemra/RoActemra is the first therapy approved for the treatment of adult patients with GCA. Actemra/RoActemra is part of a co-development agreement with Chugai Pharmaceutical Co., Ltd and has been approved in Japan since April 2005. Actemra/RoActemra is approved in 116 countries worldwide.

Actemra/RoActemra is also being investigated in a global phase III multicentre, randomised, double-blind, placebo-controlled study (NCT02453256) for patients with systemic sclerosis (SSc) also known as scleroderma. Actemra/RoActemra was granted Breakthrough Therapy Designation for SSc by the FDA in June 2015.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry eight years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 billion. 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.

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[2] Grupp, SA, et al. Analysis of a Global Registration Trial of the Efficacy and Safety of CTL019 in Pediatric and Young Adults with Relapsed/Refractory Acute Lymphoblastic Leukemia (ALL). (2016). Blood, 128(22), 221.