Media Release

Roche's Actemra/RoActemra becomes the first biologic therapy approved by the FDA for slowing the rate of decline in pulmonary function in adults with systemic sclerosis-associated interstitial lung disease, a rare, debilitating condition

- **Systemic sclerosis (SSc) is a rare disease that affects about 2.5 million people worldwide**
- **Approximately 80% of SSc patients may be affected by interstitial lung disease (ILD), a progressive disease that can significantly impact lung function and can be life-threatening**
- **In a global study, Actemra/RoActemra reduced the rate of progressive loss of lung function in people with SSc-ILD compared to placebo**
- **The U.S. Food and Drug Administration previously granted Priority Review designation to Actemra/RoActemra for the treatment of SSc-ILD**

Basel, 05 March 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the U.S. Food and Drug Administration (FDA) approved Actemra®/RoActemra® (tocilizumab) subcutaneous injection for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD), a debilitating condition with limited treatment options. Actemra/RoActemra is the first biologic therapy approved by the FDA for the treatment of the disease.

Systemic sclerosis (SSc), also known as scleroderma, is an often devastating autoimmune disease that worsens over time and has no cure. It occurs when the immune system malfunctions causing tissues of the skin and lungs to thicken and harden.[1-3] SSc affects about 2.5 million people worldwide.[4] Interstitial lung disease (ILD), which may occur in approximately 80% of SSc patients, causes inflammation and scarring of the lungs and can be life-threatening.[5]

"We are honored to offer the very first FDA-approved biologic treatment option to people living with systemic sclerosis-associated interstitial lung disease," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We worked closely with the FDA to evaluate Actemra/RoActemra's impact on lung function in this setting. This milestone approval provides a much-needed new treatment option for people living with this rare, debilitating disease."

The FDA approval is based on data from the focuSSced trial, a Phase III randomised, double-blind, placebo-controlled clinical trial of 212 adults with systemic sclerosis. Supportive information was also used from the faSScinate trial, a Phase II/III, randomised, double-blind, placebo-controlled study in patients with SSc. The focuSSced trial did not meet its primary endpoint of change from baseline to week 48 in the modified Rodnan Skin Score (mRSS), which is a standard outcome measure for skin fibrosis (the scarring or hardening of the skin) in SSc. There also was not a statistically significant effect on the primary endpoint of mRSS in the faSScinate trial.

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However, in the overall population of the focuSSced study, patients treated with Actemra/RoActemra, as compared to placebo-treated patients, were observed to have less decline from baseline to week 48 in observed forced vital capacity (FVC), a common measure of lung function that assesses how much air can be exhaled, and percent predicted forced vital capacity (ppFVC), which compares the observed FVC to that expected for a healthy person of the same age, gender, race and height. FVC results were similar in the faSScinate study.

Of the 212 patients who were randomised into the focuSSced study, 68 patients (65%) in the Actemra/RoActemra arm and 68 patients (64%) in the placebo arm had SSc-ILD at baseline, as confirmed by a visual read of high resolution computed tomograph (HRCT) by blinded thoracic radiologists. Post-hoc exploratory analyses were performed to evaluate the results within the subgroups of patients with and without SSc-ILD. The ppFVC and FVC results in the overall population were primarily driven by results in the SSc-ILD subgroup. In that subgroup, patients in the Actemra/RoActemra group had a smaller decline in mean ppFVC than patients on placebo (0.07% vs. -6.4%, mean difference 6.47%), and a smaller decline in FVC compared to placebo (mean change -14 mL vs. -255 mL, mean difference 241 mL). The mean change from baseline to week 48 in mRSS in patients receiving Actemra/RoActemra compared to placebo was -5.88 vs. -3.77, mean difference -2.11.

The safety profile for Actemra/RoActemra through week 48 in the focuSSced study was comparable for SSc-ILD and SSc patients overall, and in both the focuSSced and faSScinate studies was consistent with the known safety profile of Actemra/RoActemra. The most common adverse events in patients treated with Actemra were infections.

Actemra was previously granted Priority Review for this condition by the FDA. This designation is given to medicines that have the potential to provide significant improvements in the treatment, prevention or diagnosis of a disease. This is the sixth FDA approved indication for Actemra/RoActemra since the medicine was launched in the United States in 2010.

About the focuSSced Trial
The focuSSced (NCT02453256) study was a Phase III, multicentre, randomised, double-blind, placebo-controlled, parallel-group trial to assess the efficacy and safety of Actemra/RoActemra versus placebo in people living with systemic sclerosis. Patients were randomised in a 1:1 ratio to receive weekly subcutaneous injections of 162 mg of Actemra/RoActemra or placebo during the 48-week, double-blinded, placebo-controlled period, followed by open-label Actemra/RoActemra 162 mg administered subcutaneously every week for another 48 weeks. Rescue treatment was allowed during the treatment period after 16 weeks for >10% ppFVC decline or after 24 weeks for worsening skin fibrosis.

The primary efficacy endpoint was change from baseline at week 48 in mRSS. Change from baseline in FVC at week 48 was a key secondary endpoint. Of the 212 patients who were randomised, 68 patients (65%) in the Actemra/RoActemra arm and 68 patients (64%) in the placebo arm had SSc-ILD at baseline, as confirmed by

a visual read of high resolution computed tomograph (HRCT) by blinded thoracic radiologists. The mean ppFVC at baseline for patients with SSc-ILD identified by HRCT was 79.6% (median 80.5%). Post-hoc analyses were performed to evaluate results within the subgroups of patients with and without SSc-ILD. The results of the key FVC secondary endpoints support the effectiveness of Actemra/RoActemra in reducing the rate of progressive loss of lung function in SSc-ILD patients. However, as the trial did not provide evidence of an effect on the primary endpoint of mRSS, the estimated magnitude of effect on the FVC endpoints should be interpreted with caution and comparisons to results of other products and studies may be misleading.

About Actemra/RoActemra

Actemra/RoActemra was the first approved anti-IL-6 receptor biologic, and is 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 disease-modifying anti-rheumatic drugs (DMARDs). In Europe, RoActemra IV and SC are also approved for use in adult patients with severe, active and progressive RA who previously have not been treated with MTX. Actemra/RoActemra IV and SC are also approved globally for polyarticular juvenile idiopathic arthritis (pJIA) and systemic juvenile idiopathic arthritis (sJIA) in children two years of age and older. Actemra/RoActemra SC is approved globally for giant cell arteritis (GCA), and Actemra/RoActemra IV is approved for the treatment of chimeric antigen receptor (CAR) T-cell-induced severe or life-threatening cytokine release syndrome (CRS) in people two years of age and older. Actemra/RoActemra was the first approved treatment for sJIA, GCA and CRS. Actemra SC is now approved in the U.S. for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD). In addition to the above-mentioned indications, in Japan Actemra IV is also approved for the treatment of Castleman's disease and adult Still's disease, and the Actemra SC formulation is approved for Takayasu arteritis. 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 more than 110 countries worldwide.

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. More than 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. Moreover, for the twelfth consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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