Roche provides an update on the phase III COVACTA trial of Actemra/RoActemra in hospitalised patients with severe COVID-19 associated pneumonia

- **COVACTA trial did not meet its primary endpoint of improved clinical status in patients with COVID-19 associated pneumonia, or the key secondary endpoint of reduced patient mortality**
- **The study is the first global, randomised, double-blind, placebo-controlled phase III trial investigating Actemra/RoActemra in this setting**
- **Roche remains committed to continuing the Actemra/RoActemra clinical trial programme in COVID-19 to further explore Actemra/RoActemra in other treatment settings, including in combination with an antiviral**

Basel, 29 July - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III COVACTA study of Actemra®/RoActemra® (tocilizumab) did not meet its primary endpoint of improved clinical status in hospitalised adult patients with severe COVID-19 associated pneumonia. In addition, the key secondary endpoints, which included the difference in patient mortality at week four, were not met; however, there was a positive trend in time to hospital discharge in patients treated with Actemra/RoActemra. The COVACTA study did not identify any new safety signals for Actemra/RoActemra. Further analysis of the trial results is needed to fully understand the data. The results will be submitted for publication in a peer-reviewed journal.

"People around the world are waiting for further effective treatment options for COVID-19 and we are disappointed that COVACTA did not demonstrate a benefit for patients in either clinical status or mortality at week four. We will continue to generate evidence to provide a more complete understanding of Actemra/RoActemra in COVID-19 associated pneumonia," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are grateful for the patients and physicians around the world who helped us to complete this study quickly during a public health crisis, while upholding the highest standards of scientific rigour. We will keep working to help combat the COVID-19 pandemic."

The COVACTA trial was conducted in collaboration with the Biomedical Advanced Research and Development Authority (BARDA), part of the Office of the Assistant Secretary for Preparedness and Response at the United States Department of Health and Human Services.

COVACTA evaluated the safety and efficacy of intravenous Actemra/RoActemra added to standard-of-care treatment compared to treatment with placebo plus standard of care. The primary endpoint of clinical status in hospitalised adult patients with severe COVID-19 associated pneumonia was measured by a 7-category ordinal scale, which tracked patients' clinical status based on the need for intensive care and/or ventilator use, as well as supplemental oxygen requirements. The COVACTA trial is the first global, randomised, double-blind, placebo-controlled phase III study to investigate Actemra/RoActemra in adult patients hospitalised with severe COVID-19 associated pneumonia, with study locations in the US, Canada and Europe.

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Summary of Key COVACTA Clinical and Safety Findings

- Primary endpoint not met: The difference in clinical status between Actemra/RoActemra and placebo in patients assessed using a 7-category ordinal scale at week four was not statistically significant (p=0.36; odds ratio [95% CI] = 1.19 [0.81, 1.76], a statistically significant odds ratio greater than 1 would have favoured Actemra/RoActemra).
- There was no difference between Actemra/RoActemra and placebo in the percentage of patients that died by week four (Actemra/RoActemra = 19.7% and placebo = 19.4% with a difference [95% CI] of 0.3% [-7.6%, 8.2%], p=0.9410)
- Time to hospital discharge or 'ready to discharge' was shorter in patients treated with Actemra/RoActemra than in those treated with placebo. The median time to discharge or 'ready to discharge' for Actemra/RoActemra was 20 days and for placebo was 28 days (median time [95% CI]: Actemra/RoActemra = 20.0 [17.0, 27.0]; placebo = 28.0 [20.0, NE], p=0.0370). However, the difference cannot be considered statistically significant as the primary endpoint was not met.
- The difference in ventilator-free days between Actemra/RoActemra and placebo was not statistically significant (median of 22 days for Actemra/RoActemra and 16.5 days with placebo, difference in medians [95% CI] = 5.5 [-2.8, 13.0], p=0.3202).
- At week four, rates of infections were 38.3% and 40.6% in the Actemra/RoActemra and placebo arms, respectively, and the rates of serious infections were 21.0% and 25.9% in the Actemra/RoActemra and placebo arms, respectively. The COVACTA study did not identify any new safety signals for Actemra/RoActemra.

In addition to COVACTA, Roche has initiated several studies to further investigate Actemra/RoActemra as a potential treatment for patients with COVID-19 associated pneumonia, including two phase III clinical trials, REMDACTA and EMPACTA, as well as the phase II MARIPOSA trial. There are also a number of independent trials of Actemra/RoActemra in this setting. Actemra/RoActemra has not previously been studied in, nor approved for, COVID-19 associated pneumonia.

For more information on how Roche is responding to the global COVID-19 pandemic, please visit our COVID-19 response page.

About the COVACTA Trial

COVACTA is a global, randomised, double-blind, placebo-controlled phase III study (COVACTA, NCT04320615) evaluating the safety and efficacy of intravenous Actemra/RoActemra added to standard of care in adult patients hospitalised with severe COVID-19 associated pneumonia compared to placebo plus standard of care. The primary and secondary endpoints include clinical status, mortality, mechanical ventilation and intensive care unit (ICU) variables at week four. Patients will be followed for 60 days post randomisation.

About Actemra/RoActemra

Actemra/RoActemra was 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 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 approved globally for polyarticular juvenile idiopathic arthritis (pJIA) and in the US and Europe for systemic juvenile idiopathic arthritis (sJIA) in children two years of age and older. Actemra/RoActemra SC injection is also the first approved therapy for the treatment of giant cell arteritis (GCA) in more than 40 countries, including the US and Europe. In the US and Europe, Actemra/RoActemra IV injection 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 CRS in this setting. A prefilled auto-injector ACTPen has been approved in the US and Europe. In Japan, Actemra is also approved for the treatment of Castleman's disease, adult Still's disease and Takayasu arteritis, in addition to the above mentioned indications. 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's Response to the COVID-19 Pandemic
The COVID-19 pandemic continues to evolve globally, with varying developments from country to country. We are partnering with healthcare providers, laboratories, authorities and organisations to help ensure patients receive the tests, treatment and care that they need.

Reliable, high-quality testing is essential to help healthcare systems overcome this pandemic. On 12 March, we received FDA Emergency Use Authorisation (EUA) for a high-volume molecular test to detect SARS-CoV-2, the virus that causes COVID-19. It is also available in countries accepting the CE Mark. On 3 May, Roche announced that its COVID-19 antibody test, aimed at detecting the presence of antibodies in the blood, also received FDA EUA and is available in markets accepting the CE mark. Also in June, we received an FDA EUA for the Elecsys® IL-6 test to assist in identifying severe inflammatory response in patients with confirmed COVID-19, as well as launching Roche v-TAC, which could help simplify the screening, diagnosis and monitoring of patients with respiratory compromise in the current COVID-19 pandemic. Roche is working closely with governments and health authorities around the world, and has significantly increased production to help ensure availability of tests globally.

We are actively involved in understanding the potential of our existing portfolio for COVID-19 and are researching options for the future.

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 eleventh 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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