

Roche's phase III EMPACTA study showed Actemra/RoActemra reduced the likelihood of needing mechanical ventilation in hospitalised patients with COVID-19 associated pneumonia

- **EMPACTA is the first global phase III trial to show efficacy with Actemra/RoActemra in COVID-19 associated pneumonia and the first with a focus on enrolling largely underserved and minority patients**
- **There was no statistical difference in mortality between patients who received Actemra/RoActemra or placebo**
- **Roche plans to share these results with health authorities, including the US FDA**

Basel, 18 September 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the phase III EMPACTA study met its primary endpoint, showing that patients with COVID-19 associated pneumonia who received Actemra®/RoActemra® (tocilizumab) plus standard of care were 44% less likely to progress to mechanical ventilation or death compared to patients who received placebo plus standard of care (log-rank p-value = 0.0348; HR [95% CI] = 0.56 [0.32, 0.97]). The cumulative proportion of patients who progressed to mechanical ventilation or death by day 28 was 12.2% in the Actemra/RoActemra arm versus 19.3% in the placebo arm. The EMPACTA study did not identify any new safety signals for Actemra/RoActemra.

“The EMPACTA trial demonstrated that Actemra/RoActemra can reduce the need for mechanical ventilation in patients with COVID-19 associated pneumonia, an important outcome in this serious disease,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “We plan to share this important data with the US Food and Drug Administration (FDA) and other health authorities around the world.”

The study is the first global, phase III COVID-19 clinical trial to primarily enrol patient populations that are often underrepresented in clinical studies and have been disproportionately affected by the COVID-19 pandemic. Approximately 85% of the 389 patients were from minority racial and ethnic groups. The majority of patients were Hispanic, with significant representation of Native American and Black populations. The trial was conducted in the United States, South Africa, Kenya, Brazil, Mexico and Peru.

“We have been striving to improve inclusion and diversity in our trials,” said Jamie Freedman, M.D., Ph.D., Head of U.S. Medical Affairs. “During the COVID-19 pandemic, we saw how high the stakes were for many communities of colour and made diversity the centerpiece of this trial.”

The EMPACTA trial builds on Roche’s work in [Advancing Inclusive Research](#), a cross-organisational US initiative to help address barriers in clinical research for underrepresented racial and ethnic groups.

Summary of Key EMPACTA Clinical and Safety Findings

- Primary endpoint was met: patients with COVID-19 associated pneumonia who received Actemra/RoActemra plus standard of care were 44% less likely to progress to mechanical ventilation or death compared to patients who received placebo plus standard of care (log-rank p-value = 0.0348; HR [95% CI] = 0.56 [0.32, 0.97]). The cumulative proportion of patients who progressed to mechanical ventilation or death by day 28 was 12.2% in the Actemra/RoActemra arm versus 19.3% in the placebo arm.
- Key secondary endpoints
 - The difference in time to hospital discharge or “ready for discharge” to day 28 was not significant (median (days): Actemra = 6; placebo (PBO) = 7.5; log-rank p-value = 0.2456; HR [95% CI] = 1.16 [0.90, 1.48])
 - The difference in time to improvement in ordinal clinical status to day 28 was not significant (median (days): Actemra = 6; PBO = 7; log-rank p-value = 0.2597; HR [95% CI] = 1.15 [0.90, 1.47])
 - Time to clinical failure to day 28 was longer in the Actemra arm compared to the placebo arm (median (days): Actemra = not-estimable (NE); PBO = NE; log-rank p = 0.0217; HR [95% CI] = 0.55 [0.33, 0.92]). However, the difference cannot be considered statistically significant as other key secondary endpoints were not met.
 - There was no statistical difference in mortality between patients who received Actemra or placebo by day 28 (Actemra = 10.4%; PBO = 8.6%, p-value = 0.5146, Difference [95% CI]: 2.0% [-5.2%, 7.8%]).
- At day 28, incidence of infections was 10% and 11% in the Actemra/RoActemra and placebo arms, respectively, and the incidence of serious infections was 5.0% and 6.3% in the Actemra/RoActemra and placebo arms, respectively. The most common adverse events in patients who received Actemra/RoActemra were constipation (5.6%), anxiety (5.2%), and headache (3.2%). The EMPACTA study did not identify any new safety signals for Actemra/RoActemra.

Results from the EMPACTA trial will be submitted for publication in a peer-reviewed journal.

Actemra/RoActemra is currently being investigated as a potential treatment for COVID-19 associated pneumonia, including in combination with an antiviral in the phase III REMDACTA clinical trial. Results from the phase III COVACTA trial in patients with severe COVID-19 associated pneumonia were released in July. In addition, there are a number of independent trials of Actemra/RoActemra in this setting. Actemra/RoActemra has not been approved by any health authority 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 EMPACTA Trial

EMPACTA (Evaluating Minority Patients with Actemra) is a Phase III, randomised, double-blind, placebo-controlled multicenter study (EMPACTA, NCT04372186) to evaluate the efficacy and safety of Actemra in the treatment of hospitalised COVID-19 associated pneumonia among patients that are often underrepresented in clinical trials.

The trial enrolled hospitalised patients older than 18 years with confirmed SARS-CoV-2 (COVID-19) infection with SpO₂ <94% while on ambient air who did not require noninvasive or invasive mechanical ventilation. The primary endpoint is the cumulative proportion of participants dying or requiring mechanical ventilation by Day 28. Secondary objectives include: time to clinical failure, defined as the time to death, mechanical ventilation, ICU admission, or withdrawal (whichever occurs first); mortality rate by Day 28; and time to hospital discharge or “ready for discharge.”

The study enrolled 389 patients in the United States, South Africa, Kenya, Brazil, Mexico and Peru.

About the REMDACTA Trial

REMDACTA is a two-armed global phase III, randomised, double-blind, multi-centre study (REMDACTA, NCT04409262) to evaluate the efficacy and safety of Actemra/RoActemra plus remdesivir, versus placebo plus remdesivir in hospitalised patients with severe COVID-19 associated pneumonia receiving standard of care. The REMDACTA trial is being conducted in collaboration with Gilead Sciences, Inc. The primary endpoint of the study is clinical status as measured by a 7-Category Ordinal Scale by Day 28. Key secondary endpoints include mortality, mechanical ventilation, and intensive care variables. 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 and we are partnering with healthcare providers, laboratories, authorities and organisations to help make sure that patients receive the tests, treatment and care they need. This new test is an additional step in Roche's fight against the COVID-19 pandemic, which has already included:

- Launching COVID-19 diagnostic tests for active infection and the detection of antibodies in patients who have been exposed to the virus,
- Investigating treatments from our existing portfolio to better understand their potential to treat patients with COVID-19,
- Increasing manufacturing and supply chain capacity to meet product demand across our portfolio within the wider context of COVID-19 treatment, and
- Ensuring the supply of our existing medicines and diagnostics to patients around the world under exceptional conditions.

Reliable, high-quality testing is essential to help healthcare systems overcome this pandemic. On 13 March we received FDA Emergency Use Authorisation for a high-volume molecular test to detect SARS-CoV-2, the virus that causes COVID-19, which 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 Emergency Use Authorisation 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. In July, we added a Rapid Antibody Test, with SD Biosensor as distribution partner, to our portfolio, that allows the detection of antibodies against Covid-19 at the point of care. On 1 September we announced that we will launch a SARS-CoV-2 Rapid Antigen Test, in late September, for markets accepting the CE Mark. We also intend to file for Emergency Use Authorisation (EUA) to the U.S. Food and Drug Administration (FDA). The SARS-CoV-2 Rapid Antigen Test is for use in point of care settings for both symptomatic and asymptomatic people. 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 and are researching options for the future. Roche has an ongoing clinical trial program evaluating the role of Actemra/RoActemra (tocilizumab) in COVID-19 pneumonia. On 29 July we announced that the 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 was 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. 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. Roche has further initiated an internal early research programme focused on the development of medicines for COVID-19 and is engaged in multiple research collaborations. On 19 August, we announced a partnership with Regeneron to develop, manufacture and distribute REGN-COV2, Regeneron's investigational antiviral antibody combination, to people around the globe.

In these exceptional times, Roche stands together with governments, healthcare providers and all those working to overcome the pandemic

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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