Media Release

Positive phase III results for Roche's satralizumab in neuromyelitis optica spectrum disorder published in the New England Journal of Medicine

- **Satralizumab demonstrated robust efficacy, sustained for 144 weeks, in significantly reducing the risk of relapse in combination with baseline immunosuppressant therapy**
- **Satralizumab targets the interleukin-6 (IL-6) receptor, a potential key driver of neuromyelitis optica spectrum disorder (NMOSD)**
- **NMOSD is a rare, debilitating autoimmune disease of the central nervous system that can cause visual impairment, motor disability and even death**

Basel, 2 December 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that data from SAkuraSky, a pivotal phase III study of the investigational medicine satralizumab for the treatment of neuromyelitis optica spectrum disorder (NMOSD), were published in the 27 November 2019 online issue of the New England Journal of Medicine (NEJM).

"The positive results from the pivotal SAkuraSky study of satralizumab support the hypothesis that IL-6 plays a key role in NMOSD, which is a debilitating and potentially fatal condition," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Satralizumab has shown robust efficacy sustained for 144 weeks across a broad patient population in two phase III studies, whether given as a monotherapy or in combination with baseline therapy. We're encouraged that satralizumab may soon provide a new treatment option for people living with NMOSD."

People with NMOSD experience unpredictable, severe relapses that directly cause cumulative, permanent, neurological damage and disability. The condition is often misdiagnosed as multiple sclerosis. Satralizumab inhibits interleukin-6 (IL-6) signalling, which is believed to play a key role in the inflammation that occurs in people with NMOSD. Satralizumab can be self-administered every four weeks by subcutaneous injection.

Detailed results published in NEJM highlight that in the overall study population, only eight of 41 patients (20%) treated with satralizumab in combination with baseline immunosuppressant therapy experienced a protocol-defined relapse (PDR) compared to 18 of 42 patients (43%) treated with placebo in combination with baseline therapy (HR=0.38, 95% CI: 0.16-0.88; p=0.02). Importantly, 89%, 78% and 74% of patients on satralizumab in combination with baseline therapy were relapse-free at weeks 48, 96 and 144 compared to 66%, 59% and 49% with placebo in combination with baseline therapy. Notably, the intention-to-treat (ITT) population studied included both aquaporin-4 (AQP4-IgG) seropositive and seronegative patients, reflecting a real-world population of adolescents and adults (age 13-73 years) with NMOSD. People who are AQP4-IgG seropositive tend to experience a more severe disease course.

In the AQP4-IgG seropositive subgroup analysis, three of 27 patients (11%) treated with satralizumab experienced a PDR compared to 12 of 28 patients (43%) treated with placebo (HR=0.21, 95% CI: 0.06-0.75). In the AQP4-IgG seronegative subgroup analysis, five of 14 patients (36%) treated with satralizumab

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experienced a PDR compared to six of 14 patients (43%) receiving placebo (HR= 0.66, 95% CI: 0.20-2.24).

Overall, the proportion of patients with serious adverse events was similar between the satralizumab and placebo treatment groups. A lower rate of infections (including serious infections) was observed in patients treated with satralizumab compared with the placebo group. Most adverse events were mild to moderate, and the most common adverse events in the satralizumab group were upper respiratory tract infection, nasopharyngitis (common cold) and headache.

In October 2019, the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) accepted the marketing applications for satralizumab for the treatment of NMOSD, and the EMA granted Accelerated Assessment. The EMA's Committee for Medicinal Products for Human Use (CHMP) recommendation and the FDA decision are expected in 2020.

About the SAkuraSky study in NMOSD
SAkuraSky is a phase III multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of satralizumab added to baseline immunosuppressant therapy in patients with NMOSD. The primary endpoint was the time to first relapse as adjudicated by an independent review committee in the double-blind period.

Eighty-three male and female patients 13-73 years of age were randomised to either of the following two treatment groups in a 1:1 ratio: satralizumab (120 mg) or placebo added to baseline therapy (azathioprine, mycophenolate mofetil and/or corticosteroids). Both treatments were administered subcutaneously at Week 0, 2, and 4. The subsequent treatment was continued at 4-week intervals. The double-blind treatment ended when patients experienced a PDR; the study ended when the total number of PDRs reached 26. After experiencing a PDR or upon completion of the study, patients in both groups were offered treatment with satralizumab in an open-label extension period. Patients with AQP4-IgG seropositive or seronegative neuromyelitis optica (NMO, as defined by the diagnostic criteria in 2006) and those with AQP4-IgG seropositive NMOSD were enrolled.

About neuromyelitis optica spectrum disorder (NMOSD)
NMOSD is a rare, lifelong and debilitating autoimmune disease of the central nervous system that primarily damages the optic nerve(s) and spinal cord, causing blindness, muscle weakness and paralysis. People with NMOSD experience unpredictable, severe relapses directly causing cumulative, permanent, neurological damage and disability. In some cases, relapse can result in death. NMOSD affects over 10,000 people in Europe, 15,000 people in the United States and up to hundreds of thousands of people worldwide. The disease is most common among non-Caucasian women in their 30s and 40s.

NMOSD is commonly associated with pathogenic antibodies (AQP4-IgG) that target and damage a specific cell type, called astrocytes, resulting in inflammatory lesions of the optic nerve(s), spinal cord and brain. AQP4-IgG antibodies are detectable in the blood serum of around two-thirds of NMOSD patients.

Although most cases of NMOSD can be confirmed through a diagnostic test, people living with the condition are still frequently misdiagnosed with multiple sclerosis. This is due to overlapping characteristics of the two

disorders, including a higher prevalence in women, similar symptoms and the fact that both are relapse-based conditions.

About satralizumab
Satralizumab is an investigational humanised monoclonal antibody that targets the IL-6 receptor. The cytokine IL-6 is thought to be a key driver of NMOSD, triggering the inflammation cascade and leading to damage and disability. Positive phase III results for satralizumab, as both monotherapy and in combination with baseline immunosuppressant therapy, suggest that IL-6 inhibition may be an effective therapeutic approach for NMOSD. The Phase III clinical development program for satralizumab includes two studies: SAkuraStar and SAkuraSky.

Satralizumab has been designated as an orphan drug in the U.S., Europe and Japan. In addition, it was granted Breakthrough Therapy Designation for the treatment of NMOSD by the FDA in December 2018.

About Roche in neuroscience
Neuroscience is a major focus of research and development at Roche. The company's goal is to develop treatment options based on the biology of the nervous system to help improve the lives of people with chronic and potentially devastating diseases.

Roche has more than a dozen investigational medicines in clinical development for diseases that include multiple sclerosis, Alzheimer's disease, Huntington's disease, spinal muscular atrophy, Parkinson's disease and autism.

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 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF

56.8 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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