Roche's satralizumab significantly reduced relapse risk in second positive phase III study for neuromyelitis optica spectrum

- **Pivotal phase III SAkuraStar study shows 55% reduction in the risk of relapse for satralizumab monotherapy versus placebo presented at ECTRIMS congress 2019**
- **74% reduction in the risk of relapse for satralizumab monotherapy versus placebo in people with neuromyelitis optica spectrum disorder (NMOSD) with aquaporin-4 antibodies (AQP4-IgG seropositive patients)**
- **Satralizumab demonstrated a similar safety profile compared to placebo in two phase III studies across a broad population**
- **Satralizumab targets the interleukin-6 (IL-6) receptor, a key driver of NMOSD**

Basel, 12 September 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) presented today full pivotal phase III study results for satralizumab as a monotherapy for neuromyelitis optica spectrum disorder (NMOSD), a rare, debilitating central nervous system disease. Results from the SAkuraStar study, presented at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), show that satralizumab monotherapy achieved a 55% reduction in the risk of relapses compared to placebo in the overall population, representative of NMOSD patients (HR 0.45, 95% CI: 0.23-0.89; p=0.0184). In the large (~67%) subgroup of patients seropositive for AQP4-IgG antibodies, the effect was higher with a 74% reduction in risk of relapses (HR 0.26, 95% CI: 0.11-0.63; p=0.0014). People who are AQP4-IgG seropositive tend to experience a more severe disease course.

"The positive phase III results for satralizumab, first as an add-on therapy and now as a monotherapy are exciting to see, and importantly, it achieved efficacy in a broad range of NMOSD patients, reflective of what we see in our everyday practice. Satralizumab targets the IL-6 receptor, potentially offering a novel treatment approach," said Professor Jeffrey Bennett, University of Colorado Neurology & Ophthalmology. "Approved treatment options demonstrating favourable safety and efficacy in controlled clinical trials are urgently needed. Even one relapse may lead to blindness and debilitating motor dysfunction for people with NMOSD."

In the overall satralizumab-treated population, 76.1% were relapse-free at 48 weeks, and 72.1% relapse-free at 96 weeks, compared to 61.9% and 51.2% with placebo, respectively. Data from the AQP4-IgG seropositive subgroup showed that 82.9% were relapse-free at 48 weeks and 76.5% relapse-free at 96 weeks when treated with satralizumab, compared to 55.4% and 41.1% with placebo, respectively.

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. Through the use of a diagnostic biomarker test, most NMOSD patients are identified as AQP4-IgG seropositive; however, as many as one-third of patients with NMOSD are AQP4-IgG seronegative. The condition is often misdiagnosed as multiple sclerosis.

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Satralizumab inhibits IL-6 signalling, which is believed to play a key role in the inflammation that occurs in people with NMOSD, leading to damage and disability. People with NMOSD experience unpredictable, severe relapses that directly cause cumulative, permanent neurological damage.

“While first described 125 years ago, the underlying biology of NMOSD has only recently been understood. The positive results from the pivotal SAkuraStar and SAkuraSky studies support the hypothesis that IL-6 plays a key role in this devastating disease that can take away people’s independence,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are encouraged by these results and look forward to working with regulators over the coming months to bring satralizumab to people living with NMOSD as soon as possible.”

These SAkuraStar data add to the previously reported results for satralizumab in combination with baseline therapy for people with NMOSD. Initial phase III data for SAkuraSky were presented at the 34th ECTRIMS congress in 2018. The data showed a 62% reduction in the risk of relapses in a representative population of both AQP4-IgG seropositive and AQP4-IgG seronegative patients in the overall study population (HR 0.38, 95% CI: 0.16-0.88; p=0.0184) when used in combination with baseline therapy compared to placebo, and a 79% reduction in the risk of relapses in AQP4-IgG seropositive patients (HR 0.21, 95% CI: 0.06-0.75; p=0.0086).

Overall, the proportion of patients with serious adverse events was similar between the satralizumab monotherapy and placebo treatment groups in the SAkuraStar study; and between the satralizumab added to baseline therapy and placebo added to baseline therapy treatment groups in the SAkuraSky study. A lower rate of infections (including serious infections) was observed in patients treated with satralizumab compared with the placebo group. In both studies, most adverse events were mild to moderate, and the most common adverse events in the satralizumab group were urinary tract infections and upper respiratory tract infections in the SAkuraStar study and upper respiratory tract infections, nasopharyngitis (common cold) and headache in the SAkuraSky study. Safety analyses continue in the open-label extensions of SAkuraStar and SAkuraSky.

The data available across two controlled, randomised phase III clinical trials suggest that satralizumab could be an efficacious option for patients across a broad NMOSD patient population, whether given as a monotherapy or in combination with baseline therapy. Satralizumab is administered every four weeks by subcutaneous injection, which may be a convenient option for patients and carers.

The SAkuraStar study recruited 95 NMOSD patients from the age of 20-70 and SAkuraSky recruited 83 patients, including adolescents, aged 13-73. These studies represent one of the largest clinical trial programmes undertaken for this rare disease.

About SAkuraStar and SAkuraSky in NMOSD
SAkuraStar is a phase III multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of satralizumab monotherapy administered to patients with NMOSD. The primary endpoint is the time to first protocol-defined relapse (PDR), adjudicated by an independent review committee in the double-blind period. Secondary endpoints included the Visual Analogue Scale (VAS) score

for pain and Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue score.

Ninety-five patients aged from 20-70 years were randomised to either of the following two treatment groups in a 2:1 ratio: satralizumab (120 mg) or placebo. Both treatments were administered subcutaneously at Week 0, 2, and 4. The subsequent treatment was continued at 4-week intervals. The double-blind treatment period ended when the total number of PDRs had reached 44 or at 1.5 years after the enrollment of the last patient, whichever occurred first. 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.

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. Main secondary endpoints included change in VAS score for pain and change in FACIT Fatigue score.

Eighty-three male and female patients aged from 13 to 73 years 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 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 US 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 features 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 in 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 therapy, suggest that IL-6 inhibition may be an effective therapeutic approach for NMOSD. The phase III clinical development programme for satralizumab includes two studies: SAkuraStar and SAkuraSky.

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 tenth consecutive year, Roche has been recognised as the most sustainable company 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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