## New data show Roche's ENSPRYNG (satralizumab) significantly reduces severity and risk of relapse in neuromyelitis optica spectrum disorder (NMOSD)

- **ENSPRYNG lowered relapse severity in double-blind periods of SAkura Phase III studies.**
- **Pooled data from SAkura open-label extension (OLE) studies support continued effect of ENSPRYNG reducing risk of relapse in the longer term**
- **Ongoing data continues to show a favourable safety profile for ENSPRYNG**
- **ENSPRYNG was recently approved by the U.S. Food and Drug Administration (FDA) for adults with anti-aquaporin-4 (AQP4) antibody positive NMOSD**

Basel, 10 September 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will present new ENSPRYNG® (satralizumab) data on reducing relapse severity in the treatment of neuromyelitis optica spectrum disorder (NMOSD), a rare disease of the central nervous system. These data are being presented at MSVirtual2020, the 8th joint ACTRIMS-ECTRIMS meeting, in addition to longer-term efficacy data supporting the continued effect of ENSPRYNG on reducing the risk of NMOSD relapse, as well as its favourable benefit:risk profile.

"The data for ENSPRYNG at MSVirtual2020 are promising and suggest it significantly reduces relapse severity and frequency, which are important goals of the treatment for people with NMOSD," said Professor Anthony Traboulsee, M.D., Neurologist and Professor, University of British Columbia, and Research Chair of the MS Society of Canada. "ENSPRYNG, the first approved treatment for NMOSD that can be taken at home, offers favourable efficacy and safety, which are important for improved long-term outcomes."

In a post-hoc analysis of the ENSPRYNG-treated group, the risk of severe relapse was reduced by 79% compared to placebo (5 of 27 [19%] vs. 12 of 34 [35%]), for patients across the double-blind periods of the SAkura studies. Preventing relapses, the most severe of which cause cumulative, irreversible, neurological damage and disability, is the primary goal for NMOSD disease management. The patients treated with ENSPRYNG were also less likely to require rescue therapy for a relapse compared with placebo (OR 0.46; 95% CI, 0.25–0.86, p=0.015). A relapse was categorised as severe if it resulted in a change of ≥2 points on the Expanded Disability Status Scale.

In a separate pooled analysis, ENSPRYNG reduced the risk of relapse in the combined double-blind period and open-label extension (OLE) by 51% (HR, 0.49; 95% CI, 0.31–0.79; p=0.002) compared to those originally in the placebo group. This effect was more pronounced in aquaporin-4 antibody (AQP4-IgG) seropositive patients, who tend to experience a more severe disease course, with 66% reduction in risk of relapse (HR, 0.34; 95% CI, 0.19–0.62; P<0.001) compared to those originally in the placebo group.

"The longer-term data for ENSPRYNG further reinforce the previously observed efficacy of this medicine for this debilitating disorder that is often mistaken for multiple sclerosis," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "ENSPRYNG is the first and only FDA-approved subcutaneous, self-administered medicine for NMOSD and the first medicine for NMOSD

that is designed to target the interleukin-6 receptor, which is believed to play a key role in the inflammation associated with this disorder."

In the double-blind periods, infection rates were lower in the ENSPRYNG-treated group compared to placebo in the SAkuraStar study (99.8 vs 162.6 events/100 patient years (PY)), whereas infection rates did not differ between groups in the SAkuraSky study. Serious infection rates were comparable between both groups in each of the studies (SAkuraSky: 2.6 vs 5.0 events/100PY; SAkuraStar: 5.2 vs 9.9 events/100PY). Infection and serious infection rates for ENSPRYNG-treated patients in the combined double-blind and OLE periods were consistent with those for ENSPRYNG-treated patients in the double-blind portion in terms of the nature and rate of adverse events, and did not increase over time.

ENSPRYNG is approved in Canada, Japan, Switzerland and the U.S. Additional applications are under review with numerous regulators, including in the EU and China. ENSPRYNG 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 SAkuraStar and SAkuraSky in NMOSD**
SAkuraStar is a Phase III multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of ENSPRYNG monotherapy administered to patients with neuromyelitis optica spectrum disorder (NMOSD). The primary endpoint is the time to first protocol-defined relapse (PDR), adjudicated by an independent review committee in the double-blind period. Results from the SAkuraStar study were presented at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), September 11-13, 2019, and were published in the May 1, 2020 edition of *The Lancet Neurology*.

Ninety-five patients aged from 20-70 years were randomised to either of the following two treatment groups in a 2:1 ratio: ENSPRYNG (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 at 1.5 years after the enrolment of the last patient. After experiencing a PDR or upon completion of the study, patients in both groups were offered treatment with ENSPRYNG in an open label extension (OLE) 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 enroled. The number of AQP4-IgG seronegative patients was limited to approximately 33% of the total population of the study. Data have shown that AQP4-IgG seropositive patients may experience a greater likelihood of relapse and poorer long-term outcomes than AQP4-IgG seronegative patients.

SAkuraSky is a Phase III multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of ENSPRYNG added to baseline immunosuppressant therapy in patients with NMOSD. The primary endpoint was the time to first PDR as adjudicated by an independent review committee in the double-blind period. Results from the SAkuraSky study were published in the November 28, 2019 edition of the *New England Journal of Medicine* (NEJM).

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: ENSPRYNG (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 ENSPRYNG in an OLE 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 enroled. AQP4-IgG seronegative patients represented approximately 30% of the SAkuraSky study population.

**About neuromyelitis optica spectrum disorder (NMOSD)**
NMOSD is a rare, lifelong and debilitating autoimmune condition 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, up to 15,000 people in the US and approximately 200,000 people worldwide. NMOSD can affect individuals of any age, race and gender, but is most common among women in their 30s and 40s, and appears to occur at higher rates in people of African or Asian background. There is some evidence that people of African or Asian descent may also experience a more severe disease course.

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 70-80% of NMOSD patients.

Although most cases of NMOSD can be confirmed through diagnostic tests, 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 ENSPRYNG® (satralizumab)**
ENSPRYNG, which was designed by Chugai, a member of the Roche group, is a humanised monoclonal antibody that targets interleukin-6 (IL-6) receptor activity. The cytokine IL-6 is believed to be a key driver in NMOSD, triggering the inflammation cascade and leading to damage and disability. ENSPRYNG was designed using novel recycling antibody technology, which compared to conventional technology, allows for longer duration of the antibody and subcutaneous dosing every four weeks.

Positive Phase III results for ENSPRYNG, as both monotherapy and in combination with baseline immunosuppressant therapy, suggest that IL-6 inhibition is an effective therapeutic approach for NMOSD. The Phase III clinical development programme for ENSPRYNG includes two studies: SAkuraStar and SAkuraSky.

ENSPRYNG is approved in Canada, Japan, Switzerland and the U.S. Applications are under review with numerous regulators, including in the EU and China.

ENSPRYNG 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. Our goal is to pursue groundbreaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases.

Roche is investigating more than a dozen medicines for neurological disorders, including multiple sclerosis, Alzheimer's disease, Huntington's disease, Parkinson's disease, Duchenne muscular dystrophy and autism spectrum disorder. Together with our partners, we are committed to pushing the boundaries of scientific understanding to solve some of the most difficult challenges in neuroscience today.

**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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