CHMP recommends EU approval of Roche's ENSPRYNG (satralizumab) for adults and adolescents with neuromyelitis optica spectrum disorder (NMOSD)

- **If approved, ENSPRYNG will be the first and only treatment available to both adults and adolescents from 12 years of age with anti-aquaporin-4 antibody (AQP4-IgG) seropositive NMOSD in the EU**
- **ENSPRYNG is the only subcutaneous treatment option for NMOSD that can be administered at home every four weeks**
- **Recommendation is based on results from the two pivotal Phase III SAkuraStar and SAkuraSky studies, in which ENSPRYNG demonstrated robust and sustained efficacy in reducing the risk of relapse and a favourable safety profile**
- **NMOSD is a rare, lifelong and debilitating autoimmune disorder of the central nervous system that can cause blindness, muscle weakness and paralysis**

Basel, 23 April 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of ENSPRYNG® (satralizumab) as the first subcutaneous treatment option for adults and adolescents from 12 years of age living with anti-aquaporin-4 antibody (AQP4-IgG) seropositive neuromyelitis optica spectrum disorder (NMOSD), as a monotherapy or in combination with immunosuppressive therapy (IST). AQP4-IgG are present in around 70-80% of people with NMOSD, who tend to experience a more severe disease course.

NMOSD is a rare, lifelong and debilitating autoimmune disorder of the central nervous system, often misdiagnosed as multiple sclerosis, that primarily damages the optic nerve(s) and spinal cord, causing permanent blindness, muscle weakness and paralysis. The disease is characterised by unpredictable relapses and severe disability often occurs following the first NMOSD attack, accumulating with each subsequent relapse. Preventing these relapses is the primary goal for disease management. ENSPRYNG has been recommended for use in people who have only experienced a single NMOSD attack and adolescents, currently unserved NMOSD populations, as well as those with more advanced disease.

"Today's positive CHMP opinion is an important step toward bringing ENSPRYNG to people in the EU living with NMOSD who have limited treatment options," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. "ENSPRYNG has been shown to reduce the risk of relapse significantly, while also offering a favourable safety profile. Additionally, if approved, ENSPRYNG would be the first and only treatment that can be self-administered subcutaneously at home following appropriate training."

ENSPRYNG is a humanised monoclonal antibody designed to target and inhibit interleukin-6 (IL-6) receptor activity, believed to play a key role in the inflammation associated with NMOSD. The treatment was designed by Chugai, a member of the Roche Group, using novel recycling antibody technology which,

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compared to conventional technology, allows for longer duration of antibody circulation and subcutaneous dosing every four weeks after an initial loading dose.

The CHMP recommendation is based on the results of the Phase III SAkuraStar and SAkuraSky studies in which ENSPRYNG showed robust and sustained efficacy results in reducing the risk of relapse and a favourable safety profile in people with AQP4-IgG seropositive NMOSD. A final decision regarding the approval is expected from the European Commission in the near future.

About SAkuraStar and SAkuraSky in NMOSD
SAkuraStar was a pivotal Phase III study evaluating the efficacy and safety of ENSPRYNG monotherapy administered to adults with neuromyelitis optica spectrum disorder (NMOSD). In the anti-aquaporin-4 antibody (AQP4-IgG) seropositive subgroup, 83% treated with ENSPRYNG remained relapse free at 48 weeks, compared with 55% of those treated with placebo. At 96 weeks, 77% of those treated with ENSPRYNG remained relapse free, compared with 41% with placebo.

SAkuraSky was a pivotal Phase III study evaluating the efficacy and safety of ENSPRYNG in combination with baseline immunosuppressive therapy in adults and adolescents with NMOSD. Overall, 92% of AQP4-seropositive participants receiving ENSPRYNG in combination with immunosuppressants remained relapse free at 48 and 96 weeks, compared with 60% and 53% with placebo at 48 and 96 weeks.

The primary endpoint of both the SAkuraStar and SAkuraSky studies was time to first protocol-defined relapse (PDR) adjudicated by an independent review committee in the double-blind period.

ENSPRYNG demonstrated a favourable safety and tolerability profile in the Phase III studies.

The most common adverse reactions observed in the safety population were: headache, arthralgia, white blood cell count decrease, hyperlipidaemia and injection-related reactions.

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 permanent 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 people with NMOSD.

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 people can experience relapses in both 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 immunosuppressive 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 currently approved in 20 countries, including the United States, Canada, Japan and Switzerland. Applications are under review with numerous regulators.

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.that

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 twelfth 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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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