FDA Approves Roche's ENSPRYNG for Neuromyelitis Optica Spectrum Disorder (NMOSD)

- **First and only FDA-approved subcutaneous treatment option for anti-aquaporin-4 antibody positive NMOSD that can be self-administered by a person with NMOSD or a caregiver every four weeks**
- **First and only approved therapy for NMOSD designed to target and inhibit interleukin-6 receptor activity, using novel recycling antibody technology**
- **Approval supported by one of the largest clinical trial programmes undertaken for this rare disease**

Basel, 17 August 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the US Food and Drug Administration (FDA) has approved ENSPRYNG™ (satralizumab-mwge) as the first and only subcutaneous treatment for adults living with anti-aquaporin-4 (AQP4) antibody positive neuromyelitis optica spectrum disorder (NMOSD). 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 blindness, muscle weakness and paralysis.

"Today's FDA approval of ENSPRYNG, the first subcutaneous NMOSD treatment using novel recycling antibody technology, builds upon the work we've done in multiple sclerosis with OCREVUS to develop first-in-class medicines and further the scientific understanding of neuroimmunological diseases," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. "We thank the NMOSD community, including patients and investigators who participated in ENSPRYNG clinical trials."

ENSPRYNG is a humanised monoclonal antibody and the only approved therapy 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 compared to conventional technology, allows for longer duration of antibody circulation and subcutaneous dosing every four weeks.

"For people with NMOSD, relapses can cause devastating, irreversible and disabling neurological effects," said Professor Jeffrey Bennett, University of Colorado Neurology & Ophthalmology, and investigator for the ENSPRYNG pivotal clinical trials. "Having an approved therapy that can be administered subcutaneously in the home, and has demonstrated an impact on the frequency of relapses, is an important advancement for patients."

"We are very optimistic the addition of this new approved treatment option will make a meaningful difference for those living with NMOSD, those who love and support them and the doctors who treat them," said Victoria Jackson, founder, The Guthy-Jackson Charitable Foundation. "When my daughter was diagnosed with NMOSD in 2008, there were no approved treatment options, and a critical lack of resources

and understanding for people living with this disabling disorder. After years of dedicated effort and collaboration, the FDA approval of ENSPRYNG exemplifies how patients, industry, and academia can find solutions together."

ENSPRYNG can be administered in the home by a person living with NMOSD or a caregiver following training from a healthcare provider. ENSPRYNG treatment is administered every four weeks after an initial loading dose.

ENSPRYNG will be available in the United States in two weeks.

FDA approval is based on results from one of the largest pivotal clinical trial programmes undertaken for this rare neurological disorder

This approval is supported by results from two randomised controlled Phase III clinical trials, the SAkuraStar and SAkuraSky studies, in which ENSPRYNG demonstrated robust and sustained efficacy and a favourable safety profile in adults with AQP4 antibody positive NMOSD. Results were sustained for 96 weeks, significantly reducing the risk of relapse compared with placebo as a monotherapy and when used concurrently with baseline immunosuppressant therapy (IST), which has commonly been used to manage NMOSD symptoms associated with relapses.

In the SAkuraStar monotherapy study's AQP4 antibody positive subgroup, 76.5% of ENSPRYNG-treated patients were relapse-free at 96 weeks, compared to 41.1% with placebo. In the SAkuraSky study, which evaluated ENSPRYNG when used concurrently with baseline IST, 91.1% of ENSPRYNG-treated AQP4 antibody positive subgroup patients were relapse-free at 96 weeks, compared to 56.8% with placebo. The primary endpoint of both SAkuraStar and SAkuraSky was time to first protocol-defined relapse (PDR) adjudicated by an independent review committee in the double-blind period.

The most common adverse reactions with ENSPRYNG (incidence ≥ 15%) were nasopharyngitis, headache, upper respiratory tract infection, gastritis, rash, arthralgia, extremity pain, fatigue and nausea.

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 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 Lancet Neurology in April 2020.

Ninety-five adult patients 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 aquaporin-4 (AQP4) antibody positive or negative neuromyelitis optica (NMO, as defined by

the diagnostic criteria in 2006) and those with AQP4 antibody positive NMOSD were enrolled. The number of AQP4 antibody negative patients was limited to approximately 33% of the total population of the study. Data have shown that AQP4 antibody positive patients may experience a greater likelihood of relapse and poorer long-term outcomes than AQP4 antibody negative 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 relapse 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).

Seventy-six adult patients 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 antibody positive or negative neuromyelitis optica (NMO, as defined by diagnostic criteria in 2006) and those with AQP4 antibody positive NMOSD were enrolled. AQP4 antibody negative 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) that target and damage a specific cell type, called astrocytes, resulting in inflammatory lesions of the optic nerve(s), spinal cord and brain. AQP4 antibodies are detectable in the blood serum of around 70-80% 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 ENSPRYNG™ (satralizumab-mwge)
ENSPRYNG, which was designed by Chugai, a member of the Roche group, is a humanised monoclonal antibody that targets 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 antibody recycling 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 used concurrently 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 also approved in Canada, Japan and Switzerland. Applications are under review with numerous regulators, including in the EU and China.

ENSPRYNG has been designated as an orphan drug in the US, 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, neuromyelitis optica spectrum disorder, 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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