Media Release

Roche's ENSPRYNG® (satralizumab) approved in Japan for adults and children with neuromyelitis optica spectrum disorder

- **ENSPRYNG is Japan's first and only approved therapy for both adults and children with neuromyelitis optica spectrum disorder (NMOSD)**
- **ENSPRYNG is the first and only approved therapy targeting the interleukin-6 (IL-6) receptor given subcutaneously every four weeks**
- **Approval is supported by data demonstrating ENSPRYNG's robust efficacy, which was well-tolerated with a consistent safety profile, in a broad NMOSD population as a monotherapy and as an add-on therapy**
- **Asia has a high prevalence of NMOSD with limited treatment options**

Basel, 29 June 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that Japan's Ministry of Health, Labour and Welfare (MHLW) has approved ENSPRYNG® (satralizumab) for the prevention of relapses of neuromyelitis optica spectrum disorder (NMOSD), including NMO, for aquaporin-4 antibody (AQP4-IgG) seropositive adults and children. ENSPRYNG demonstrated robust efficacy and significantly reduced the risk of relapse across a broad NMOSD patient population in two pivotal Phase III studies, as a monotherapy and as an add-on therapy to baseline immunosuppressant therapy (IST), and is dosed subcutaneously every four weeks.

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, and these patients tend to experience a more severe disease course. Although most cases of NMOSD can be confirmed through a diagnostic test, up to 30% of people living with the condition are still frequently misdiagnosed with multiple sclerosis.

"Today's approval in Japan is the first for ENSPRYNG in Asia, providing a new treatment option to help reduce NMOSD relapses that cause irreversible disability, such as vision loss and paralysis," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Japan has a high prevalence of NMOSD in both adults and children, but limited approved treatment options. ENSPRYNG offers robust efficacy, is well-tolerated, and is the first and only approved therapy targeting the interleukin-6 (IL-6) receptor given subcutaneously every four weeks."

ENSPRYNG is a humanised monoclonal antibody that targets the IL-6 receptor, believed to play a key role in the inflammation that occurs in people with NMOSD. ENSPRYNG was designed by Chugai Pharmaceutical Co., a member of the Roche group, using novel antibody recycling technology. Compared to conventional technology, this allows for longer duration of antibody circulation and maximum inhibition of IL-6 signalling, while minimising safety risks in a chronic disease setting. People with NMOSD experience unpredictable, severe relapses directly causing cumulative, irreversible neurological damage and disability.

Preventing relapses through early treatment can have a positive impact on preventing disability and is the primary goal for NMOSD disease management.

ENSPRYNG was recently approved in Canada under priority review, as a monotherapy or as an add-on therapy to baseline IST, for the treatment of NMOSD in adult and adolescent patients who are AQP4-IgG seropositive. In October 2019, the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) accepted the marketing applications for ENSPRYNG for the treatment of NMOSD. The EMA's Committee for Medicinal Products for Human Use (CHMP) recommendation and the FDA decision are expected in 2020. In April 2020, China's Centre for Drug Evaluation (CDE) accepted a licensing application for ENSPRYNG.

The approval of ENSPRYNG in Japan is based on data including the two pivotal Phase III studies, SAkuraStar and SAkuraSky, evaluating the efficacy and safety of ENSPRYNG as a monotherapy and as an add-on therapy to baseline IST, respectively.

- In the overall population, a reduction in the risk of relapse was observed in both pivotal studies:
    - In SAkuraSky, the risk of relapse was reduced by 62% (HR, 0.38; 95% CI, 0.16–0.88; p=0.0184) with ENSPRYNG, compared to placebo (both treatment arms as an add-on therapy to baseline IST)
    - In SAkuraStar, the risk of relapse was reduced by 55% (HR, 0.45; 95% CI, 0.23–0.89; p=0.0184) with ENSPRYNG monotherapy, compared to placebo
- In the pre-specified subgroup of AQP4-IgG seropositive patients, a reduction in the risk of relapse was observed in both pivotal studies:
    - In SAkuraSky, the risk of relapse was reduced by 79% (HR, 0.21; 95% CI, 0.06–0.75) with ENSPRYNG, compared to placebo (both treatment arms as an add-on therapy to baseline IST)
    - In SAkuraStar, the risk of relapse was reduced by 74% (HR, 0.26; 95% CI, 0.11–0.63) with ENSPRYNG monotherapy, compared to placebo
- Overall, the proportion of patients with serious adverse events was similar between the ENSPRYNG and placebo groups in both studies. A lower rate of infections (including serious infections) was observed in patients treated with ENSPRYNG compared with the placebo group. The safety profile in longer term follow up is consistent with the double-blind period.

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) in 2019, and were published in The Lancet Neurology in April 2020.

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 enrollment 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 enrolled. The overall population in the SAkuraStar study is representative of the types of NMOSD patients seen in real-world clinical practice, which includes 70-80% of patients diagnosed as AQP4-IgG seropositive.

SAkuraSky is a Phase III multicentre, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of ENSPRYNG as an add-on therapy to baseline IST 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 enrolled. The overall population in the SAkuraSky study is representative of the types of NMOSD patients seen in real-world clinical practice, which includes 70-80% of patients diagnosed as AQP4-IgG seropositive.

About ENSPRYNG® (satralizumab)
ENSPRYNG, which was designed by Chugai, a member of the Roche group, 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. ENSPRYNG was designed using novel antibody recycling technology. Compared to conventional technology, this allows for longer duration of antibody circulation and maximum inhibition of IL-6 signalling, while minimising safety risks in a chronic disease setting.

Positive Phase III results for ENSPRYNG, as both monotherapy and as an add-on to baseline IST, suggest that IL-6 inhibition may be an effective therapeutic approach for NMOSD. The Phase III clinical development programme for ENSPRYNG includes two studies: SAkuraStar and SAkuraSky.

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 approximately 200,000 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 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 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 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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