Media & Investor Release

Positive Phase III results for Roche's OCREVUS (ocrelizumab) twice a year, 10-minute subcutaneous injection in patients with multiple sclerosis

- **Phase III OCARINA II trial met primary and secondary endpoints**
- **OCREVUS twice a year, 10-minute injection has the potential to further improve the treatment experience and expand OCREVUS usage in MS centres with IV capacity limitations or without IV infrastructure**
- **OCREVUS remains the first and only therapy approved for both RMS and PPMS, and more than 300,000 people have been treated globally**

Basel, 13 July 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the Phase III OCARINA II trial evaluating OCREVUS® (ocrelizumab) as a twice a year 10-minute subcutaneous injection met its primary and secondary endpoints in patients with relapsing forms of MS or primary progressive MS (RMS or PPMS). OCREVUS subcutaneous injection was shown to be non-inferior to OCREVUS given by intravenous infusion (IV), as measured by pharmacokinetics (levels in the blood) over 12 weeks. OCREVUS subcutaneous injection was also comparable with OCREVUS IV in controlling magnetic resonance imaging (MRI) lesion activity in the brain over 12 weeks. The safety profile of OCREVUS subcutaneous injection was consistent with that of OCREVUS IV.

The OCREVUS 10-minute injection is designed to be administered without the need for IV infrastructure so it has the potential to expand the usage of OCREVUS in MS centres without IV infrastructure or those with IV capacity limitations. It also retains the twice-yearly dosing regimen of OCREVUS IV that has shown high persistence and adherence since becoming a standard of care MS treatment.[1] This provides an additional delivery option so that the administration of OCREVUS can be matched to the individual needs of patients and healthcare professionals.

"These results give people living with MS the possibility to receive the transformational benefits of OCREVUS in the way best suited to their lives while freeing up time and healthcare resources," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "This new subcutaneous injection will allow OCREVUS to be administered in 10 minutes twice a year, helping people living with MS to spend less time in treatment for this disease."

Detailed results from the trial will be presented at an upcoming medical meeting and submitted to health authorities around the world. Roche is committed to advancing innovative clinical research programmes to broaden the scientific understanding of MS, further reduce

disability progression in RMS and PPMS and improve the treatment experiences for those living with the disease.

About the OCARINA II study

OCARINA II is a Phase III, global, multicentre, randomised study evaluating the pharmacokinetics, safety and radiological and clinical effects of the subcutaneous formulation of OCREVUS compared with OCREVUS intravenous (IV) infusion in 236 patients with relapsing MS (RMS) or primary progressive MS (PPMS). The primary endpoint is non-inferiority in serum area under the curve (AUC) from day 1 to 12 weeks after subcutaneous injection compared to IV infusion. Secondary endpoints include maximum serum concentration (Cmax) of OCREVUS, the total number of active, gadolinium-enhancing T1 lesions at 8 and 12 weeks, and new or enlarging T2 lesions at 12 and 24 weeks, as well as safety and immunogenicity outcomes. Exploratory endpoints include patient-reported outcomes.

About the subcutaneous formulation of OCREVUS (ocrelizumab)

The investigational subcutaneous formulation combines OCREVUS with Halozyme Therapeutics' Enhanze® drug delivery technology.

OCREVUS is a humanised monoclonal antibody designed to target CD20-positive B cells, a specific type of immune cell thought to be a key contributor to myelin (nerve cell insulation and support) and axonal (nerve cell) damage. This nerve cell damage can lead to disability in people with MS. Based on preclinical studies, OCREVUS binds to CD20 cell surface proteins expressed on certain B cells, but not on stem cells or plasma cells, suggesting that important functions of the immune system may be preserved.

The Enhanze drug delivery technology is based on a proprietary recombinant human hyaluronidase PH20 (rHuPH20), an enzyme that locally and temporarily degrades hyaluronan – a glycosaminoglycan or chain of natural sugars in the body – in the subcutaneous space. This increases the permeability of the tissue under the skin, allowing space for large molecules like OCREVUS to enter, and enables the subcutaneous formulation to be rapidly dispersed and absorbed into the bloodstream.

OCREVUS IV is the first and only therapy approved for both RMS (including relapsing-remitting MS [RRMS] and active, or relapsing secondary progressive MS [SPMS], in addition to clinically isolated syndrome [CIS] in the U.S.) and PPMS. OCREVUS IV is administered by intravenous infusion every six months. The initial dose is given as two 300 mg infusions given two weeks apart. Subsequent doses are given as single 600 mg infusions.

About multiple sclerosis

Multiple sclerosis (MS) is a chronic disease that affects more than 2.8 million people worldwide. MS occurs when the immune system abnormally attacks the insulation and support around nerve cells (myelin sheath) in the central nervous system (brain, spinal cord and optic nerves), causing inflammation and consequent damage. This damage can cause a wide range of symptoms, including muscle weakness, fatigue and difficulty seeing, and may eventually lead to disability. Most people with MS experience their first symptom between 20 and 40 years of age, making the disease the leading cause of non-traumatic disability in younger adults.

People with all forms of MS experience disease progression – permanent loss of nerve cells in the central nervous system – from the beginning of their disease even if their clinical symptoms aren't apparent or don't appear to be getting worse. Delays in diagnosis and treatment can negatively impact people with MS, in terms of their physical and mental health, and contribute to the negative financial impact on the individual and society. An important goal of treating MS is to slow, stop and ideally prevent disease activity and progression as early as possible.

Relapsing-remitting MS (RRMS) is the most common form of the disease and is characterised by episodes of new or worsening signs or symptoms (relapses) followed by periods of recovery. Approximately 85% of people with MS are initially diagnosed with RRMS. The majority of people who are diagnosed with RRMS will eventually transition to secondary progressive MS (SPMS), in which they experience steadily worsening disability over time. Relapsing forms of MS (RMS) include people with RRMS and people with SPMS who continue to experience relapses. Primary progressive MS (PPMS) is a debilitating form of the disease marked by steadily worsening symptoms but typically without distinct relapses or periods of remission. Approximately 15% of people with MS are diagnosed with the primary progressive form of the disease. Until the FDA approval of OCREVUS, there had been no FDA-approved treatments for PPMS.

About Roche in Neuroscience

Neuroscience is a major focus of research and development at Roche. Our goal is to pursue ground-breaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases. Roche and Genentech are investigating more than a dozen medicines for neurological disorders, including MS, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease, acute ischemic stroke, Duchenne muscular dystrophy and Angelman syndrome. 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

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognising our endeavour to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

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.

References

[1] Engmann NJ, Sheinson D, Bawa K, Ng CD, Pardo G. Persistence and adherence to ocrelizumab compared with other disease-modifying therapies for multiple sclerosis in U.S. commercial claims data. *J Manag Care Spec Pharm*. 2021;27(5):639-649.

Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

Hans Trees, PhD
Phone: +41 79 407 72 58

Nathalie Altermatt
Phone: +41 79 771 05 25

Karsten Kleine
Phone: +41 79 461 86 83

Nina Mählitz
Phone: +41 79 327 54 74

Kirti Pandey
Phone: +49 172 6367262

Sileia Urech
Phone: +41 79 935 81 48

Roche Investor Relations

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America

Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com