Media & Investor Release

FDA approves OCREVUS ZUNOVO™ as the first and only twice-a-year 10-minute subcutaneous injection for people with relapsing and progressive multiple sclerosis

- **OCREVUS ZUNOVO™ has the potential to expand treatment options to centres without IV infrastructure or with IV constraints, like at a doctor's office**
- **This approval is backed by a decade of proven safety and efficacy data of Ocrevus® IV, with over 350,000 people treated globally**
- **OCREVUS ZUNOVO™ offers people with multiple sclerosis (MS) more options to access treatment based on their individual needs**

Basel, 16 September 2024 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced that the United States Food and Drug Administration (U.S. FDA) has approved OCREVUS ZUNOVO™ (ocrelizumab & hyaluronidase-ocsq) for the treatment of relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS). OCREVUS ZUNOVO is the first and only twice-a-year, healthcare professional (HCP)-administered approximately 10-minute subcutaneous (SC) injection approved for both these forms of multiple sclerosis, giving people living with MS more treatment options.

“OCREVUS ZUNOVO gives patients and providers another option for receiving OCREVUS, building on a decade of robust safety and efficacy data for OCREVUS in multiple sclerosis,” said Levi Garraway, M.D., Ph.D., Roche’s chief medical officer and head of Global Product Development. “This approval may offer greater flexibility for healthcare providers and people living with multiple sclerosis, based on their individual treatment needs.”

“People are living longer with chronic illnesses and with fewer disabilities because of the extensive progress that has been made in the development of medicines that can slow their progression,” said Natalie Blake, Executive Director of the MS Foundation. “But still, not everyone has access to these medicines. It’s crucial to acknowledge each experience with MS is as unique as the individual navigating it, so providing choices to address each person’s needs is essential. We are pleased that with a new method of delivery, there is now an additional option for those who need flexibility in the route of administration or treatment time.”

After the first dose, the time for treatment with OCREVUS ZUNOVO could be as little as 55 minutes. Patients will be required to take premedications at least 30 minutes prior to each dose. Following the first dose, patients will be monitored by their HCP for at least 60 minutes. Patients will be monitored for at least 15 minutes post-injection for subsequent doses.

The FDA approval is based on pivotal data from the Phase III OCARINA II trial, which showed no clinically significant difference in the levels of OCREVUS in the blood when administered subcutaneously, and a safety and efficacy profile consistent to the IV formulation in people with RMS and PPMS. Out of the exploratory outcomes measured, OCREVUS ZUNOVO was consistent with IV, demonstrating suppression of relapse activity (97%) and MRI lesions (97%) through 48 weeks. Additionally, one of several patient-reported outcomes measured during the study showed more than 92% of trial participants reported being satisfied or very satisfied with the SC administration of OCREVUS ZUNOVO.

In the Phase III OCARINA II trial, the safety profile of OCREVUS ZUNOVO was consistent with the well-established safety profile of OCREVUS® IV, with the exception of injection reactions. The most common adverse events with OCREVUS ZUNOVO were injection reactions. Injection reactions were more frequently reported with the first injection, with 49% of trial participants experiencing an injection reaction after the first injection. All injection reactions were either mild or moderate, and none led to treatment withdrawal.

Roche is dedicated to advancing innovative clinical research programmes to broaden the scientific understanding of multiple sclerosis, further reducing disability progression in RMS and PPMS and improving the treatment experiences for those living with the disease. Roche has more than 30 ongoing multiple sclerosis clinical trials designed to help us better understand the disease and its progression.

Developing new formulations of our medicines is part of our commitment to improve the patient experience and support people living with different illnesses at every step of their treatment journey. With OCREVUS ZUNOVO and Genentech and Roche's 14 subcutaneous therapies – available across various diseases – we offer additional administration options to meet the diverse preferences of patients.

About OCREVUS ZUNOVO (ocrelizumab & hyaluronidase-ocsq)

OCREVUS ZUNOVO 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 multiple sclerosis. 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 OCREVUS to enter, and enabling it to be rapidly dispersed and absorbed into the bloodstream.

OCREVUS and OCREVUS ZUNOVO are the only therapies approved for both RMS (including relapsing-remitting multiple sclerosis [RRMS] and active, or relapsing secondary progressive multiple sclerosis [SPMS], as well as clinically isolated syndrome [CIS] in the U.S.) and PPMS.

About the OCARINA II study

OCARINA II (NCT05232825) was a Phase III, global, multicentre, randomised study that evaluated the pharmacokinetics, safety and clinical and radiological efficacy of the subcutaneous (SC) formulation of OCREVUS compared with OCREVUS intravenous (IV) infusion in 236 patients with relapsing multiple sclerosis (RMS) or primary progressive multiple sclerosis (PPMS).

The trial met its primary and secondary endpoints, demonstrating SC injection was non-inferior to IV infusion based on OCREVUS levels in the blood, and consistent control of clinical (relapses) and radiological (MRI lesions) disease activity. The safety profile of OCREVUS SC was also consistent with the well-established safety profile of OCREVUS IV with the exception of injection site reactions.

About multiple sclerosis

Multiple sclerosis is a chronic disease that affects more than 2.9 million people worldwide. Multiple sclerosis 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 weakness, fatigue and difficulty seeing, and may eventually lead to disability. Most people with multiple sclerosis experience their first symptom between 20 and 40 years of age, making the disease the leading cause of acquired non-traumatic disability in younger adults.

People with all forms of multiple sclerosis experience disease progression – permanent loss of nerve cells in the central nervous system – from the beginning of their disease even if their symptoms aren't apparent or don't appear to be getting worse. Delays in diagnosis and treatment can negatively impact people with multiple sclerosis, 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 multiple sclerosis is to slow, stop and ideally prevent progression as early as possible.

Relapsing-remitting multiple sclerosis (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 multiple sclerosis are initially diagnosed with RRMS. The majority of people who are diagnosed with RRMS will eventually

transition to secondary progressive multiple sclerosis (SPMS), in which they experience steadily worsening disability over time. Relapsing forms of multiple sclerosis (RMS) include people with RRMS and people with SPMS who continue to experience relapses. Primary progressive multiple sclerosis (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 multiple sclerosis 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 and OCREVUS and OCREVUS ZUNOVO are still the only approved treatments for PPMS.

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 neuromuscular diseases: Duchenne muscular dystrophy, facioscapulohumeral muscular dystrophy and spinal muscular atrophy; neuro immune diseases: multiple sclerosis and neuromyelitis optica spectrum disorder; and neurodegenerative diseases: Alzheimer's disease, Huntington's disease and Parkinson's disease. 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.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

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