Media & Investor Release

Roche provides update on Phase III OCREVUS high dose study in people with relapsing multiple sclerosis

- **MUSETTE trial was designed to determine whether a higher dose of the currently approved OCREVUS IV 600 mg would provide additional benefit to people living with relapsing multiple sclerosis**
- **The trial did not meet its primary endpoint; results support OCREVUS IV 600 mg as the optimal dose to slow disability progression**
- **High dose was well tolerated with an overall comparable safety profile to OCREVUS IV 600 mg and no new safety signals observed**
- **These data further support the efficacy and safety profile of OCREVUS IV 600 mg dose for RMS**
- **OCREVUS set a new standard of care in multiple sclerosis and is the most prescribed disease modifying therapy in the United States with more than 400,000 people treated globally**

Basel, 02 April 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the Phase III MUSETTE trial comparing a high dose of OCREVUS® (ocrelizumab) intravenous (IV) infusion to the currently approved OCREVUS IV 600 mg dose in people with relapsing multiple sclerosis (RMS) did not meet its primary endpoint in showing additional benefit in slowing disability progression, as measured by a composite disability endpoint over a period of at least 120 weeks of treatment. The rates of disability progression were low and consistent with rates observed in the previous pivotal studies of OCREVUS IV 600 mg. In addition, in several predefined analyses on disease activity, OCREVUS IV 600 mg showed clinically meaningful results with the lowest annualised relapse rate (ARR) observed during the double-blind period of a Phase III study in RMS. The MUSETTE data further support the efficacy and safety profile of the currently approved OCREVUS IV 600 mg dose for RMS.

“OCREVUS is the first and only B-cell therapy approved for RMS and PPMS and after more than ten years of treatment, the majority of people with RMS remain free from disease progression,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “These findings reaffirm that the current OCREVUS IV 600 mg is optimally dosed to significantly slow disability progression. Moreover, in several predefined analyses on disease activity, OCREVUS showed clinically meaningful results on relapses with a relapse occurring approximately once every 16 years, a first for an anti-CD20 RMS medicine.”

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Since its launch, OCREVUS has set a new standard of care in MS and is the most prescribed disease modifying therapy in the United States with more than 400,000 people treated globally. With the recent launch of OCREVUS subcutaneous formulation we aim to improve the treatment experience for people living with multiple sclerosis and expand OCREVUS usage in centres without IV infrastructure or those with IV capacity limitations. In addition, we are developing a novel high concentration formulation for even more convenient on-body device delivery to bring OCREVUS treatment closer to home.

In addition to OCREVUS, Roche has a diverse and promising pipeline of formulations and targets, such as Brainshuttle™ CD20 and a monoacylglycerol lipase (MAGL) inhibitor in early-stage development and Bruton's tyrosine kinase (BTK) inhibitor fenebrutinib in Phase III studies for both RMS and primary progressive multiple sclerosis (PPMS).

Full data from MUSETTE will be presented at an upcoming medical meeting.

About the MUSETTE study

MUSETTE (NCT04544436) is a Phase III randomised, double-blind, controlled, parallel-group, multicentre trial to evaluate the efficacy, safety and pharmacokinetics of a high dose of OCREVUS intravenous (IV) infusion (1,200 mg for patients <75 kg or 1,800 mg for patients ≥75 kg) in adult patients with relapsing multiple sclerosis (RMS) compared with the currently approved OCREVUS IV 600 mg dose. Patients received treatment with OCREVUS high dose or IV 600 mg every 24 weeks for a minimum of 120 weeks.

The primary endpoint was the time to first onset of 12-week composite confirmed disability progression (cCDP), defined as any of the following events sustained for 12 weeks: an increase of ≥1.0 point from the baseline Expanded Disability Status Scale (EDSS) score if the baseline EDSS score was ≤5.5 or an increase of ≥0.5 points if the baseline EDSS score was >5.5; a ≥20% increase in time to perform the timed 25-foot walk (T25FW); a ≥20% increase in time to perform the nine-hole peg test (9HPT).

About OCREVUS (ocrelizumab)

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.

OCREVUS IV and OCREVUS subcutaneous (SC; marketed as OCREVUS ZUNOVO® [ocrelizumab hyaluronidase-ocsq] in the U.S.) 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 primary

progressive multiple sclerosis (PPMS). Both OCREVUS IV and SC are administered every six months. The initial IV dose is given as two 300 mg infusions two weeks apart with subsequent doses given as single 600 mg infusions. OCREVUS SC is given as a single 920 mg subcutaneous injection every six months.

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 non-traumatic disability in younger adults.

People with all forms of multiple sclerosis experience disease progression from the beginning of their disease. Therefore, 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.

Approximately 85% of people with multiple sclerosis have a relapsing form of the disease (RMS) characterised by relapses and also worsening disability over time. 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 is still the only approved treatment 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 multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular dystrophy. 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.

For more information, please visit www.roche.com.

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