Media & Investor Release

Early treatment with Roche's OCREVUS leads to reduced disease progression and healthcare costs; nine-year safety data reinforce favourable benefit-risk profile

- **77% of early-stage relapsing-remitting multiple sclerosis (RRMS) patients who had not received prior treatment achieved no evidence of disease activity (NEDA) at two years**
- **Initiation of OCREVUS as first-line treatment reduces relapses, hospitalisations and costs compared with using OCREVUS in second-line setting**
- **Nine-year long-term safety data for OCREVUS further reinforce favourable benefit-risk profile; more than 250,000 people have been treated globally**
- **Pregnancy outcomes reported for more than 2,000 women with multiple sclerosis (MS) treated with OCREVUS do not suggest an increased risk of adverse pregnancy and infant outcomes**

Basel, 26 October 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new OCREVUS® (ocrelizumab) data on disease progression and healthcare costs in patients with early-stage RRMS and long-term safety from all clinical trials in patients with relapsing MS (RMS) and primary progressive MS (PPMS). Data from the largest database of pregnancy outcomes for an anti-CD20 therapy in MS suggest consistent outcomes with epidemiological data in pregnant women and was an oral presentation today at the 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS).

“MS often impacts young people at a time in their lives when they are starting a career or planning a family,” said Levi Garraway, M.D., Ph.D. Roche's Chief Medical Officer and Head of Global Product Development. “These new data show that using OCREVUS as a first-line treatment brings substantial clinical and cost benefits to patients, thereby further emphasizing the efficacy that OCREVUS may bring with continued long-term use.”

Two-year interim analysis of open-label Phase IIIb ENSEMBLE: No evidence of disease progression in early-stage RRMS

OCREVUS treatment provided consistent benefit over two years in patients who were recently diagnosed with RRMS and had not received prior disease modifying treatment (DMT) in an interim analysis of open-label Phase IIIb study ENSEMBLE. After 96 weeks of OCREVUS treatment, 77% of patients achieved no evidence of disease activity (NEDA; no relapses, no worsening of disability or no evidence of MRI lesion activity with pre-specified MRI re-baselining at 8 weeks). The majority of patients had no relapses (93%), no MRI lesion activity (89%) and no 24-week confirmed disability progression (91%).

Over two years, the average annualised relapse rate (ARR) across all patients in the ENSEMBLE study was low (0.033), which equates to 1 relapse every 30 years. The mean Expanded Disability Status Scale (EDSS) score from baseline significantly improved from 1.8 to 1.67 ($p<0.0001$). The safety profile of OCREVUS in this trial was consistent with its overall favourable safety profile.

U.S. claims analysis: Early initiation of OCREVUS may benefit both patients and the healthcare system

Patients who were newly diagnosed and initiated OCREVUS treatment had a lower rate of annualised events often associated with a relapse (EOAR; 0.36) compared with patients who initiated OCREVUS as a second-line or later treatment (0.51). Additionally, patients treated with first-line OCREVUS had lower hospitalisation rates within one year compared with patients treated with second-line or later OCREVUS (0.02 vs. 0.042, respectively).

Costs were also lower after first-line OCREVUS treatment, including the total annual non-DMT costs ($18,389 vs. $26,225, respectively) and MS-related/non-DMT costs ($8,837 vs. $14,758, respectively) compared with patients treated with second-line or later OCREVUS.

Non-DMT costs were defined as total costs for emergency department visits, inpatient care, outpatient care and non-DMT prescriptions. MS-related costs were defined similarly but could also be attributed to the disease.

The findings from the study suggest that the early initiation of OCR, instead of escalation from lower-efficacy DMTs, can provide benefits for both patients and the healthcare system.

These clinical and economic analyses were performed on U.S. commercial claims data between 1 January 2015 and 30 June 2021.

Long-term safety from OCREVUS clinical trials consistent for nine years

New safety data as of November 2021 will be presented, representing 5,848 patients with relapsing MS (RMS) and primary progressive MS (PPMS) and 25,153 patient-years of exposure to OCREVUS, across all OCREVUS clinical trials. These findings further demonstrate the consistently favourable benefit-risk profile of OCREVUS over nine years.

“Nine-year data presented at ECTRIMS in relapsing and primary progressive MS continue to show significant efficacy against disease activity and progression with a consistent long-term safety profile, which is very encouraging for patients living with this disease and their physicians,” said Stephen Hauser, M.D., chair of the Scientific Steering Committee of the OPERA studies and director of the Weill Institute for Neurosciences at the University of California, San Francisco. “OCREVUS has significantly changed the treatment paradigm for more than 250,000 people with MS since its approval more than five years ago.”

More than 250,000 people with MS have now been treated with OCREVUS globally, and data continue to show a consistent and favourable benefit-risk profile in clinical trial and real-world settings. OCREVUS is approved in 101 countries across North America, South America, the Middle East, Eastern Europe, as well as in Australia, Switzerland, the United Kingdom and the EU.

Roche safety data do not suggest increased risk of adverse pregnancy and infant outcomes in women treated with OCREVUS

As of 31 March 2022, 2,020 cumulative MS pregnancies were reported, of which 705 (35%) had in utero exposure to OCREVUS.

Of the 532 pregnancies with in utero exposure of OCREVUS that were also prospectively reported, 286 had known outcomes: 79% live births; 1% ectopic pregnancies; 12% therapeutic/elective abortions; 8% spontaneous abortions; 0.3% still birth.

In women living with MS and treated with OCREVUS who reported pregnancies, cumulative data do not suggest an increased risk of preterm birth, major congenital anomalies or other adverse outcomes and are consistent with epidemiological data, and in-line with previous reports, providing important information for women living with MS who are or may become pregnant.

Regulatory agencies advise the use of contraception while on treatment with OCREVUS, and for 6-12 months after the last dose. The benefit-risk of OCREVUS in mothers and infants is being prospectively assessed in two Phase IV studies, MINORE in pregnant women and SOPRANINO in lactating women, both of which are currently enrolling.

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 and gradual worsening of disability – at 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 the progression of disability 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 OCREVUS (ocrelizumab)

OCREVUS is the first and only therapy approved for both RMS (including RRMS and active, or relapsing SPMS, in addition to clinically isolated syndrome [CIS] in the U.S.) and PPMS. 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. OCREVUS 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 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 has both approved and investigational medicines across multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, myasthenia gravis, 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.

In recognising our endeavor 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.

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