Phase III efficacy results of investigational medicine OCREVUS® (ocrelizumab) reinforced by exploratory analyses in two forms of multiple sclerosis

- 75 percent higher proportion of relapsing multiple sclerosis (RMS) patients achieved No Evidence of Disease Activity (NEDA) with OCREVUS compared with interferon beta-1a (Rebif®)
- 47 percent higher proportion of primary progressive multiple sclerosis (PPMS) patients achieved No Evidence of Progression (NEP) with OCREVUS compared with placebo

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today new analyses from the three OCREVUS® (ocrelizumab) Phase III studies in relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS) will be presented during the 32nd congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), from 14th to 17th September in London, England.

OCREVUS increased disease control in patients with RMS and PPMS in separate post-hoc analyses. In these analyses, two composite endpoints measured disease control using a combination of clinical and MRI outcomes: No Evidence of Disease Activity (NEDA) in patients with RMS and No Evidence of Progression (NEP) in patients with PPMS. These composite endpoints are emerging as new treatment targets.

A NEDA analysis of pooled data from the Phase III OPERA I and OPERA II studies compared no evidence of disease activity during different time periods over two years of study. NEDA is achieved when a patient has no relapses, no confirmed disability progression, no gadolinium-enhancing MRI lesions and no new or enlarging MRI lesions. The data showed that OCREVUS significantly increased the proportion of RMS patients achieving NEDA by 75 percent compared with interferon beta-1a over 96 weeks (0-96 weeks, p<0.0001). Additionally, compared with interferon beta-1a, OCREVUS treatment significantly increased the relative proportion of patients achieving NEDA by 33 percent in weeks 0-24 and by 72 percent in weeks 24-96 (both p<0.0001). A majority of patients achieved NEDA in the first 24 weeks of OCREVUS treatment (60.8 percent) and this proportion increased during weeks 24-96 of the study (72.2 percent).
“Controlling clinical and sub-clinical disease activity as early as possible is an important treatment goal for people living with MS,” said Professor Gavin Giovannoni, Scientific Steering Committee Member of the OPERA I and II studies and Chair of Neurology at Barts and The London School of Medicine and Dentistry. “These new data suggest that ocrelizumab consistently impacts disease progression and has the potential to change how we approach treating both relapsing and primary progressive MS.”

New post-hoc analyses of the ORATORIO study in PPMS patients measured NEP, which includes three measures of physical disability (confirmed disability progression, walking speed and upper extremity function) and reflects no evidence of worsening of a person’s physical disability. Patients who achieved NEP had no evidence of confirmed disability progression sustained for at least 12 weeks and less than 20 percent worsening of performance on the timed 25-foot walk and 9-hole peg test. OCREVUS treatment significantly increased the proportion of PPMS patients with NEP by 47 percent at week 120 compared with placebo (p=0.0006).

“With no approved treatment options, primary progressive MS remains a challenge for physicians and people with MS,” said Xavier Montalban, M.D., Ph.D., Professor of Neurology and Neuroimmunology at Vall d’Hebron University Hospital, Research Institute and Cemcat, Barcelona, Spain. “OCREVUS significantly impacted three key disability measurements, which further highlight its clinical significance in people with primary progressive MS.”

In addition, new patient-reported outcomes data from the ORATORIO study highlighting the unmet need of people with PPMS, including the effect OCREVUS had on fatigue measures, will be presented.

Leading investigators will present the following oral and poster presentations:

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<th>Abstract Title</th>
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<td>An exploratory analysis of 12- and 24-week composite confirmed disability progression in patients with primary progressive multiple sclerosis in the ORATORIO trial</td>
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<td>Infusion-related reactions with ocrelizumab in</td>
<td>P720 (poster), Thursday, 15 September, 3:45 –</td>
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<td>relapsing multiple sclerosis and primary progressive multiple sclerosis</td>
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<td>Evaluation of no evidence of progression using composite disability outcome measures, in patients with primary progressive multiple sclerosis in the ORATORIO trial</td>
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<td>Effect of ocrelizumab on magnetic resonance imaging markers of neurodegeneration in patients with relapsing multiple sclerosis: analysis of the Phase III, double-blind, double-dummy, interferon beta-1a-controlled OPERA I and OPERA II studies</td>
<td>P1011 (poster), Friday, 16 September, 3:30 – 5:00 p.m. BST</td>
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<td>Baseline assessment of fatigue and health-related quality of life in patients with primary progressive multiple sclerosis in the ORATORIO study</td>
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<td>Exploration and verification of a patient-powered research network to provide patient insights in multiple sclerosis</td>
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<td>NEDA epoch analysis of patients with relapsing multiple sclerosis treated with ocrelizumab: Results</td>
<td>P1593 (poster), Friday, 16 September, 3:30 – 5:00 p.m. BST</td>
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from OPERA I and OPERA II, Phase III studies

| Real-world treatment observation in multiple sclerosis: development of an online platform to measure patients’ treatment awareness and experiences, access barriers and decision-making | ePoster will be displayed on terminals during the congress |

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As previously announced, the European Medicines Agency (EMA) and US Food and Drug Administration (FDA) have accepted marketing applications for OCREVUS, each submitted for RMS and PPMS.

OCREVUS® is the proprietary name submitted to global regulatory authorities for the investigational medicine ocrelizumab.

**About OCREVUS® (ocrelizumab)**

OCREVUS is an investigational, humanised monoclonal antibody designed to selectively 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, and therefore important functions of the immune system may be preserved.

The Phase III clinical development programme for OCREVUS (ORCHESTRA) includes three studies: OPERA I, OPERA II and ORATORIO. OPERA I and OPERA II are identical Phase III, randomised, double-blind, double-dummy, global multi-centre studies that evaluated the efficacy and safety of OCREVUS (600 mg administered by intravenous infusion every six months) compared with Rebif® (interferon beta-1a; 44 mcg administered by subcutaneous injection three times per week) in 1,656 people with relapsing forms of MS (i.e., relapsing-remitting MS and secondary-progressive MS with relapses). ORATORIO is a Phase III, randomised, double-blind, global multi-centre study that evaluated the efficacy and safety of OCREVUS (600 mg administered by intravenous infusion every six months) compared with placebo in 732 people with primary progressive MS.
The most common adverse events associated with OCREVUS were infusion-related reactions and infections, which were mostly mild to moderate in severity.

About multiple sclerosis
Multiple sclerosis (MS) is a chronic disease that affects an estimated 2.3 million people around the world, for which there is currently no cure. MS occurs when the immune system abnormally attacks the insulation and support around nerve cells (myelin sheath) in the 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.

Relapsing MS is the most common form of the disease. Disease activity and progression can occur even when people do not show signs or symptoms of MS, despite available relapsing MS treatments. 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 one in 10 people with MS are diagnosed with the primary progressive form of the disease. There are no approved treatments for PPMS.

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, 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.

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. 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.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. Twenty-nine 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry eight years in a row by the Dow Jones Sustainability Indices.

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2015 employed more than 91,700 people worldwide. In 2015, Roche invested CHF 9.3 billion in R&D and posted sales of CHF 48.1 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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References


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