New data at AAN reinforce clinical benefit of Roche's OCREVUS™ (ocrelizumab) for relapsing and primary progressive multiple sclerosis

- OCREVUS rapidly suppressed signs of disease activity in relapsing MS (RMS) patients
- In patients with early RMS – recently diagnosed and without prior treatment – OCREVUS was superior to Rebif® (interferon beta-1a) in controlling disease activity
- OCREVUS decreased fatigue versus placebo in people with primary progressive multiple sclerosis (PPMS)
- In open-label extension studies of over 2,200 patients with RMS and PPMS, OCREVUS continued to show a favourable benefit-risk profile

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that new data from the OCREVUS™ (ocrelizumab) clinical trial programmes will be presented during the 69th American Academy of Neurology (AAN) Annual Meeting in Boston, Massachusetts. The presentations will highlight new efficacy and safety analyses from the OCREVUS Phase II and Phase III trials, as well as from the open-label extensions. Data from these four studies further support OCREVUS as a potential treatment option for patients with relapsing or primary progressive forms of multiple sclerosis (MS).

Within the first eight weeks of treatment, OCREVUS reduced the relapse rate by 55 percent compared with Rebif® (interferon beta-1a) (p=0.0045), in a pooled exploratory analysis of the Phase III OPERA I and OPERA II studies in RMS. In a separate Phase II study in relapsing-remitting MS (RRMS) patients, OCREVUS demonstrated rapid and near-complete suppression of brain MRI activity at eight weeks, including new active areas of damage (T1 gadolinium-enhancing lesions) and new or newly enlarging areas of damage (hyperintense T2 lesions), compared with placebo.
Additional analyses of the Phase III OPERA I and II studies demonstrated the efficacy of OCREVUS in people with early RMS (recently diagnosed and without previous treatment). OCREVUS suppressed more than 90 percent of active MRI lesions over two years compared with interferon beta-1a (p<0.0001) in these patients. In the same early RMS patients, OCREVUS also increased the proportion who achieved No Evidence of Disease Activity (NEDA) by 76 percent compared with interferon beta-1a over two years (p<0.0001). 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. These data were consistent with NEDA results observed in the overall OCREVUS-treated population.

“The rapid effect seen with OCREVUS in clinical trials provides insight into how this newly FDA-approved therapy could change the way MS is treated”, said Stephen Hauser, MD, Chair of the Scientific Steering Committee of the OPERA studies, Director of the Weill Institute for Neurosciences and Chair of the Department of Neurology at the University of California, San Francisco. “Following the FDA approval of OCREVUS for relapsing or primary progressive forms of MS, it is encouraging to see the medicine’s favourable benefit-risk profile continue to play out in the data.”

In an analysis of pooled data from the Phase III RMS open-label extension (OLE) studies, patients who switched from interferon beta-1a to OCREVUS experienced reductions in relapse rates (unadjusted annualised relapse rate of 0.102 after switching) and MRI brain lesions (0.01 mean number of active lesions (T1 gadolinium-enhancing) and 0.37 new or enlarging T2 lesions after switching). Furthermore, patients who were treated with OCREVUS from the start of the studies showed a sustained benefit after three years.

In the ORATORIO study, PPMS patients with confirmed disability progression (CDP) had a greater increase in fatigue (p=0.0003), underlining the importance of preventing disease progression in people with PPMS. Furthermore, patients treated with OCREVUS who didn’t experience disability progression reported a significant reduction in fatigue compared to those taking placebo (p=0.0337).

Additionally, in open-label extension studies of over 2,200 patients with RMS and PPMS, OCREVUS safety was consistent with the controlled treatment periods.
The most common side effects associated with OCREVUS in all Phase III studies were infusion reactions and upper respiratory tract infections, which were mostly mild to moderate in severity.

OCREVUS is approved for use in the U.S. The OCREVUS Marketing Authorisation Application (MAA) has been validated by the European Medicines Agency (EMA) and is currently under review.

About the OPERA I and OPERA II studies in relapsing forms of MS
OPERA I and OPERA II are Phase III, randomised, double-blind, double-dummy, global multi-centre studies evaluating the efficacy and safety of OCREVUS (600 mg administered by intravenous infusion every six months) compared with interferon beta-1a (44 mcg administered by subcutaneous injection three times per week) in 1,656 people with relapsing forms of MS. In these studies, relapsing MS (RMS) was defined as relapsing-remitting MS (RRMS) and secondary progressive MS (SPMS) with relapses. A similar proportion of patients in the OCREVUS group experienced serious adverse events and serious infections compared with patients in the high-dose interferon beta-1a group in the RMS studies.

About the ORATORIO study in primary progressive MS
ORATORIO is a Phase III, randomised, double-blind, global multi-centre study evaluating the efficacy and safety of OCREVUS (600 mg administered by intravenous infusion every six months; given as two 300 mg infusions two weeks apart) compared with placebo in 732 people with primary progressive MS (PPMS). The blinded treatment period of the ORATORIO study continued until all patients had received at least 120 weeks of either OCREVUS or placebo and a predefined number of confirmed disability progression (CDP) events was reached overall in the study. A similar proportion of patients in the OCREVUS group experienced adverse events and serious adverse events compared with patients in the placebo group in the PPMS study.

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.\(^1\)\(^2\) 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.\(^3\)\(^4\)\(^5\) 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.\(^6\)
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. 7,8 Approximately 85 percent of people with MS are initially diagnosed with RRMS. 9 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. 9 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 percent of people with MS are diagnosed with the primary progressive form of the disease. 9 Until now, there have been no FDA approved treatments for PPMS.

People with all forms of MS experience disease activity – inflammation in the nervous system and permanent loss of nerve cells in the brain – even when their clinical symptoms aren’t apparent or don’t appear to be getting worse. 10 An important goal of treating MS is to reduce disease activity as soon as possible to slow how quickly a person’s disability progresses. 11 Despite available disease-modifying treatments (DMTs), some people with RMS continue to experience disease activity and disability progression.

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 (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.

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. 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. 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.

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.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims for improving patient access to medical innovations by working with all relevant stakeholders. 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 (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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](http://www.roche.com).

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References

6 Multiple Sclerosis International Federation. What is MS? Available at http://www.msif.org/about-ms/what-is-ms/.
9 National Multiple Sclerosis Society. Types of MS. Available at http://www.nationalmssociety.org/What-is-MS/Types-of-MS.