Basel, 23 June 2017

New data at EAN show Roche’s OCREVUS (ocrelizumab) significantly reduced multiple measures of disease progression in relapsing and primary progressive multiple sclerosis

- OCREVUS increased the number of patients with relapsing MS (RMS) and primary progressive MS (PPMS) who maintained No Evidence of Progression or Active Disease (NEPAD) versus Rebif (interferon beta-1a) in RMS and placebo in PPMS
- OCREVUS significantly reduced the risk of RMS and PPMS patients requiring mobility aids versus comparators
- In PPMS patients, OCREVUS reduced the risk of more severe forms of disability progression versus placebo

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that new post-hoc analyses from the OCREVUS® (ocrelizumab) Phase III clinical trial programme in people with relapsing and primary progressive forms of multiple sclerosis (RMS and PPMS) will be presented at the 3rd Congress of the European Academy of Neurology (EAN) from 24 June to 27 June in Amsterdam, Netherlands.

OCREVUS significantly reduced disease activity and disability progression in patients with RMS and PPMS, as measured by No Evidence of Progression or Active Disease (NEPAD), a novel composite endpoint in MS. In RMS, OCREVUS significantly increased the proportion of patients maintaining NEPAD by 82 percent compared with Rebif® (interferon beta-1a) at 96 weeks in a pooled exploratory analysis of the Phase III OPERA I and II studies (p<0.001). In PPMS patients, OCREVUS more than tripled the proportion of those who maintained NEPAD compared with placebo at 120 weeks in an exploratory analysis of the Phase III ORATORIO study (29.9 percent with OCREVUS versus 9.4 percent with placebo, p<0.001).
NEPAD is considered a clinically meaningful endpoint because it signifies a patient has no relapses, no confirmed disability progression measured by the Expanded Disability Status Scale (EDSS), no progression equal to or above 20 percent on the timed 25-foot walk (T25-FW) and the nine-hole peg test (9-HPT), no gadolinium-enhancing T1 MRI lesions and no new or enlarging T2 MRI lesions.

These results underline that the significant effects of OCREVUS on disability progression are clinically meaningful,” said Ludwig Kappos, MD, Chair of the Department of Neurology, University Hospital, Basel, Switzerland. “Slowing disability progression, or preventing people with MS from having to use a cane or wheelchair, makes a great difference to their daily lives. It is particularly exciting to see these benefits in people with PPMS, a disabling form of MS without approved treatments in Europe.”

In separate post-hoc analyses of the OPERA I and II studies, OCREVUS significantly reduced the risk of patients with RMS losing the ability to walk long distances unassisted (EDSS ≥4) or requiring a cane or crutch (EDSS ≥6) compared with interferon beta-1a at 96 weeks (p≤0.005). In the ORATORIO study, OCREVUS significantly reduced the risk of becoming wheelchair-bound (EDSS ≥7) compared with placebo at 120 weeks in PPMS patients with baseline EDSS ≤6 (p≤0.028).

Furthermore, in a post-hoc analysis of the placebo-controlled ORATORIO study, OCREVUS consistently reduced the risk of 12- and 24-week confirmed disability progression (CDP) across three different definitions of the measure meant to capture more severe disability worsening than traditionally assessed in PPMS patients.

In addition, interim results from FLOODLIGHT, a sensor-based digital monitoring study to determine adherence and correlation with in-clinic testing in people with and without MS, will be presented. Pregnancy outcomes in all female patients treated with OCREVUS will also be presented.

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.
Leading investigators will present the following oral and poster presentations:

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In parallel to EAN, Roche will be hosting a live MS Forum: ‘Shifting mindsets in Multiple Sclerosis – the need for policy change and better outcomes across Europe’, Monday 26 June at 4.00 – 5.00pm CET.

Registration can be made here: [http://livestream.videum.com/roche/ms/?utm_source=T&utm_medium=E&utm_campaign=](http://livestream.videum.com/roche/ms/?utm_source=T&utm_medium=E&utm_campaign=)

Follow Roche on Twitter via @Roche and keep up to date with EAN 2017 news and updates by using the hashtag #EAN2017.

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. 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 to improve patient access to medical innovations by working with all relevant stakeholders. Thirty 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.
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