Roche to present new OCREVUS (ocrelizumab) data analyses showing significant reduction of disability progression in relapsing and primary progressive multiple sclerosis at the AAN Annual Meeting

- New analyses show the effect of OCREVUS on reducing the risk of disability progression is associated with exposure and lower B-cell levels
- Long-term data in RMS and PPMS show that earlier treatment with OCREVUS significantly reduced the risk of permanent disability progression
- Over 100,000 people have been treated with OCREVUS globally, in clinical trial and real-world settings; data presented at the AAN Annual Meeting highlights a consistent and favourable benefit-risk profile

Basel, 8 May 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new OCREVUS® (ocrelizumab) data in relapsing and primary progressive multiple sclerosis (MS) were presented at the 71st American Academy of Neurology (AAN) Annual Meeting from 4-10 May in Philadelphia, Pennsylvania. New analyses on OCREVUS show its effect on reducing the risk of disability progression is associated with higher exposure to the medicine and lower B-cell levels, and show the positive impact of OCREVUS in significantly reducing disability progression.

With rapidly growing real-world experience and more than 100,000 patients treated globally, OCREVUS is the first and only therapy with six-month dosing approved for both relapsing MS (RMS), (including RRMS and active, or relapsing, secondary progressive MS) and primary progressive MS (PPMS). Additionally, new safety data presented at AAN representing 4,501 patients with RMS and PPMS and 12,559 patient years of exposure to OCREVUS, across all OCREVUS clinical trials, remain consistent with the medicine’s favourable benefit-risk profile.

“These are the first data to show that higher OCREVUS exposure is associated with greater control of disability progression without impacting safety,” said Stephen Hauser, MD, 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. “These analyses, along with long-term data that show OCREVUS reduced the risk of permanent disability progression, create a compelling case for initiating the therapy early in the disease course and provide important information that clinicians can use to inform treatment decisions.”

New data from pharmacokinetic, pharmacodynamic and exposure analyses – or how OCREVUS is processed in an individual’s body over time – show higher exposure to OCREVUS correlated with lower B-cell levels and lower rates of disability progression in patients. In patients with RMS, OCREVUS reduced the risk of 24-week confirmed disability progression (CDP) at all exposure levels compared with interferon beta-1a. There was lower risk of disability progression with higher exposure to OCREVUS.
A similar pattern was observed for patients with PPMS, in which OCREVUS reduced the risk of 24-week CDP at all exposure levels compared with placebo. OCREVUS reduced T1 gadolinium-enhancing and new/enlarging T2 MRI lesions to nearly undetectable levels in RMS and PPMS patients and reduced annualized relapse rates to low levels (0.13-0.18) in RMS patients across all exposure segments. Notably, safety findings remained consistent across all OCREVUS exposure levels, suggesting that higher exposure does not increase the likelihood of adverse events.

Long-term data, of over five years, from the Phase III OPERA and ORATORIO open-label extension (OLE) trials in RMS and PPMS, show that earlier treatment with OCREVUS significantly reduced the risk of permanent disability progression and this effect was sustained over time. In the OPERA OLE, the proportion of RMS patients with 48-week CDP was lower for those treated with continuous OCREVUS (total of five years on OCREVUS) compared with patients who switched to OCREVUS after two years of interferon beta-1a treatment in the double-blind period (total of three years on OCREVUS) (10.4% vs. 15.7%; p=0.004). In the ORATORIO OLE, the proportion of PPMS patients with 48-week CDP was lower in those treated with continuous OCREVUS over five and a half years compared with patients who switched to OCREVUS from placebo after the 120-week double-blind period (43.7% vs 53.1%; p=0.03).

Additionally, interim results of the Phase III Ocrelizumab Biomarker Outcome Evaluation (OBOE) study show that OCREVUS reduced the presence of a nerve cell damage and inflammation biomarker in serum and cerebrospinal fluid at 12, 24 and 52 weeks in patients with RMS. These one-year data add to the growing body of evidence to identify biomarkers of disease progression in MS and the benefit of OCREVUS on these markers.

OCREVUS is now approved in 85 countries across North America, South America, the Middle East, Eastern Europe, as well as in Australia, Switzerland and the European Union.

Full session details and data presentation listings for the 2019 AAN Annual Meeting can be found at the meeting website: https://www.aan.com/conferences-community/annual-meeting/.

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**About multiple sclerosis**

Multiple sclerosis (MS) is a chronic disease that affects up to a million people in the U.S., 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-remitting MS (RRMS) is the most common form of the disease and is characterized by episodes of new or worsening signs or symptoms (relapses) followed by periods of recovery. 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. Relapsing forms of MS (RMS) include people with RRMS and people with active 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. Until the FDA approval of OCREVUS, 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. An important goal of treating MS is to reduce disease activity as soon as possible to slow how quickly a person’s disability progresses.

**About OCREVUS (ocrelizumab)**
OCREVUS is the first and only therapy approved for both RMS (including RRMS and active, or relapsing, SPMS) and PPMS, with six-month dosing. OCREVUS is a humanized 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, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer’s disease, Huntington’s disease, Parkinson’s disease, Duchenne muscular dystrophy 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. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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