

OCREVUS (ocrelizumab) data show early initiation of treatment reduces disability progression over five years in relapsing and primary progressive multiple sclerosis

- **People with relapsing MS (RMS) treated sooner with OCREVUS had earlier reduction in disease activity and less disability progression vs. those who switched from interferon beta-1α**
- **People with primary progressive MS (PPMS) treated with OCREVUS earlier had less disability and upper limb progression than those who switched from placebo**
- **Longer-term safety data are consistent with OCREVUS' favourable benefit-risk profile for both RMS and PPMS**
- **OCREVUS approved in 68 countries, with over 70,000 patients treated globally**

Basel, 10 October 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that new OCREVUS® (ocrelizumab) data will be presented at the 34th Congress of the European Committee for the Treatment and Research in Multiple Sclerosis (ECTRIMS) from 10 October to 12 October in Berlin, Germany. Five-year data from the Phase III open-label extension studies of OPERA I, OPERA II and ORATORIO show OCREVUS efficacy is maintained on key measures of disease activity and that people treated earlier with OCREVUS had superior disability progression outcomes compared with RMS patients who switched from interferon beta-1α or PPMS patients who switched from placebo.

“From the moment of diagnosis, reducing disease progression is an important goal for people with MS. The new data presented at ECTRIMS demonstrate that OCREVUS' efficacy continued over five years in relapsing and primary progressive MS, and notably, include the largest body of evidence for any medicine to significantly slow disability progression in primary progressive MS,” said Stephen Hauser, MD, chair of the Scientific Steering Committee of the OPERA studies, professor of neurology at the University of California, San Francisco, and director of the UCSF Weill Institute for Neurosciences. “The data also suggest that OCREVUS rapidly suppressed relapse and MRI disease activity in people with relapsing MS who switched from interferon beta-1α, and additionally, that earlier treatment with OCREVUS reduced disability progression and brain atrophy.”

In the open-label extension of the Phase III OPERA I and OPERA II trials, people with RMS who had continuous OCREVUS treatment over five years had better outcomes in brain atrophy and confirmed disability progression (CDP) than patients who switched to OCREVUS after the first two years of interferon beta-1α treatment. People with RMS who initiated OCREVUS two years earlier maintained lower whole brain, white matter and cortical grey matter tissue loss after five years of continuous treatment. People with RMS who initiated OCREVUS treatment two years earlier achieved significant and sustained reductions in 24-week CDP compared to those who switched from interferon beta-1α (16.1 percent vs. 21.3 percent progression after Year 5, respectively, p=0.014).

Additionally, people with RMS who switched to OCREVUS from interferon beta-1 α after the controlled trial period had a rapid suppression of disease activity, measured with annualized relapse rate and MRI measures of T1-gadolinium enhancing (T1-Gd+) lesions and new/enlarging T2 (N/E T2) lesions. Switching to OCREVUS reduced the annualized relapse rate from 0.2 pre-switch to 0.07 after three years of OCREVUS treatment. People also experienced near-complete suppression of T1-gadolinium enhancing (T1-Gd+) lesions from 0.49 lesions/scan on interferon beta-1 α treatment to 0.004 lesions/scan after three years of OCREVUS treatment. Similarly, the number of new or enlarging T2 (N/E T2) lesions were suppressed from 2.58 to 0.038 lesions/scan.

PPMS patients who were treated with OCREVUS three to five years earlier had less disability progression in the open-label extension study of the Phase III ORATORIO trial. Disability progression was significantly reduced by 9.6 percent in people who were continuously treated with OCREVUS compared with those who switched from placebo as measured by 24-week CDP ($p=0.023$). Upper limb disability progression, measured by the nine-hole peg test (9-HPT), was significantly reduced by 13.4 percent in people who were continuously treated with OCREVUS compared with those who switched from placebo ($p=0.001$).

Furthermore, data from the open-label Phase IIIb CHORDS study evaluating OCREVUS in people with relapsing-remitting MS (RRMS) who had a suboptimal response to at least six months of treatment with another disease-modifying therapy will be presented. An interim analysis shows 59 percent of people who switched to OCREVUS had no relapse, no T1-Gd+ lesion MRI activity, no N/E T2 lesion MRI activity and no 24-week CDP at 48 weeks.

Ongoing safety data presented atECTRIMS representing 3,811 RMS and PPMS patients and 10,919 patient years of exposure to OCREVUS, across all OCREVUS clinical trials, remain consistent with the medicine's favourable benefit-risk profile.

A post-hoc analysis of the ORATORIO study demonstrating OCREVUS treatment increased the proportion of patients with PPMS who achieved no evidence of progression or active disease (NEPAD), a comprehensive measure of MS, compared to placebo were published 29 August in *Annals of Neurology*.

<https://onlinelibrary.wiley.com/doi/10.1002/ana.25313>

OCREVUS is now approved in 68 countries across North America, South America, the Middle East, Eastern Europe, as well as in Australia, Switzerland and the European Union. As of October 2018, over 70,000 people have been treated globally with OCREVUS. Marketing applications are currently under review in more than 20 countries across the world.

About OCREVUS (ocrelizumab)

OCREVUS is a 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 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. 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 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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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