

Roche presents new OCREVUS (ocrelizumab) biomarker data that increase understanding of disease progression in multiple sclerosis at ECTRIMS

- **Blood neurofilament light chain (NfL) levels were significantly lowered following OCREVUS treatment in analyses of Phase III studies in RMS and PPMS**
- **New data show NfL may be a biomarker for predicting future disability outcomes**
- **Separate analyses presented from one of the first studies to demonstrate NfL levels are correlated with active MRI lesions in PPMS**

Basel, 10 September 2019 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new data from OCREVUS® (ocrelizumab) trials in relapsing and primary progressive multiple sclerosis (MS). The analyses provide new insights into the biology of MS that advance the understanding of disease progression, with the goal of identifying and slowing disease progression as early as possible to preserve patient function over the long term. Findings will be presented at the 35th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) from 11-13 September in Stockholm, Sweden.

Following OCREVUS treatment, blood neurofilament light chain (NfL) levels were lowered to a healthy donor range¹ in relapsing MS (RMS) and primary progressive MS (PPMS) patients. NfL is a protein that provides structural support to nerve fibres in the brain. An increase in the amount of NfL may be associated with nerve cell damage, and detection of increased NfL levels in blood or cerebrospinal fluid (CSF) may serve as a biomarker of nerve cell damage. In the Phase III OPERA I study in RMS and the ORATORIO study in PPMS, blood NfL levels were significantly lower after treatment with OCREVUS. In RMS, blood serum NfL levels were reduced by 43 percent from baseline to 96 weeks after OCREVUS treatment compared with a 31 percent reduction with interferon beta-1a ($p < 0.001$). In PPMS, blood plasma NfL levels were reduced by 16 percent from baseline to 96 weeks after OCREVUS treatment compared with 0.2 percent reduction with placebo ($p < 0.001$). Additionally, these analyses showed higher blood NfL levels at the start of the study were correlated with more disability progression in upper and lower limbs in PPMS and overall disability in the interferon beta-1a RMS treatment group at 96 weeks.

Few studies have described the relationship between NfL levels and MRI in a well-characterised PPMS patient group. New data from the Phase III OBOE study in PPMS and RMS show that PPMS patients with active MRI lesions (gadolinium-enhancing T1 lesions) had median cerebrospinal fluid (CSF) NfL levels twice as high as those without these lesions. As previously reported, RMS patients with active MRI lesions also had significantly higher NfL levels. Collectively, these data around NfL in MS advance the understanding of it as a potential biomarker of disease progression and may provide insight into the potential neuroprotective effects following OCREVUS treatment.

“These analyses from the OCREVUS trials strengthen the evidence for pursuing neurofilament light chain as a potential biomarker of disease activity and progression in MS, including its potential to predict future disability outcomes,” said Amit Bar-Or, MD, FRCP, FAAN, FANA, chair of the Scientific Steering Committee of the OBOE study and chief of the Multiple Sclerosis Division of the Department of Neurology

at the Perelman School of Medicine, University of Pennsylvania, Philadelphia. “Disease progression in MS can be challenging to identify without noticeable relapses or disability progression, and continued investigation into neurofilament light chain may help us better understand the underlying progression in all forms of this disease.”

OCREVUS is the first and only therapy approved for both RMS (including relapsing-remitting MS (RRMS) and active, or relapsing, secondary progressive MS, in addition to clinically isolated syndrome in the U.S.) and PPMS. OCREVUS is dosed every six months, with rapidly increasing real-world experience and more than 120,000 people with MS treated globally. OCREVUS is now approved in 89 countries across North America, South America, the Middle East, and Eastern Europe, as well as in Australia, Switzerland and the European Union.

Full session details and data presentation listings for ECTRIMS can be found at the congress website: <https://www.ectrims-congress.eu/2019.html>.

Follow Roche on Twitter via @Roche and keep up to date with ECTRIMS news and updates by using the hashtag #ECTRIMS2019.

About multiple sclerosis

Multiple sclerosis (MS) is a chronic disease that affects more than 2.3 million people globally, 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 clinically isolated syndrome, RRMS and active, or relapsing, SPMS) and PPMS, with six-monthly dosing. 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, suggesting that 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. More than 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.

All trademarks used or mentioned in this release are protected by law.

References

[1] Samples were taken from 118 healthy donors to establish healthy donor NfL ranges of 5.5–9.8 pg/mL for blood serum and 4.3–7.9 pg/mL for blood plasma. Healthy donor range was defined as the 90th percentile of an age-matched healthy cohort.

Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Daniel Grotzky
- Karsten Kleine
- Nathalie Meetz
- Barbara von Schnurbein