Investor Update

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New OCREVUS (ocrelizumab) data at ECTRIMS advance clinical understanding of underlying progression in multiple sclerosis

- Data show superiority of OCREVUS compared to Rebif (interferon beta-1a) in significantly reducing disability Progression Independent of Relapse Activity (PIRA) in people with relapsing multiple sclerosis (RMS)
- Data demonstrates first method to automatically detect and characterise Slowly Evolving Lesions (SELs) as a potential measure of underlying disease activity in the brain using MRI
- New results from FLOODLIGHT study suggest smartphone-based disease progression monitoring can augment in-clinic tests, such as hand/arm function and walking behaviour

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that new OCREVUS® (ocrelizumab) data are being presented at the 7th Joint European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) – Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Meeting in Paris, France. The data presented showcase clinical advances around underlying disease activity and disability progression in relapsing and progressive forms of multiple sclerosis (MS), through the exploration of newly emerging endpoints and precision monitoring.

OCREVUS significantly reduced the proportion of people with RMS who experienced Progression Independent of Relapse Activity (PIRA) in a post-hoc analysis compared to Rebif® (interferon-beta 1a). This effect was particularly seen in those who were potentially at higher risk of progressive disease course based on their baseline Expanded Disability Status Scale (EDSS). Specifically, in this analysis, OCREVUS treatment reduced the risk of PIRA by 25 percent and 23 percent confirmed at 12 and 24 weeks, respectively (p=0.008 and p=0.039, respectively).
PIRA is a newly emerging MS endpoint intended to measure an increase in disability, which is related to underlying disease activity in RMS. These data were generated through a post-hoc analysis of more than 1,600 people randomly assigned to treatment in OPERA I and OPERA II, and assessed for PIRA, as measured by cCDP. cCDP is a measure of the risk of a person’s physical disability getting worse and is based on three measures of physical disability – confirmed disability progression, walking speed and upper extremity function.

“These new analyses of data from the large controlled studies with OCREVUS help advance our understanding of how in relapsing MS the disease may progress independent of relapses. These insights have implications for daily decisions made together with patients,” said Ludwig Kappos, MD, Chair of the Department of Neurology, University Hospital, Basel, Switzerland. “Even without experiencing relapses, people with RMS may still have underlying disease activity, which can cause irreversible decline in their mobility and day-to-day quality of life. Recognising and understanding this process supports early indication of more efficacious treatment.”

A platform presentation, also highlighting underlying disease activity, showed that a new algorithm using conventional MRI can be used as a possible biomarker to automatically detect Slowly Evolving Lesions (SELS), as a potential measure of chronic disease activity outside of acute lesions in the brain. SELs were shown to evolve independently of acute lesions leading to enhanced focal brain tissue loss, as measured by T1 black hole evolution. Further research is needed, but this algorithm for automatic detection of SELs using conventional brain MRI may provide a marker of chronic disease activity in MS lesions.

“This new ability to detect both acute and underlying disease activity with conventional MRI may advance the way we monitor for MS progression and how we think about overall patient management,” 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. “While we’ve seen SELs can occur across MS subtypes, this finding may be particularly promising for people with PPMS whose worsening of disability may be related to the presence of SELs. This study also highlights the importance of continued research in MS, not only for development of new treatments such as OCREVUS, but for the insights that are gained about the fundamental cause of this debilitating disease.”
New data from the FLOODLIGHT clinical trial program, which is designed to assess sensor-based outcomes from a series of active neurological tests and passive monitoring through the use of a smartphone is also being presented. The tool enables a continuous stream of precise, real-world MS disease progression data to be collected and analysed using dedicated algorithms and machine learning.

Data at ECTRIMS – ACTRIMS demonstrate strong patient adherence to the FLOODLIGHT technology. Hand/arm function measured with a smartphone-based pinching test may detect subclinical impairment in those who have normal Nine-Hole Peg Test (9-HPT) performances. Turning speed measured with a smartphone-based U-Turn Test was shown to correlate with the Timed 25-Foot Walk (T25-FW) (p<0.001), and may detect subclinical activity compared to normal in-clinic performances. The data support FLOODLIGHT as a potential complement to in-clinic testing to provide a more complete and consistent picture of a patient’s disease progression.

Additionally, OPERA I, OPERA II and ORATORIO Phase III open-label extension data presented at ECTRIMS – ACTRIMS continue to show a favourable benefit-risk profile for OCREVUS.

OCREVUS has been approved for use in countries across North America, South America, the Middle East, Eastern Europe, as well as in Australia and Switzerland.

Follow Roche on Twitter via @Roche and keep up to date with Joint ECTRIMS – ACTRIMS Meeting news and updates by using the hashtag #MSParis2017.

**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. 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 characterised 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 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.

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. 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 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine 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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