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## **Phase II study showed ocrelizumab maintained significant reduction in disease activity for multiple sclerosis patients for almost two years**

### **Phase III trials underway to investigate ocrelizumab in two forms of MS**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced 96-week results<sup>1</sup> from a Phase II study of ocrelizumab in patients with relapsing-remitting multiple sclerosis (RRMS), the most common clinical form<sup>2</sup> of the disease. The study showed that the significant reduction in disease activity as measured by the total number of active brain lesions and relapses previously reported for 24 weeks, was maintained through 96 weeks. The data is being presented today atECTRIMS (European Committee for Treatment and Research in Multiple Sclerosis) the world's largest annual international conference devoted to basic and clinical research in multiple sclerosis.

People with RRMS suffer from relapses and disabling symptoms caused by damage to the central nervous system (the brain, spinal cord and optic nerves) which can significantly affect their quality of life. Symptoms are unpredictable and vary between patients. Most people experience their first symptoms between the ages of 20 and 40.

Results from the trial showed that during the 24-96 week treatment period no patient who received a dose of 600mg ocrelizumab developed a new or enlarging brain lesion (as measured by MRI). The annualised relapse rate (ARR), the rate of clinical attacks or flare-ups per patient-year, was less than 0.2 attacks per patient per year across the 96-week period. The data also showed that, of the patients who completed the study, two-thirds of the patients in the 600mg group were free of any disease activity (as measured by MRI, relapses or neurological progression) over the 96-week treatment period.

"This demonstration of long-term efficacy of ocrelizumab confirms the compelling benefit demonstrated in the first 24-week treatment period", said Hal Barron, M.D., Head of Global Development and Chief Medical Officer for Roche. "These results indicate a high likelihood of success of the ongoing Phase III program in patients with relapsing-remitting multiple sclerosis. Additionally, a study is underway to evaluate the potential benefit of ocrelizumab in patients with primary progressive multiple sclerosis."

The safety profile of ocrelizumab over the 96 weeks of the study was consistent with that demonstrated in the earlier 24-week data. No opportunistic infections were reported and the rate of infections (and serious infections) did not increase over the treatment period. Serious infection rates were similar for ocrelizumab 600mg (1.97 events/100 patient/years) and ocrelizumab 1000 mg (1.93 events/100 patient/years) and did not increase with time on ocrelizumab treatment.

### **About the study**

- A Phase II, randomised, multicenter, placebo-controlled study in 220 patients with RRMS.
- A randomised, open-label, rater-blinded, interferon beta-1a (30mcg IM weekly) group was enrolled as an active comparator arm.
- In the primary analyses, the efficacy and safety profile of the two dose regimens of ocrelizumab were evaluated over 24 weeks versus placebo.
- At day one and day 15, patients either received intravenous infusions of 300mg ocrelizumab, 1000mg ocrelizumab or placebo. An additional group received open-label interferon beta-1a (30 mcg IM weekly).
- As reported previously, the total number of gadolinium enhancing T1 lesions (based on MRI scans at weeks 12, 16, 20 and 24), was significantly decreased by 89% in the 2 x 300mg arm and 92% in the 2 x 1000mg arm, compared to both placebo and interferon beta 1-a ( $p < 0.0001$  for both doses).
- ARR was significantly reduced by 80% ( $p = 0.0005$ ) with ocrelizumab 2 x 300mg and by 73% ( $p = 0.0014$ ) with ocrelizumab 2 x1000 mg versus placebo at week 24.
- At 24 weeks in the double-blinded treatment groups (ocrelizumab 600mg, ocrelizumab 2000mg vs. placebo) SAEs (serious adverse events) included: systemic inflammatory response syndrome [SIRS] (0.0 percent, 1.8 percent vs. 0.0 percent), hypersensitivity (1.8 percent, 0.0 percent vs. 0.0 percent), oral herpes (0.0 percent, 0.0 percent vs. 1.9 percent), squamous cell carcinoma of the skin (pre-existing lesion) (0.0 percent, 1.8 percent vs. 0.0 percent) and anxiety (0.0 percent, 1.8 percent vs. 0.0 percent).
- At week 24 patients on placebo and interferon beta-1a were switched to ocrelizumab, given as 2 x300 mg infusions through week 48 and single 600mg infusions through week 96.
- Patients who began on 2 x 300mg and 2 x 1000mg ocrelizumab continued on 600mg or 1000mg, given as single infusions, until week 72, at which time patients were switched to single 600mg infusions through to week 96.
- All groups were treated in open-label fashion after week 24.
- Overall, at week 96, there were no gadolinium-enhancing T1 lesions observed by magnetic resonance imaging (MRI) scans of the brain in any patient in either of the ocrelizumab 600mg or 1000mg groups.

- No new and/or enlarging T2 lesions were observed from weeks 24 to 96 in any patient in the ocrelizumab 600mg group.
- The ARR for weeks 0–96 was 0.18 (95% CI: 0.11–0.31) for the ocrelizumab 600mg group and 0.22 (0.13–0.35) for the ocrelizumab 1000mg group.
- Overall, 67.3% patients in the ocrelizumab 600mg group and 76.4% of patients in the ocrelizumab 1000mg group had no relapses and no confirmed EDSS progression from week 0–96 ('clinical disease activity free'); 78.2% and 80.0% of patients, respectively, were relapse-free.
- There was no imbalance in the total number of serious adverse events observed across the treatment groups to week 96.
- As has been previously reported, one death occurred in a patient receiving 2 x 1000mg, at week 14, secondary to a complicated course of systemic inflammatory response syndrome
- Serious infection rates were similar for ocrelizumab 600mg (1.97 events/100 patient/years [95% CI: 0.49–7.98]) and ocrelizumab 1000mg (1.93 events/100 patient/years [95% CI: 0.48–7.71]) and did not increase with time on ocrelizumab treatment.
- No opportunistic infections were reported and the rate of infections (and serious infections) did not increase over the treatment period.

### **About the phase III clinical program**

The ocrelizumab Phase III clinical program (Orchestra), consists of two studies in patients with relapsing-remitting multiple sclerosis (Opera I and II) and one study in patients with primary progressive multiple sclerosis (Oratorio). The program has now begun enrolling patients into all of its trials. There is no approved therapy to treat PPMS, a much rarer form of the disease, affecting about 10% of those with MS.

### **About ocrelizumab**

Ocrelizumab is an investigational, humanised monoclonal antibody designed to selectively target CD20-positive B-cells, which are believed to play a critical role in multiple sclerosis (MS). It then interacts with the body's immune system to eliminate CD20-positive B-cells.

### **About multiple sclerosis**

Multiple sclerosis (MS) is a highly debilitating, autoimmune-mediated disease of the central nervous system (CNS) and is one of the leading causes of neurological disability in young adults<sup>3,4</sup>. The immune system incorrectly attacks healthy nerve tissue in the CNS which affects the transfer of messages from the CNS to the rest of the body<sup>5</sup>. Symptoms are unpredictable and vary between patients, but include tingling, numbness,

pain, slurred speech and blurred or double vision. Some patients may experience muscle weakness, poor balance or coordination and tremors as well as altered sensation, memory and concentration problems. Over time (without treatment) most patients develop permanent disability, including partial or complete paralysis and difficulties with vision, speech and memory. According to estimates of the World Health Organisation, approximately 1.3 million people worldwide have been diagnosed with multiple sclerosis<sup>6</sup>. Most people experience their first symptoms between the ages of 20 and 40 years<sup>7</sup>. Relapsing-remitting multiple sclerosis (RRMS) is the most common clinical form of MS and accounts for around 85% of all cases<sup>2</sup> at onset. RRMS is characterised by infrequent, acute exacerbations with full or partial recovery between attacks.

### **About Roche**

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company with truly differentiated medicines in oncology, virology, inflammation, metabolism and CNS. Roche is also the world leader in in-vitro diagnostics, tissue-based cancer diagnostics and a pioneer in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostic tools that enable tangible improvements in the health, quality of life and survival of patients. In 2010, Roche had over 80'000 employees worldwide and invested over 9 billion Swiss francs in R&D. The Group posted sales of 47.5 billion Swiss francs. Genentech, United States, is a wholly owned member of the Roche Group. Roche has a majority stake in Chugai Pharmaceutical, Japan. For more information: [www.roche.com](http://www.roche.com).

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