# Media & Investor Release

## Roche to present new key clinical and real-world data at ECTRIMS-ACTRIMS 2023 showcasing strength of long-term outcomes in MS and NMOSD

- **Late-breaking results from Phase III trial of OCREVUS (ocrelizumab) subcutaneous injection and Phase II trial of BTK inhibitor fenebrutinib in multiple sclerosis (MS) will be presented**
- **10-year OCREVUS efficacy and safety data show significant benefit in slowing long-term disability progression and consistent long-term safety profile in MS**
- **Additional OCREVUS real-world and clinical data show impact for underrepresented populations including more than 3,200 pregnant women and Black and Hispanic/Latinx patients with MS**
- **Longer-term safety data and late-breaking efficacy data from Phase III trial of ENSPRYNG (satralizumab) in neuromyelitis optica spectrum disorder (NMOSD) will be presented**

Basel, 02 October 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will present new data for OCREVUS® (ocrelizumab) and investigational Bruton's tyrosine kinase (BTK) inhibitor fenebrutinib for multiple sclerosis (MS), and ENSPRYNG® (satralizumab) for neuromyelitis optica spectrum disorder (NMOSD). In total, Roche will be presenting 36 abstracts at the 9th Joint ECTRIMS-ACTRIMS Meeting (European and Americas Committees for Treatment and Research in Multiple Sclerosis) from 11-13 October 2023. Late-breaking data in MS includes the Phase Ib OCARINA I and Phase III OCARINA II studies evaluating an investigational subcutaneous OCREVUS injection. In addition, the Phase II FENopta study of fenebrutinib for people living with MS and late-breaking ENSPRYNG data for people with NMOSD, which includes longer-term data from the Phase III SAkuraMoon study, will also be presented.

"It is gratifying to see that OCREVUS and ENSPRYNG continue to show a favourable benefit/risk profile over many years in MS and NMOSD, and we are also pleased to share late-breaking results from our investigational MS medicine fenebrutinib and OCREVUS subcutaneous injection," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We've developed these latest innovations with the goal of further improving the day-to-day lives of those living with MS."

## Multiple sclerosis (MS)

Roche will present 29 abstracts in MS, including three late-breaking presentations from the Phase Ib OCARINA I and Phase III OCARINA II studies on the OCREVUS subcutaneous injection in people with MS and the Phase II FENopta study of BTK inhibitor fenebrutinib in people with MS.

Highlights also include 10-year milestone data from the open-label extensions of Phase III OPERA I and II studies in relapsing MS (RMS) and ORATORIO study in primary progressive MS (PPMS) that show benefit on slowing long-term disability progression. OCREVUS is the only medicine approved for both RMS and PPMS, and by slowing disability progression it has fundamentally changed the landscape of MS treatment, with more than 300,000 patients treated globally. Safety outcomes from more than 6,000 patients across 12 OCREVUS clinical trials further support the medicine's consistent favourable safety profile over 10 years.

Roche safety data will report pregnancy and infant outcomes from more than 3,200 pregnancies, and separate real-world data on pregnant women in the international MSBase registry will provide insights on the impact of OCREVUS and other disease-modifying therapies on relapses during and post-pregnancy. Further, one-year data from the first-ever clinical trial in Black and Hispanic/Latinx people with MS (Phase IV CHIMES trial) will show OCREVUS effectively controlled disease activity.

## Neuromyelitis optica spectrum disorder (NMOSD)

Roche will present seven NMOSD abstracts, including late-breaking, longer-term data from the Phase III SAkuraMoon open-label extension study and real-world data evaluating ENSPRYNG in people with NMOSD.

Infection is a major comorbidity in people with NMOSD, and analyses comparing infection rates across clinical trials, post-marketing settings and U.S. claims data suggest overall lower rates in the ENSPRYNG-treated population.

Follow Roche on X via @Roche and keep up to date with ECTRIMS-ACTRIMS 2023 news and updates by using the hashtag #MSMilan2023. Below are the details of all Roche presentations.

| Medicine | Abstract title | Presentation number (type)<br><br>Presentation date (session)<br><br>Time |
|---|---|---|
| Regular abstracts available from 01 October at 8:00 CEST.<br>*Late-breaking abstracts available from 11 October 2023 at 8:00 CEST. | | |
| OCREVUS for MS | Subcutaneous ocrelizumab in patients with multiple sclerosis: results of the Phase III OCARINA II study | P370 (poster)<br><br>11 October (Late Breaking Abstracts*, Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Subcutaneous ocrelizumab in patients with multiple sclerosis: results of the Phase Ib dose-finding OCARINA I study | P371 (poster)<br><br>11 October (Late Breaking Abstracts*, Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | The patient impact of 10 years of ocrelizumab treatment in multiple sclerosis: long-term data from the Phase III OPERA and ORATORIO studies | P302 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Safety of ocrelizumab in multiple sclerosis: updated analysis in patients with relapsing and primary progressive multiple sclerosis | P304 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Disease activity during pre-conception, pregnancy and postpartum in women with MS receiving ocrelizumab or other disease-modifying therapies in a real-world cohort | O173 (oral)<br><br>13 October (Scientific Session 20: Female health)<br><br>12:35 - 12:42 CEST |

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| | One-year analysis of efficacy and safety in Black and Hispanic patients with relapsing multiple sclerosis receiving ocrelizumab treatment in the CHIMES trial | P691 (poster)<br><br>12 October (Poster Presentation Session 2)<br><br>17:00 - 19:00 CEST |
| | Ocrelizumab dose selection for treatment of paediatric relapsing-remitting multiple sclerosis: preliminary pharmacokinetic, safety and efficacy results from the OPERETTA 1 study | P034 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Pregnancy and infant outcomes in women receiving ocrelizumab for the treatment of multiple sclerosis: analysis of the largest available outcome database | P061 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Cerebrospinal fluid neurofilament heavy levels correlate with spinal cord lesions and disability in multiple sclerosis | P241 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Combining measures from clinical assessments, imaging and fluid biomarkers at one year to predict MS progression at two years | P258 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Composite confirmed disability worsening is a useful clinical trial endpoint for multiple sclerosis focusing on disability progression | P283 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Reduction of intrathecal immunoglobulin levels with ocrelizumab treatment in relapsing and primary progressive multiple sclerosis | P653 (poster)<br><br>12 October (Poster Presentation Session 2)<br><br>17:00 - 19:00 CEST |

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| | Low disability accumulation after 4-year ocrelizumab therapy in treatment-naive patients with early-stage relapsing-remitting multiple sclerosis; data from the Phase IIIb ENSEMBLE study | P688 (poster)<br><br>12 October (Poster Presentation Session 2)<br><br>17:00 - 19:00 CEST |
| | Persistence to ocrelizumab compared with other disease-modifying therapies for multiple sclerosis in the German NeuroTransData registry | P732 (poster)<br><br>12 October (Poster Presentation Session 2)<br><br>17:00 - 19:00 CEST |
| | Utility and implementation of a federated research infrastructure to assess lack disease stability as a real-world surrogate of PIRA, by combining MS clinical trial and real-world cohort data (the INTONATE MS consortium) | P1181 (e-poster) |
| | Immunological signatures associated with ocrelizumab treatment in early relapsing-remitting multiple sclerosis (RRMS): new data on T cell function and pro/anti-inflammatory monocytes of the 12-month interim analysis from the MA30143 Phase IIIb (ENSEMBLE) substudy | P1460 (e-poster) |
| | Real-world safety data from up to 4.5 years of ocrelizumab in relapsing and primary progressive multiple sclerosis - a CONFIDENCE interim analysis | P333 (e-poster) |
| | Real-world effectiveness of ocrelizumab in patients with primary progressive multiple sclerosis grouped by EDSS at baseline – a CONFIDENCE study interim analysis | P336 (e-poster) |
| | Specific unmet medical needs in the care of patients with relapsing multiple sclerosis: final results from the PROFILE RMS study | P738 (eposter) |

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| | Disease-related knowledge and patient perceptions in relapsing-remitting multiple sclerosis | P1189 (e-poster) |
| | MS patients treated with ocrelizumab using BRISA - an MS specific app in Germany | P1594 (e-poster) |
| | Ocrelizumab safety under real-world conditions: Contrasting investigator-reported safety with patient-reported safety in people with multiple sclerosis (CONFIDENCE, COMPASS and TrotzMS) | P334 (e-poster) |
| | Development of a self-assessment tool for the autonomy of patients with multiple sclerosis (ms) | P1190 (e-poster) |
| | Implications of progression independent of relapse activity (PIRA) for multiple sclerosis clinical trials: item banks could provide the precise patient-reported outcome measures needed | P478 (e-poster) |
| | Unsupervised analysis reveals that memory IgA B cells are spared by ocrelizumab treatment | P762 (e-poster)<br><br>11 October (Late Breaking Abstracts*, Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Drug combination discovery for treatment of Multiple Sclerosis using machine learning | P790 (poster)<br><br>11 October (Late Breaking Abstracts*, Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| Fenebrutinib for MS | Cerebrospinal fluid and MRI analyses of fenebrutinib treatment in multiple sclerosis reveal brain penetration and early reduction of new lesion activity: results from the Phase II FENopta study | O187 (oral)<br><br>13 October (Scientific Session 22: Late Breaking Abstracts*)<br><br>16:03 - 16:10 CEST |
| | Fenebrutinib, a noncovalent, reversible, Bruton's tyrosine kinase inhibitor, potently blocks neuroinflammation induced by Fcy receptor | P686 (poster)<br><br>12 October (Poster Presentation Session 2) |

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| | activation in human microglial systems: implications for multiple sclerosis treatment | 17:00 - 19:00 CEST |
| Floodlight™ in MS | Smartphone-based passive monitoring of gait in people with progressive multiple sclerosis | P100 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| ENSPRYNG for NMOSD | Long-term efficacy of satralizumab in patients with AQP4-IgG+ NMOSD: updated analysis from the open-label SAkuraMoon study | P362 (poster)<br><br>11 October (Late Breaking Abstracts*, Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Infection in NMOSD: an analysis of the patterns of infection in SAkuraMoon (an open-label study to evaluate the long-term safety and efficacy of satralizumab) with post-marketing data and US-based health claims data | P301 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Clarification of blood-retinal barrier on AQP4-peptide immunized mice | P115 (poster)<br><br>11 October (Poster Presentation Session 1)<br><br>16:30 - 18:30 CEST |
| | Addressing the burdens of neuromyelitis optica spectrum disorder amid challenges of the COVID-19 pandemic: real-world perspectives from patients | P1014 (e-poster) |
| | Satralizumab treatment in adults with AQP4-IgG-seropositive neuromyelitis optica spectrum disorder: a retrospective case series | P1036 (e-poster) |
| | Relapse under the prescription of satralizumab in neuromyelitis optica spectrum disorder: analysis of a Japanese claims database | P1557 (e-poster) |
| | Use of immunosuppressive therapy among patients with NMOSD using satralizumab treatment: a study based on Japanese real-world data | P1574 (e-poster) |

## About multiple sclerosis

Multiple sclerosis (MS) is a chronic disease that affects more than 2.8 million people worldwide. MS occurs when the immune system abnormally attacks the insulation and support around nerve cells (myelin sheath) in the central nervous system (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.

People with all forms of MS experience disease progression – permanent loss of nerve cells in the central nervous system – from the beginning of their disease even if their clinical symptoms aren't apparent or don't appear to be getting worse. Delays in diagnosis and treatment can negatively impact people with MS, in terms of their physical and mental health, and contribute to the negative financial impact on the individual and society. An important goal of treating MS is to slow, stop and ideally prevent disease activity and progression as early as possible.

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% 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% of people with MS are diagnosed with the primary progressive form of the disease. Until the FDA approval of OCREVUS, there had been no FDA-approved treatments for PPMS.

## About OCREVUS (ocrelizumab)

OCREVUS is the first and only therapy approved for both RMS (including RRMS and active, or relapsing SPMS, in addition to clinically isolated syndrome [CIS] in the U.S.) and PPMS. 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 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 fenebrutinib

Fenebrutinib is an investigational oral, reversible and non-covalent Bruton's tyrosine kinase (BTK) inhibitor that blocks the function of BTK. BTK, also known as tyrosine-protein kinase BTK, is an enzyme that regulates B-cell development and activation and is also involved in the activation of innate immune system myeloid lineage cells, such as macrophages and microglia. Pre-clinical data have shown fenebrutinib to be potent and highly selective, and it is the only reversible inhibitor currently in Phase III trials for MS. Fenebrutinib has been shown to be 130 times more selective for BTK vs. other kinases. These design features may be important as the high selectivity and reversibility can potentially reduce off-target effects of a molecule.

Fenebrutinib is a dual inhibitor of both B-cell and microglia activation. This dual inhibition may be able to reduce both MS disease activity and progression, thereby potentially addressing the key unmet medical need in people living with MS. The Phase III programme includes two identical trials in RMS (FENhance 1 & 2) with an active teriflunomide comparator and one trial in primary progressive MS (PPMS) (FENtrepid) in which fenebrutinib is being evaluated against OCREVUS® (ocrelizumab). To date, more than 2,500 patients and healthy volunteers have been treated with fenebrutinib in Phase I, II and III clinical programmes across multiple diseases, including MS and other autoimmune disorders.

## About ENSPRYNG (satralizumab)

ENSPRYNG, which was designed by Chugai, a member of the Roche Group, is a humanised monoclonal antibody that targets interleukin-6 (IL-6) receptor activity. ENSPRYNG was designed using novel recycling antibody technology which, compared to conventional technology, allows for longer duration of the antibody and subcutaneous dosing every four weeks.

Positive Phase III results for ENSPRYNG, as both monotherapy and in combination with baseline immunosuppressive therapy, demonstrate that IL-6 inhibition is an effective therapeutic approach for neuromyelitis optica spectrum disorder (NMOSD). ENSPRYNG is currently approved for NMOSD in 85 countries with further applications under review with numerous regulators. Roche continues to investigate ENSPRYNG in other autoantibody-mediated rare neurological diseases characterised by elevated IL-6 levels, indications including generalised Myasthenia Gravis (gMG), Myelin Oligodendrocyte Glycoprotein Antibody-associated Disease (MOGAD) and Autoimmune Encephalitis (AIE).

ENSPRYNG was granted Breakthrough Therapy Designation for the treatment of NMOSD by the FDA in December 2018 and designated as an orphan drug for NMOSD in the United States, Europe, Russia and Japan.

In addition,the FDA has designated satralizumab as an investigational orphan drug for gMG, MOGAD and AIE (NMDAR).

## About Roche in Neuroscience

Neuroscience is a major focus of research and development at Roche. Our goal is to pursue ground-breaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases. Roche and Genentech are investigating more than a dozen medicines for neurological disorders, including MS, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease, acute ischemic stroke, Duchenne muscular dystrophy and Angelman syndrome. Together with our partners, we are committed to pushing the boundaries of scientific understanding to solve some of the most difficult challenges in neuroscience today.

## About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognising our endeavour to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

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