Media Release

Roche to present pivotal data for satralizumab in neuromyelitis optica spectrum disorder and six-year OCREVUS data in multiple sclerosis at ECTRIMS

- **Investigational medicine satralizumab significantly reduces the risk of relapse in pivotal SAkuraStar monotherapy study for neuromyelitis optica spectrum disorder**
- **New data provide insights into neurofilament light chain levels as a potential biomarker for predicting MS disability progression; new longer-term OCREVUS® (ocrelizumab) data of more than six years show reduction of disability progression in relapsing and primary progressive MS**
- **Breadth of data reinforce Roche's commitment to following the science to gain a better understanding of complex nervous system disorders**

Basel, 4 September 2019 – Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that new data across its neuroscience portfolio 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. Presentations include complete Phase III results from the SAkuraStar study investigating satralizumab for the treatment of neuromyelitis optica spectrum disorder (NMOSD), and new multiple sclerosis (MS) research, which provides insights into disease progression, including data from OCREVUS® (ocrelizumab) trials that advance understanding of neurofilament light chain (NfL) levels as a potential biomarker for predicting disability outcomes. Additionally, longer-term data of more than six years to be presented continue to show consistent safety and efficacy outcomes for patients treated with OCREVUS earlier.

“Disorders of the nervous system are some of the most complex and difficult to treat, and we have increased our commitment in neuroscience to advance care and scientific understanding for conditions such as multiple sclerosis and neuromyelitis optica spectrum disorder. Data being presented at ECTRIMS include positive Phase III results for satralizumab as a monotherapy, taking a novel approach to treating neuromyelitis optica spectrum disorder, and new insights using biomarkers to identify disease progression in multiple sclerosis,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Similar to our approach with OCREVUS in multiple sclerosis, targeting B-cells as a key driver of disease, we aim to offer satralizumab as a highly effective treatment option in neuromyelitis optica spectrum disorder, targeting the interleukin-6 receptor.”

Neuromyelitis Optica Spectrum Disorder (NMOSD)
Complete pivotal data from the SAkuraStar study investigating satralizumab as a subcutaneous monotherapy compared to placebo for the treatment of NMOSD will be presented. The primary and subgroup analyses show that satralizumab significantly reduces the risk of relapse in patients who were seropositive for aquaporin-4 auto-antibodies (AQP4-IgG), as well as the overall ITT population representative of NMOSD patients. Satralizumab also demonstrates a similar safety profile compared to placebo.

NMOSD is a rare, lifelong and debilitating autoimmune disease of the central nervous system commonly misdiagnosed as MS. It is associated with pathogenic auto-antibodies (AQP4-IgG) that target and damage a

specific cell type, called astrocytes, resulting in inflammatory lesions of the optic nerve(s), spinal cord and brain. Through the use of a diagnostic biomarker test, the majority of people with NMOSD are identified as AQP4-IgG seropositive and tend to experience a more severe disease course; however, as many as one-third of those with NMOSD are AQP4-IgG seronegative. At ECTRIMS, two analyses of U.S. healthcare insurance claims databases will be presented that reflect the low utilisation of AQP4-IgG diagnostic testing and the subsequent frequency of misdiagnosis of NMOSD patients.

Additionally, two pre-clinical in-vitro models will be presented that show satralizumab reduces the degradation of the blood brain barrier, supporting evidence of its multi-faceted mechanism of action.

Multiple Sclerosis (MS)
New analyses will be presented that advance understanding of NfL as a potential biomarker for predicting future MS disability outcomes, including data from the Phase III studies showing blood NfL levels in primary progressive MS (PPMS) and relapsing MS (RMS) patients were significantly lowered following OCREVUS treatment. NfL is a protein that provides structural support to nerve fibres in the brain, and an increase in the amount of NfL in blood serum or cerebrospinal fluid may serve as a marker for axonal (nerve) damage. Studying NfL may provide more information on how to quickly measure MS disease activity and progression. This is important because a key goal of treatment is to reduce disease activity to delay disability progression as soon as possible.

Longer-term data of more than six years from the Phase III open-label extension studies of OPERA I, OPERA II and ORATORIO showed that patients who were treated earlier with OCREVUS had lower rates of disability progression compared with RMS patients who switched from interferon beta-1α or PPMS patients who switched from placebo after the double-blind phase. Additionally, updated safety data being presented remain consistent with findings from the Phase III studies, supporting OCREVUS' favourable benefit-risk profile.

Over 120,000 people have been treated with OCREVUS globally, both in clinical trial and real-world settings, and OCREVUS is now approved in 89 countries.

Follow Roche on Twitter via @Roche and keep up to date with ECTRIMS 2019 news and updates by using the hashtag #ECTRIMS2019.

Roche presentations at ECTRIMS 2019
A full list of Roche presentations can be found at: https://www.ectrims-congress.eu/2019/scientific-programme/scientific-programme.html.

Presentations at ECTRIMS 2019 include:

Medicine	**Abstract Title**	**Presentation Number (type)** **Presentation Date** **Time**
Satralizumab for Neuromyelitis Optica Spectrum Disorder	Efficacy and Safety of Satralizumab Monotherapy for Relapse Prevention in Neuromyelitis Optica Spectrum Disorder (NMOSD): Results from SAkuraStar, a Double-Blind Placebo-Controlled Phase 3 Clinical Study	#P603 (poster presentation) Wednesday, September 11 5:15 – 7:15 PM CEST
	Identifying Patients with Neuromyelitis Optica Spectrum Disorder in US Insurance Claims Databases	#P408 (poster presentation) Wednesday, September 11 5:15 – 7:15 PM CEST
	Efficacy of Satralizumab as Monotherapy in Pre-Specified Subgroups of SAkuraStar, a Double-Blind Placebo-Controlled Phase 3 Clinical Study in Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)	#141 (oral presentation) Thursday, September 12 8:54 – 9:06 AM CEST
	Temporal Trends in the Diagnosis of Neuromyelitis Optica Spectrum Disorder in US Claims Databases From 2001-2017	#P1130 (poster presentation) Friday, September 13 12:15 – 2:15 PM CEST
	Efficacy and safety of Satralizumab for Relapse Prevention in Neuromyelitis Optica Spectrum Disorder: a Pooled Analysis from Two phase III clinical trials	#614 (poster presentation) Friday September 13 12:45 – 14:15 CEST
	The effect of Neuromyelitis Optica (NMO)-IgG and Anti-IL-6 Receptor Monoclonal Antibody (SA237; satralizumab) for Barrier Function at the Blood-Brain Barrier in Vitro	#P473 (poster presentation) Wednesday, September 11 17:15-19:15 PM CEST
	Anti-IL-6 Receptor Antibody Prevents Blood-Brain Barrier Disruption in Mice with Experimental Autoimmune	#EP1497 (ePoster) ePosters will be displayed on terminals during the congress, not presented

	Encephalomyelitis (EAE)	during specific sessions.
OCREVUS (ocrelizumab) for Multiple Sclerosis	Serum Immunoglobulin Levels and Risk of Serious Infections in the Pivotal Phase III Trials of Ocrelizumab in Multiple Sclerosis and their Open-Label Extensions	#65 (oral presentation) Wednesday, September 11 2:49 – 3:01 PM CEST
	Effect of Ocrelizumab Versus Interferon β-1a on Retinal Thinning and Association with Brain Volume Loss in the OPERA I and OPERA II Phase III Trials in Relapsing Multiple Sclerosis	#92 (oral presentation) Wednesday, September 11 4:37 – 4:49 PM CEST
	Efficacy and Safety of Ocrelizumab in Patients with Relapsing- Remitting Multiple Sclerosis with a Suboptimal Response to Previous Disease-Modifying Therapies (1- Year Interim Results)	#P690 (poster presentation) Wednesday, September 11 5:15 – 7:15 PM CEST
	Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Primary Progressive Multiple Sclerosis	#P648 (poster presentation) Wednesday, September 11 5:15 – 7:15 PM CEST
	Blood Neurofilament Light Levels are Lowered to a Healthy Donor Range in Patients with RMS and PPMS Following Ocrelizumab Treatment	#152 (oral presentation) Thursday, September 12 9:06 – 9:18 AM CEST
	Sustained Reduction in Confirmed Disability Progression in Patients with Primary Progressive Multiple Sclerosis Treated with Ocrelizumab in the Open-Label Extension Period of the Phase III ORATORIO Trial: 6.5-Study Year Follow-Up Data	#159 (oral presentation) Thursday, September 12 11:16 – 11:28 AM CEST
	Pregnancy Outcomes in Patients Treated with Ocrelizumab	#P780 (poster presentation) Thursday, September 12 5:15 – 7:15 PM CEST
	Real-World Experience with Ocrelizumab in the MS Base Registry	#P1017 (poster presentation) Thursday, September 12 5:15 – 7:15 PM CEST
	Pretreatment Cerebrospinal Fluid (CSF) and Serum Neurofilament Light (NfL) Levels in Patients with PPMS in	#P948 (poster presentation) Thursday, September 12 5:15 – 7:15 PM CEST

	the OBOE Study are Correlated and are Higher in Patients with PPMS with T1 Gd+ Brain Lesions	
	Long-Term Reduction of Relapse Rate and Confirmed Disability Progression After 6 Years of Ocrelizumab Treatment in Patients with Relapsing Multiple Sclerosis	#P1015 (poster presentation) Thursday, September 12 5:15 – 7:15 PM CEST
	Cases Reported as Progressive Multifocal Leukoencephalopathy in Ocrelizumab-Treated Patients with Multiple Sclerosis	#P970 (poster presentation) Thursday, September 12 5:15 – 7:15 PM CEST
	FlywheelMS: A Novel, Patient-Centred Study to Better Understand Multiple Sclerosis Using Electronic Health Records and Other Real-World Data Sources	#P758 (poster presentation) Thursday, September 12 5:15 – 7:15 PM CEST
	Baseline Cognitive Functioning Using the Brief International Cognitive Assessment for MS Tests in Patients with Relapsing- Remitting Multiple Sclerosis Enrolled in Phase IIIb Studies of Ocrelizumab (ENSEMBLE and CASTING)	#P1170 (poster presentation) Friday, September 13 12:15 – 2:15 PM CEST
	Evaluation of Shorter Infusion Times for Ocrelizumab Treatment in an Extension Substudy of the Phase IIIb CHORDS Trial	#P1408 (poster presentation) Friday, September 13 12:15 – 2:15 PM CEST
	Safety Results for Administering Ocrelizumab per a Shorter Infusion Protocol in Patients with Primary Progressive and Relapsing Multiple Sclerosis	#P1406 (poster presentation) Friday, September 13 12:15 – 2:15 PM CEST
	Ocrelizumab treatment satisfaction in patients with Suboptimal Response to Previous Disease-Modifying Therapies	#EP1479 (ePoster) ePosters will be displayed on terminals during the congress, not presented during specific sessions.

About satralizumab
Satralizumab is an investigational humanised monoclonal antibody that represents a novel approach to treating NMOSD. The cytokine IL-6 is thought to be a key driver of NMOSD, triggering the inflammation cascade and leading to damage and disability. Positive Phase III results for satralizumab, as both monotherapy and add-on to baseline immunosuppressant therapy, suggest that IL-6 inhibition may be an effective therapeutic approach for NMOSD.

The Phase III clinical development programme for satralizumab includes two studies: SAkuraSky, which studied satralizumab in combination with baseline immunosuppressant therapy, and SAkuraStar, which studied the efficacy and safety of satralizumab as a monotherapy.

Satralizumab has been designated as an orphan drug in the U.S. and Europe. In addition, it was granted Breakthrough Therapy Designation for the treatment of NMO and NMOSD by the U.S. Food and Drug Administration in December 2018.

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 dosing every six months. OCREVUS is a humanized 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.

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