New Roche data at the 2019 AAN Annual Meeting showcase breadth and promise of neuroscience portfolio

- **Risdiplam data from Part 1 of pivotal FIREFISH study show infants with Type 1 spinal muscular atrophy achieve key motor milestones and improved survival after one year of treatment**
- **New analyses in relapsing and primary progressive multiple sclerosis suggest that higher OCREVUS (ocrelizumab) exposure and lower B-cell levels are important for control of disability progression**
- **Satralizumab significantly reduces the risk of relapse in neuromyelitis optica spectrum disorder in pivotal SAkuraSky study**
- **New data in Huntington's disease support dose selection for Phase III trial and provide insight on mutant huntingtin protein (mHTT) reduction**

Basel, 29 April 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new data for its approved and investigational medicines for the treatment of neurological conditions will be presented at the 71st American Academy of Neurology (AAN) Annual Meeting from 4-10 May in Philadelphia, PA. Presentations include data from a pivotal study for risdiplam in spinal muscular atrophy (SMA), which has the potential to become the first oral treatment for this community. New research for OCREVUS® (ocrelizumab) in relapsing and primary progressive multiple sclerosis shows that its effect on reducing the risk of disability progression is associated with higher exposure and lower B-cell levels. Additional OCREVUS data demonstrate the importance of earlier treatment. New data for investigational medicines in neuromyelitis optica spectrum disorder (NMOSD), Huntington's disease (HD), Alzheimer's disease and Duchenne muscular dystrophy will also be shared.

"The great need for therapeutic options in areas of neuroscience such as SMA, HD and NMOSD means that every development is a collective step forward," said Sandra Horning, M.D., chief medical officer and head of Global Product Development. "We continue to invest in research and partnerships to develop new treatment options for these diseases that severely reduce quality of life. We are pleased to contribute to the greater understanding and clinical progress of neurologic diseases at this year's AAN Annual Meeting to help make a difference in the lives of people and families impacted by these conditions."

Spinal Muscular Atrophy (SMA)
New data will be presented for risdiplam, an investigational oral survival motor neuron 2 (SMN2) splicing modifier for SMA, which is designed to increase and sustain SMN protein levels in the central nervous system (CNS) and throughout the body. Platform presentations include one-year data from the dose-finding Part 1 of the pivotal FIREFISH study on key motor milestones, motor function and survival in infants with Type 1 SMA. Updated safety, tolerability and pharmacokinetics / pharmacodynamics (PK/PD) data, as well as an exploratory efficacy analysis from Part 1 of the pivotal SUNFISH study in people aged 2-25 years with SMA Types 2 or 3 will also be presented.

F. Hoffmann-La Roche Ltd 4070 Basel Switzerland
Investor Relations email: investor.relations@roche.com
Tel. +41 61 68-88880 Fax +41 61 69-10014 www.roche.com

Multiple Sclerosis (MS)
New analyses in relapsing and primary progressive multiple sclerosis suggest that higher OCREVUS exposure and lower B-cell levels are important for control of disability progression. Additionally, new long-term data from the Phase III OPERA and ORATORIO open-label extension trials showed earlier treatment with OCREVUS significantly reduced the risk of permanent disability progression. Updated safety data being presented remain consistent with findings from the controlled Phase III trials, supporting OCREVUS' favourable benefit-risk profile.

Neuromyelitis Optica Spectrum Disorder (NMOSD)
A subgroup analysis based on AQP4-Ig serostatus from the pivotal phase III SAkuraSky trial investigating satralizumab compared to placebo as add-on to baseline immunosuppressants and/or corticosteroids for the treatment of NMOSD will be presented. The subgroup data shows that satralizumab significantly reduced the risk of NMOSD relapse in a clinically-relevant population, especially in AQP4-Ig positive patients, with a favourable benefit-risk profile. The Phase III trial SAkuraStar, investigating satralizumab compared to placebo as a monotherapy, met its primary endpoint and will be presented at a future congress.

Satralizumab is a humanized IgG2 anti-human interleukin-6 (IL-6) receptor neutralizing monoclonal antibody that represents a novel approach to treating NMOSD by selectively inhibiting the inflammatory effects of IL-6, thought to be a key driver in the pathogenesis of the disease. There are currently no approved treatments for NMOSD, a rare, lifelong and debilitating autoimmune disease of the central nervous system that damages the optic nerve and spinal cord, causing blindness, muscle weakness and paralysis.

Huntington's Disease (HD)
The HD platform session will include results from a translational modelling approach developed from preclinical data and includes clinical RG6042 data from the ongoing, open label extension study in HD patients, including a safety update and mutant huntingtin (mHTT) protein reduction in the cerebrospinal fluid. These data also support the dose selection for the recently initiated Phase III GENERATION HD1 clinical trial investigating RG6042 in manifest Huntington's disease.

RG6042 (formerly known as Ionis HTT-Rx) is an antisense oligonucleotide (ASO) designed to reduce the production of the toxic mHTT protein, the disease-causing protein in people with Huntington's disease, by targeting human huntingtin RNA.

Alzheimer's disease (AD)
Data and safety findings from the gantenerumab SCarlet RoAD and Marguerite RoAD open-label extension studies will be presented that show consistently large amyloid reductions in AD patients with and without ARIA-E. Roche continues to advance the development of gantenerumab in the Phase III GRADUATE trials and the anti-tau molecule RO7105705 (MTAU9937A, RG6100) into its second Phase II clinical trial (LAURIET), which is currently enrolling patients with moderate Alzheimer's disease.

The study design, methodology and baseline characteristics from the crenezumab Phase III CREAD study will be presented in a poster at AAN. Data from the crenezumab interim analysis of the now discontinued CREAD program were presented at the 14th International Conference on Alzheimer's & Parkinson's

Diseases in March 2019. Additional analyses, including biomarker data, will be presented at future medical conferences. Crenezumab continues to be studied in a landmark Alzheimer's Prevention Initiative trial of cognitively healthy individuals in Colombia with an autosomal dominant mutation who are at risk to develop familial AD (fAD).

Duchenne Muscular Dystrophy (DMD)
Results will be shared from a Phase Ib/II study of the anti-myostatin adnectin RG6206 in ambulatory boys with DMD showing no drug-related safety findings leading to withdrawal from the study through 72 weeks of treatment. RG6042 successfully lowered myostatin levels in the blood of boys with DMD and MRI and DXA imaging suggested that RG6206 had a positive effect on muscle in boys with DMD.

The full range of data from Roche's late-stage clinical development program in neuroscience being presented at AAN include:

Medicine	**Abstract Title**	**Presentation Number (type), Presentation Date, Time**
Risdiplam for spinal muscular atrophy	FIREFISH Part 1: 1-year results on motor function in babies with Type 1 SMA receiving risdiplam (RG7916)	S25.003 (platform), Tuesday, 7 May, 1:22 – 1:33 p.m. EDT
	Update from SUNFISH Part 1: Safety, tolerability and PK/PD from the dose-finding study, including exploratory efficacy data in patients with Type 2 or 3 spinal muscular atrophy (SMA) treated with risdiplam (RG7916)	S25.007 (platform), Tuesday, 7 May, 2:06 – 2:17 p.m. EDT
	FIREFISH Part 1: Survival, ventilation and swallowing ability in infants with Type 1 SMA receiving risdiplam (RG7916)	S25.008 (platform), Tuesday, 7 May, 2:17 – 2:28 p.m. EDT
OCREVUS (ocrelizumab) for multiple sclerosis	Reduction in 48-Week Confirmed Disability Progression After 5.5 Years of Ocrelizumab Treatment in Patients with Primary Progressive Multiple Sclerosis	P3.2-031 (poster), Tuesday, 7 May, 5:30 – 6:30 p.m. EDT
	Long-Term Reduction in 48-Week Confirmed Disability Progression After 5 Years of Ocrelizumab Treatment in Patients with Relapsing Multiple Sclerosis	P3.2-054 (poster), Tuesday, 7 May, 5:30 – 6:30 p.m. EDT
	Evaluation of Shorter Infusion Times with Ocrelizumab in Patients with Relapsing-Remitting Multiple Sclerosis	P3.2-034 (poster), Tuesday, 7 May, 5:30 – 6:30 p.m. EDT

	Ocrelizumab Treatment Effect on Upper Limb Function in PPMS Patients with Disability: Subgroup Results of the ORATORIO Study to Inform the ORATORIO-HAND Study Design	P3.2-091 (poster), Tuesday, 7 May, 5:30 – 6:30 p.m. EDT
	Reduced Rate of Brain Atrophy in Patients with PPMS Receiving Ocrelizumab Earlier and Continuously Versus Those Initiating Ocrelizumab Later: Results of ORATORIO 5-Year Follow-Up	P3.2-042 (poster), Tuesday, 7 May, 5:30 – 6:30 p.m. EDT
	FLOODLIGHT: Smartphone-Based Self-Monitoring Is Accepted by Patients and Provides Meaningful, Continuous Digital Outcomes Augmenting Conventional In-Clinic Multiple Sclerosis Measures	P3.2-024 (poster), Tuesday, 7 May, 5:30 – 6:30 p.m. EDT
	Pharmacokinetics, Pharmacodynamics and Exposure-Response Analyses of Ocrelizumab in Patients with Multiple Sclerosis	N4.001 (platform), Wednesday, May 8, 2:00 – 2:15 p.m. EDT
	VERISMO: A Post-Marketing Safety Study to Determine the Incidence of All Malignancies and Breast Cancer in Patients with Multiple Sclerosis Treated with Ocrelizumab	P4.2-043 (poster), Wednesday, 8 May, 5:30 – 6:30 p.m. EDT
	Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Primary Progressive Multiple Sclerosis	P4.2-025 (poster), Wednesday, 8 May, 5:30 – 6:30 p.m. EDT
	One-Year Interim Analysis Results of the Phase IIIb CHORDS Study Evaluating Ocrelizumab Effectiveness and Safety in Patients with Relapsing-Remitting Multiple Sclerosis Who Had Suboptimal Response with Prior Disease-Modifying Treatments	S56.007 (platform), Friday, 10 May, 2:06 – 2:17 p.m. EDT
	Ocrelizumab Treatment Reduced Levels of Neurofilament Light Chain and Numbers of B cells in the Cerebrospinal Fluid of Patients with Relapsing Multiple Sclerosis in the OBOE Study	S56.008 (platform), Friday, 10 May, 2:17 – 2:28 p.m. EDT
Satralizumab for Neuromyelitis Optica Spectrum Disorder	Efficacy of Satralizumab (SA237) in Subgroups of Patients in SAkuraSky: A Phase III Double-Blind, Placebo-Controlled, Add-On Study in Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)	S43.008 (platform), Wednesday, 8 May, 4:47 – 4:58 p.m. EDT

RG6042 for Huntington's disease	Preliminary Reliability and Validity of a Novel Digital Biomarker Smartphone Application to Assess Cognitive and Motor Symptoms in Huntington's Disease	P1.8-042 (poster), Sunday, 5 May, 5:30 – 6:30 p.m. EDT
	Defining Clinically Meaningful Change on the Composite Unified Huntington's Disease Rating Scale (cUHDRS)	P1.8-043 (poster), Sunday, 5 May, 5:30 – 6:30 p.m. EDT
	Translational Pharmacokinetic/Pharmacodynamic (PK/PD) Modelling Strategy to Support RG6042 Dose Selection in Huntington's Disease	S16.005 (platform), Monday, 6 May, 1:44 – 1:54 p.m. EDT
Gantenerumab for Alzheimer's disease	Consistently Large Amyloid Reductions in Patients with and Without ARIA-E in the Gantenerumab SCarlet RoAD and Marguerite RoAD Open-Label Extension Studies	S9.007 (platform), Sunday, 5 May, 4:36 – 4:47 p.m. EDT
Crenezumab for Alzheimer's disease	Baseline Characteristics from a Phase III Trial of Crenezumab in Early (Prodromal-to Mild) Alzheimer's Disease (CREAD)	P4.1-002 (poster) Wednesday, 8 May, 5:30 – 6:30 p.m. EDT
RG6206 for Duchenne muscular dystrophy	A Phase 1b/2 Study of the Anti-Myostatin Adnectin RG6206 (BMS-986089) in Ambulatory Boys with Duchenne Muscular Dystrophy: A 72-Week Treatment Update	P1.6-062 (poster), Sunday, 5 May, 5:30 – 6:30 p.m. EDT

Full session details and data presentation listings for the 2019 AAN Annual Meeting can be found at the meeting website: https://www.aan.com/conferences-community/annual-meeting/.

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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. 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.

Roche Investor Relations
Dr. Karl Mahler
Phone: +41 61 68-78503
e-mail: karl.mahler@roche.com

Jon Kaspar Bayard
Phone: +41 61 68-83894
e-mail: jon_kaspar.bayard@roche.com

Dr. Sabine Borngräber
Phone: +41 61 68-88027
e-mail: sabine.borngraeber@roche.com

Dr. Bruno Eschli
Phone: +41 61 68-75284
e-mail: bruno.eschli@roche.com

Dr. Birgit Masjost
Phone: +41 61 68-84814
e-mail: birgit.masjost@roche.com

Dr. Gerard Tobin
Phone: +41 61 68-72942
e-mail: gerard.tobin@roche.com

Investor Relations North America
Loren Kalm
Phone: +1 650 225 3217
e-mail: kalm.loren@gene.com

Dr. Lisa Tuomi
Phone: +1 650 467 8737
e-mail: tuomi.lisa@gene.com