

## **New Roche data at 2021 AAN highlight impact and breadth of expanding neuroscience portfolio**

- **EVRYSDI 2-year FIREFISH Part 2 data show improvement in motor function in infants with Type 1 spinal muscular atrophy (SMA)**
- **OCREVUS data show its consistent benefit on slowing disease progression in relapsing multiple sclerosis (RMS) and primary progressive MS (PPMS)**
- **Data for ENSPRYNG in neuromyelitis optica spectrum disorder (NMOSD) reinforce safety and efficacy, including in patients with concomitant autoimmune diseases (CAIDs)**
- **Data for investigational MS medicine fenebrutinib support its safety profile and high potency**
- **Additional presentations on investigational programmes, including Alzheimer's disease and Huntington's disease, help advance scientific understanding of neurological disorders**

Basel, 8 April 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that new data for its approved and investigational medicines for the treatment of neurological disorders will be presented at the 73rd American Academy of Neurology (AAN) Annual Meeting being held virtually April 17-22, 2021. These new data include 23 abstracts highlighting the expanding Roche neuroscience portfolio across six therapeutic areas, including EVRYSDI™ (risdiplam) for spinal muscular atrophy (SMA), OCREVUS® (ocrelizumab) in relapsing and primary progressive multiple sclerosis (RMS and PPMS), investigational Bruton's tyrosine kinase inhibitor (BTKi) fenebrutinib in Phase III trials for RMS and PPMS, ENSPRYNG® (satralizumab) in neuromyelitis optica spectrum disorder (NMOSD), and data from investigational programmes in Alzheimer's disease (AD) and Huntington's disease (HD).

“Following U.S. FDA and global approvals for our groundbreaking therapies in SMA and NMOSD, Roche's data at AAN reflect our continued commitment to meaningful therapeutic progress for people living with neurological disorders,” said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. “We are proud to collaborate with patient advocates, academia, industry and the broader healthcare community through cutting-edge research and partnerships to advance the scientific understanding of neurological conditions, which have historically been among the hardest disorders to study, diagnose and treat.”

### **Spinal Muscular Atrophy (SMA)**

Roche will present data from five studies from the EVRYSDI clinical development programme, which was designed to represent a broad spectrum of people living with SMA. The programme includes infants aged 2 months to adults aged 60 years with varying degrees of disability, including people with scoliosis or joint contractures, and those previously treated for SMA with another medication.

New 2-year findings from Part 2 of the Phase II/III FIREFISH trial show longer-term efficacy and safety of EVRYSDI in infants with symptomatic Type 1 SMA treated with EVRYSDI. This includes the number of infants able to sit without support for 5 and 30 seconds, a key motor milestone not normally seen in the

natural course of the disease, as well as data on event-free survival and reduced hospitalisations.

Additional data being presented across EVRYSDI's broad clinical trial programme include updated data from the JEWELFISH trial evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of EVRYSDI in patients previously treated with SMA targeting therapies, as well as updated pooled safety analyses from the FIREFISH, SUNFISH, RAINBOWFISH and JEWELFISH trials.

### **Multiple Sclerosis (MS)**

Roche will be presenting data from its MS Franchise, including five presentations covering OCREVUS and results from studies on the investigational BTKi fenebrutinib. Real-world data continue to show the highest persistence and adherence to OCREVUS, the only MS therapy with a twice-yearly dosing schedule, over one year compared to other disease-modifying therapies (DMTs). Additionally, a post-hoc analysis of the ORATORIO Phase III PPMS study will be presented, which suggests OCREVUS significantly slowed atrophied T2-lesion volume accumulation, a subclinical measure of disease progression. Furthermore, interim analysis of the open-label Phase IIIb ENSEMBLE study shows OCREVUS treatment provided consistent benefit over one year in patients who were recently diagnosed with relapsing-remitting multiple sclerosis (RRMS) and had not received prior DMT.

Roche is continuing to advance the science in MS and is exploring the investigational medicine fenebrutinib. Data from fenebrutinib, a highly selective, non-covalent, reversible oral BTKi, support its safety profile in several autoimmune diseases and high potency, which is encouraging for the ongoing Phase III studies in RMS and PPMS. Fenebrutinib is a dual inhibitor of both B-cell and myeloid lineage-cell activation, which may offer a novel approach to slowing disease progression by targeting both acute and chronic inflammatory aspects of MS.

### **Neuromyelitis Optica Spectrum Disorder (NMOSD)**

Roche will present five sets of data on adults living with NMOSD. Data from the Phase III SAKuraStar and SAKuraSky clinical trials reinforce the favourable safety and efficacy of this therapy for those living with NMOSD, including patients with concomitant autoimmune diseases (CAIDs).

New longitudinal, observational data from the CIRCLES study, conducted in collaboration with the Guthy-Jackson Charitable Foundation, a patient advocacy organisation dedicated to funding research on NMOSD epidemiology, pathogenesis and treatment, will also be presented. The CIRCLES study explored factors that influence treatment change in people living with NMOSD, including those who have experienced only one relapse.

### **Alzheimer's Disease (AD)**

Roche will present data on the increased use of home nursing capabilities in the Phase III GRADUATE studies of gantenerumab during the COVID-19 pandemic, which enabled home-bound trial participants to continue dosing to maintain medicine exposure.

Gantenerumab is a late-stage investigational anti-beta-amyloid antibody being evaluated in two Phase III studies (GRADUATE I and II), which are the only late-stage AD clinical trials to offer subcutaneous administration. We expect data from the studies in 2022.

### Huntington's Disease (HD)

Roche will also present an analysis of the Enroll-HD study and REGISTRY database, which will highlight the role that genetic factors and medical history may have in predicting the rate of disease progression in HD. These data may help advance the understanding of HD and inform future treatment approaches for this rare, neurological condition.

The full range of data from Roche's clinical development programme in neuroscience being presented at 2021 AAN include:

Medicine and/or Therapeutic Area	Abstract Title	Presentation Number (type), Session Title Presentation Date Time
EVRYSOI (risdiplam) for Spinal Muscular Atrophy	FIREFISH Part 2: 24-month Efficacy and Safety of Risdiplam in Infants with Type 1 Spinal Muscular Atrophy (SMA)	P6.062 P6: Neuromuscular Disorders and Clinical Trials
	SUNFISH Part 2: 24-month Efficacy and Safety of Risdiplam in Patients with Type 2 or Non-ambulant Type 3 Spinal Muscular Atrophy (SMA)	P6.060 P6: Neuromuscular Disorders and Clinical Trials
	JEWELFISH: Safety and Pharmacodynamic Data in Non-naïve Patients with Spinal Muscular Atrophy (SMA) Receiving Treatment with Risdiplam	P6.064 P6: Neuromuscular Disorders and Clinical Trials
	Pooled Safety Data from the Risdiplam Clinical Trial Development Program	P6.067 P6: Neuromuscular Disorders and Clinical Trials
	RAINBOWFISH: A study of Risdiplam in Newborns with Presymptomatic Spinal Muscular	P6.076 P6: Neuromuscular Disorders

	Atrophy (SMA)	and Clinical Trials 2
OCREVUS (ocrelizumab) for Multiple Sclerosis	B-Cell Subset Depletion Following Ocrelizumab Treatment in Patients with Relapsing Multiple Sclerosis	P15.206 P15: MS Therapeutics MOA and Safety
	Evolution of Lesions that Shrink or Disappear into Cerebrospinal Fluid (Atrophied T2 Lesion Volume) in Primary-Progressive Multiple Sclerosis: Results from the Phase III ORATORIO Study	P15.151 P15: MS Neuroimaging
	Recently Diagnosed Early-Stage RRMS: NEDA, ARR, Disability Progression, Serum Neurofilament and Safety: 1-Year Interim Data from the Ocrelizumab Phase IIIb ENSEMBLE Study	P15.099 P15: MS Clinical Trials and Therapeutics
	Adherence and Persistence to Disease-modifying Therapies for Multiple Sclerosis and Their Impact on Clinical and Economic Outcomes in a U.S. Claims Database	P15.228 P15: MS Health Care System/Policy Based Research
	Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Primary Progressive Multiple Sclerosis	P15.203 P15: MS Therapeutics MOA and Safety
Fenebrutinib for Multiple Sclerosis	The Safety of Fenebrutinib in a Large Population of Patients with Diverse Autoimmune Indications Supports Investigation in Multiple Sclerosis (MS)	S25.005 (oral presentation) S25: MS and CNS Inflammatory Disease: Emerging Therapeutics and Biomarkers Tuesday, April 20 at 4:40 pm ET
	Fenebrutinib Demonstrates the Highest Potency of Bruton Tyrosine Kinase Inhibitors (BTKis) in Phase 3 Clinical Development for Multiple Sclerosis (MS)	P15.091 P15: MS Clinical Trials and Therapeutics
ENSPRYNG (satralizumab) for	Satralizumab in Patients with Neuromyelitis Optica Spectrum Disorder and Concomitant Autoimmune Disease	P2.019 P2: Autoimmune Neurology: Advances in Neuromyelitis

Neuromyelitis Optica Spectrum Disorder		Optica Spectrum Disorder (NMOSD)
Neuromyelitis Optica Spectrum Disorder	Disease Phenotype Correlates with Treatment Change in NMOSD Patients of the CIRCLES Cohort	P2.091 P2: Autoimmune Neurology: Clinical Observations and Advances
	Demographic and Relapse Correlates of Treatment Change in NMOSD Patients: Analysis of the CIRCLES Study	P2.013 P2: Autoimmune Neurology: Advances in Neuromyelitis Optica Spectrum Disorder (NMOSD)
	Relapse Profile Correlates with Treatment Change in NMOSD Patients of the CIRCLES Cohort	P2.012 P2: Autoimmune Neurology: Advances in Neuromyelitis Optica Spectrum Disorder (NMOSD)
	Correlates of Rituximab Discontinuation in Patients with NMOSD: a CIRCLES Cohort Analysis	P2.014 P2: Autoimmune Neurology: Advances in Neuromyelitis Optica Spectrum Disorder (NMOSD)
Alzheimer's Disease	Linking Amyloid to Cognition in the Pathogenesis and Treatment of Alzheimer's Disease: Toward the Development of a "Quantitative A/T/N Model"	P1.052 P1: Aging and Dementia: Biomarkers
Gantenerumab for Alzheimer's Disease	Utilization of Home Nursing to Mitigate the Impact of COVID-19 on the Conduct of the Gantenerumab GRADUATE Trials	P1.014 P1: Aging and Dementia: Clinical Trials
Semorinemab for Alzheimer's Disease	A Disease Progression Model for Alzheimer's Disease Predicts Longitudinal Trajectory of CDR- SB Score Across Different Stages of the Disease	P1.061 P1: Aging and Dementia: Neuropsychology

Huntington's Disease	Burden of Illness among U.S. Medicare Beneficiaries with Late-onset Huntington's Disease	P14.043 P14: Huntington's Disease
	Clinical Characteristics of Late-Onset Huntington's Disease in North Americans from the Enroll-HD Study	P14.046 P14: Huntington's Disease
	Clustering and Prediction of Disease Progression Trajectories in Huntington's Disease: An Analysis of the Enroll-HD and REGISTRY Database Using a Machine Learning Approach	P14.147 P14: Clinical Trials, Surveys, and Studies in Movement Disorders

#### **About EVRYSDI™ (risdiplam)**

EVRYSDI is a survival of motor neuron 2 (SMN2) splicing modifier designed to treat SMA by increasing production of the survival of motor neuron (SMN) protein. SMN protein is found throughout the body and is critical for maintaining healthy motor neurons and movement. EVRYSDI is administered daily at home in liquid form by mouth or by feeding tube.

The U.S. Food and Drug Administration (FDA) approved EVRYSDI for the treatment of SMA in adults and children 2 months of age and older. EVRYSDI was granted PRIME designation by the European Medicines Agency (EMA) in 2018 and Orphan Drug Designation by FDA and EMA in 2017 and 2019, respectively. At this time, EVRYSDI has been approved in 38 countries and submitted in a further 33 countries.

#### **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 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. With rapidly growing real-world experience and more than 200,000 people treated globally, OCREVUS is the first and only therapy approved for relapsing MS (RMS; including RRMS and active, or relapsing, secondary progressive MS [SPMS], in addition to clinically isolated syndrome [CIS] in the U.S.) and PPMS. At Roche, we are constantly striving to optimise the care for people with MS and a shorter two-hour OCREVUS

infusion time, dosed twice yearly (six-monthly), is now approved for eligible people with RMS or PPMS in the U.S and EU.

OCREVUS is approved in 95 countries across North America, South America, the Middle East, Eastern Europe, as well as in Australia, Switzerland, the United Kingdom and the European Union (EU).

### **About ENSPRYNG<sup>®</sup> (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. The cytokine IL-6 is believed to be a key driver in NMOSD, triggering the inflammation cascade and leading to damage and disability. 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, suggest that IL-6 inhibition is an effective therapeutic approach for NMOSD. The Phase III clinical development programme for ENSPRYNG includes two studies: SAKuraStar and SAKuraSky.

ENSPRYNG is currently approved in 18 countries, including the United States, Canada, Japan and Switzerland. Applications are under review with numerous regulators.

ENSPRYNG has been designated as an orphan drug in the U.S., Europe and Japan.

### **About Roche in Neuroscience**

Neuroscience is a major focus of research and development at Roche. Our goal is to pursue groundbreaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases.

Roche is investigating more than a dozen medicines for neurological disorders, including spinal muscular atrophy, multiple sclerosis, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease, Duchenne muscular dystrophy and autism spectrum disorder. 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**

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 twelfth consecutive year, Roche has been recognised as one of the most sustainable companies 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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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](http://www.roche.com).

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## References

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