Media & Investor Release

Roche's fenebrutinib maintains near-complete suppression of disease activity and disability progression for up to two years in people with relapsing multiple sclerosis

- **Patients on fenebrutinib had low relapse rates with data showing no active brain lesions or disability progression after nearly two years of treatment**
- **Phase III studies for fenebrutinib in relapsing and primary progressive multiple sclerosis are expected to start reading out at year end**

Basel, 30 May 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today new, 96-week data for fenebrutinib demonstrating that patients with relapsing multiple sclerosis (RMS) maintained no disability progression and low levels of disease activity for up to two years. The latest results for this investigational Bruton's tyrosine kinase (BTK) inhibitor from the Phase II FENopta open-label extension (OLE) study were presented at the Consortium of Multiple Sclerosis Centers (CMSC) Annual Meeting in Phoenix, Arizona.

"These data show that patients treated with fenebrutinib experienced an annualised relapse rate equal to one relapse every 17 years and no observed disability progression up to two years,'' said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Fenebrutinib is potent, highly selective and the only reversible BTK inhibitor currently in Phase III trials for multiple sclerosis, and we look forward to seeing the first of those results later this year."

Ninety-nine patients entered the OLE and 93 remained in the OLE after 96 weeks. During the OLE period, patients treated with fenebrutinib for up to 96 weeks had a low annualised relapse rate (ARR) of 0.06, and during this time there was no disability progression, as measured by the Expanded Disability Status Scale (EDSS).

MRI scans showed that fenebrutinib treatment suppressed disease activity in the brain. At 96 weeks zero new T1 gadolinium-enhancing (T1-Gd+) lesions, which are markers of active inflammation, were detected. In the treatment group that switched from placebo to fenebrutinib in the OLE, the annualised rate of new or enlarging T2 lesions, which represent chronic disease burden, decreased from 6.72 at the end of the 12 week double-blind period to 0.34 by 96 weeks.

The safety profile of fenebrutinib in the OLE was consistent with previously reported data, with no new safety concerns identified at 96 weeks. The most common adverse events (AEs) in ≥5% of patients were COVID-19 (10%), urinary tract infection (10%), pharyngitis (6%) and respiratory tract infection (5%). Serious AEs occurred in two patients (2%). During the OLE, one patient experienced asymptomatic alanine aminotransferase elevation at OLE week 4, after 16 weeks on treatment, which resolved with treatment discontinuation.

Three Phase III clinical trials are ongoing, including the FENhance 1 and 2 trials in RMS and the FENtrepid trial in primary progressive multiple sclerosis (PPMS). The first data from these studies, which will characterise the effects of fenebrutinib on disease progression across the multiple sclerosis spectrum, are expected at the end of 2025.

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. Preclinical data have shown fenebrutinib to be potent and highly selective, and it is the only reversible BTK inhibitor currently in Phase III trials for multiple sclerosis. Fenebrutinib has been shown to be 130 times more selective for BTK vs. other kinases.

Fenebrutinib is a dual inhibitor of both B-cell and microglia activation. This dual inhibition may be able to reduce both multiple sclerosis disease activity and disability progression, thereby potentially addressing the key unmet medical need of disability progression in people living with multiple sclerosis. The fenebrutinib Phase III programme includes two identical trials in relapsing multiple sclerosis (RMS) (FENhance 1 & 2) with active comparator teriflunomide and the only trial in primary progressive multiple sclerosis (PPMS) (FENtrepid) in which a BTK inhibitor is being evaluated against OCREVUS. To date, more than 2,700 patients and healthy volunteers have been treated with fenebrutinib in Phase I, II and III clinical programmes across multiple diseases, including multiple sclerosis and other autoimmune disorders.

About the FENopta study

The FENopta study was a global Phase II, randomised, double-blind, placebo-controlled 12-week study to investigate the efficacy, safety and pharmacokinetics of fenebrutinib in 109 adults aged 18-55 years with relapsing multiple sclerosis (RMS). The primary endpoint was the total number of new T1 gadolinium-enhancing (T1-Gd+) lesions as measured by MRI scans of the brain at 4, 8 and 12 weeks. Secondary endpoints included the number of new or enlarging T2-weighted lesions as measured by MRI scans of the brain at 4, 8 and 12 weeks, and the proportion of patients free from any new T1-Gd+ lesions and new or enlarging T2-weighted lesions as measured by MRI scans of the brain at 4, 8 and 12 weeks. The goal of the FENopta study was to characterise the effect of fenebrutinib on MRI and soluble biomarkers of disease activity and progression, and it included an optional substudy to measure cerebrospinal fluid fenebrutinib levels and biomarkers of neuronal injury.

Data from the 12-week study showed that fenebrutinib is central nervous system (CNS) penetrant (crosses the blood-brain barrier) and has the potential to impact mechanisms underlying chronic progressive disease biology in multiple sclerosis patients. Fenebrutinib significantly reduced new T1-Gd+ lesions and new/enlarging T2 lesions compared to placebo.

The safety profile of fenebrutinib was consistent with previous and ongoing fenebrutinib clinical trials and there were no new safety concerns identified.

Patients who completed the FENopta study were given the option to take part in an open-label extension (OLE) study, in which all patients receive fenebrutinib up to 192 weeks.

About multiple sclerosis

Multiple sclerosis is a chronic disease that affects more than 2.9 million people worldwide. Multiple sclerosis 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 weakness, fatigue and difficulty seeing, and may eventually lead to disability. Most people with multiple sclerosis 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 multiple sclerosis experience disease progression from the beginning of their disease. Therefore, delays in diagnosis and treatment can negatively impact people with multiple sclerosis, 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 multiple sclerosis is to slow, stop and ideally prevent progression as early as possible.

Approximately 85% of people with multiple sclerosis have a relapsing form of the disease (RMS) characterised by relapses and also worsening disability over time. Primary progressive multiple sclerosis (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 multiple sclerosis 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 and OCREVUS is still the only approved treatment for PPMS.

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 multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular dystrophy. 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.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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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