Media & Investor Release

Roche's fenebrutinib is the first investigational medicine in over a decade that reduces disability progression in primary progressive multiple sclerosis (PPMS)

- **Late-breaking Phase III FENtrepid results presented at ACTRIMS show investigational fenebrutinib met its primary endpoint of non-inferiority compared to the current standard of care, OCREVUS, in reducing disability progression in PPMS**
- **Fenebrutinib numerically reduced the risk of disability progression by 12% compared to OCREVUS as early as 24 weeks; additional analysis showed potential benefit in upper limb function**
- **Fenebrutinib has the potential to become first-in-class in multiple sclerosis, as an oral, brain-penetrant BTK inhibitor for PPMS and relapsing multiple sclerosis (RMS)**
- **Regulatory submission for fenebrutinib in both PPMS and RMS is planned following the Phase III FENhance 1 readout, expected mid first half of 2026**

Basel, 07 February 2026 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today new late-breaking data from the Phase III FENtrepid study showing the investigational Bruton's tyrosine kinase (BTK) inhibitor fenebrutinib met its primary endpoint of non-inferiority compared to OCREVUS (ocrelizumab) in reducing disability progression in patients with primary progressive multiple sclerosis (PPMS). Fenebrutinib showed a 12% reduction in the risk of disability progression compared to OCREVUS, the only approved medicine for PPMS, as measured by the time to onset of 12-week composite confirmed disability progression (cCDP12) (hazard ratio [HR] 0.88; 95% confidence interval [CI]: 0.75, 1.03) with curves separating as early as 24 weeks. A consistent treatment effect on cCDP12 was observed across patient subgroups and for the entire treatment duration.

The cCDP12 primary endpoint included the confirmed disability progression (CDP) based on the Expanded Disability Status Scale (EDSS) for functional disability, the timed 25-foot walk (T25FW) for walking speed and the nine-hole peg test (9HPT) for upper limb function. The strongest treatment effect was observed on the risk of worsening on the 9HPT by 26% (HR 0.74; 95% CI: 0.56, 0.98) compared to OCREVUS.

"Fenebrutinib showed a consistent clinical benefit as early as week 24, notably in upper limb function, which is essential for preserving independence and daily functioning," said Professor Amit Bar-Or, Director of the Center for Neuroinflammation and Neurotherapeutics, Perelman School of Medicine, University of Pennsylvania. "With only one disease-modifying therapy available for people with PPMS, fenebrutinib has the potential to be a high-efficacy,

oral treatment option that acts directly in the brain, targeting progressive biology, and may slow disability."

"Fenebrutinib represents the first potential scientific breakthrough for the PPMS community in over a decade, demonstrating a meaningful clinical benefit in reducing disability progression in a study versus the only approved treatment in PPMS," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We look forward to advancing our regulatory submission following the upcoming readout of our second pivotal RMS study, FENhance 1."

Additionally, a post-hoc analysis showed that fenebrutinib was superior to OCREVUS on a composite endpoint including two of the three components of cCDP12 (EDSS and 9HPT), with a 22% reduction in risk (HR 0.78; 95% CI: 0.64, 0.95).

Adverse events (AEs) commonly (≥10%) observed in the fenebrutinib group were comparable to OCREVUS: infections (67.0% vs 70.9%), nausea (12.0% vs 7.1%) and haemorrhage (10.2% vs 8.1%). Transient and reversible liver enzyme elevations were observed more often in the fenebrutinib group (13.3% vs 2.9%), and all cases resolved after study drug discontinuation. No Hy's law cases (an indicator for potential severe liver injury) were observed. Serious AEs were reported in 19.1% of patients receiving fenebrutinib (vs 18.9% on OCREVUS) and led to 4.3% withdrawing from treatment (vs 3.0% on OCREVUS). In the FENtrepid study there were 1.4% fatal cases in the fenebrutinib arm vs 0.2% in the OCREVUS arm, all of which were assessed as unrelated to the study treatment by the investigators and no pattern was observed in timing or cause. Epidemiological studies have shown that fatality rates are higher in people living with MS compared to the general population.[1-4]

Results were shared today as a late-breaking oral presentation at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2026 in San Diego, California. These data follow Roche's announcement in November 2025 that the FENtrepid study and the first of two Phase III relapsing multiple sclerosis (RMS) studies (FENhance 2) met their primary endpoints. Once the second RMS study (FENhance 1) has read out, which is expected in the first half of 2026, data from all Phase III fenebrutinib trials will be submitted to regulatory authorities.

About the FENtrepid study

FENtrepid is a Phase III multicentre, randomised, double-blind, double-dummy, parallel-group study to evaluate the efficacy and safety of fenebrutinib compared with OCREVUS in 985 adult patients with primary progressive multiple sclerosis (PPMS). Eligible participants were randomised 1:1 to receive treatment with either daily oral fenebrutinib (and placebo matched to intravenous [IV] OCREVUS) or IV OCREVUS (and placebo matched to oral fenebrutinib) for at least 120 weeks.

The primary endpoint is the time to onset of 12-week composite confirmed disability progression (cCDP12). The cCDP incorporates three measures of disability – total functional disability measured by the confirmed disability progression (CDP) based on the Expanded Disability Status Scale (EDSS), walking speed measured by the timed 25-foot walk (T25FW) and upper limb function measured by the nine-hole peg test (9HPT). This comprehensive composite endpoint offers greater sensitivity than the EDSS alone, capturing additional aspects of disability and often earlier. Key secondary endpoints include the time to onset of 24-week composite confirmed disability progression (cCDP24), 12-week confirmed disability progression (CDP12) and 24-week confirmed disability progression (CDP24).

Following the double-blind treatment period, patients have the option to enter an open-label extension (OLE) phase, in which all patients receive treatment with fenebrutinib.

About fenebrutinib

Fenebrutinib is an investigational oral, central nervous system (CNS)-penetrant, reversible and non-covalent Bruton's tyrosine kinase (BTK) inhibitor with an optimised pharmacokinetics (PK) profile and high potency. While most current BTK inhibitors are covalent and irreversible, meaning they form a permanent chemical bond with the enzyme, fenebrutinib binds and then eventually releases the enzyme. These design features may help limit off-target effects.

Fenebrutinib has a selectivity for BTK 130 times greater than other kinases which means that it can bind to its intended BTK target without interfering in other kinases. Fenebrutinib can act throughout the body and also cross the blood-brain barrier into the CNS to target chronic inflammation. It is uniquely designed to target relapsing and progressive biology by inhibiting cells in the immune system known as B cells and microglia. Targeting B cells helps control the acute inflammation that causes relapses, while targeting microglia inside the brain addresses the chronic damage that is thought to drive long-term disability progression.

The fenebrutinib Phase III programme includes two similarly designed trials in relapsing multiple sclerosis (RMS) (FENhance 1 and 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 multiple sclerosis

Multiple sclerosis is a chronic disease that affects more than 2.9 million people worldwide. People with all forms of multiple sclerosis experience disease progression from the beginning of their disease. Therefore, 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.

For more information, please visit www.roche.com.

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