Media & Investor Release

Ad hoc announcement pursuant to Art. 53 LR

Roche's fenebrutinib confirms its potential as first and only BTK inhibitor for relapsing and primary progressive MS in third positive Phase III study (FENhance 1)

- **FENhance 1 met its primary endpoint, showing investigational fenebrutinib significantly reduced relapses by 51% compared to teriflunomide in relapsing multiple sclerosis (RMS), consistent with FENhance 2 results showing 59% reduction**
- **FENhance 1 is the final study readout of the fenebrutinib pivotal clinical development programme in MS, following positive results for FENhance 2 in RMS and for FENtrepid in primary progressive multiple sclerosis (PPMS)**
- **Fenebrutinib has the potential to become the first and only high-efficacy oral, brain-penetrant treatment for both RMS and PPMS, showing a profound benefit on relapsing and progressive disease biology**
- **Totality of data from all three Phase III fenebrutinib studies will be submitted to regulatory authorities**

Basel, 02 March 2026 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the pivotal Phase III study (FENhance 1) of fenebrutinib in RMS met its primary endpoint, showing clinically meaningful and statistically significant results. The study demonstrated that fenebrutinib, an investigational Bruton's tyrosine kinase (BTK) inhibitor, markedly reduced the annualised relapse rate (ARR) by 51% compared to teriflunomide over a period of at least 96 weeks of treatment, consistent with FENhance 2 results showing a 59% reduction in ARR. Together, these results equate to approximately one relapse every 17 years. Secondary endpoints in both RMS studies show statistically significant and clinically meaningful reductions in brain lesions. Additionally, all progression endpoints show favorable trends for fenebrutinib.

Full data from the FENhance 1 and 2 studies will be shared at the American Academy of Neurology (AAN) Annual Meeting 2026 and submitted to regulatory authorities together with data from the FENtrepid study.

"These pivotal results, together with the earlier data, provide convincing evidence that fenebrutinib can become the first high-efficacy oral treatment for RMS and PPMS," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Building on a decade of transforming MS treatment, we are committed to advancing innovation to one day allow people with MS to live a life without disability."

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The positive FENhance 1 study follows positive results for FENhance 2 in RMS and for FENtrepid in PPMS, which were both announced in November. The collective positive results across all three pivotal studies demonstrate that fenebrutinib consistently shows a profound benefit on relapsing and progressive disease biology.

In both RMS studies, liver transaminase elevations were comparable with teriflunomide. In the FENhance 1 study, there was one Hy's Law case in the fenebrutinib arm and one in the teriflunomide arm. Both cases were asymptomatic and resolved after study drug discontinuation. There were no additional Hy's Law cases across all of the fenebrutinib clinical development programme in MS or in other autoimmune diseases.

In the FENhance 1 and 2 studies in RMS, 1 fatal case was reported in the teriflunomide arm and 8 fatal cases with various causes and at different points in treatment in the fenebrutinib arms. Further analyses are ongoing to better understand these findings.

Fenebrutinib targets 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. Fenebrutinib, a non-covalent BTK inhibitor, is designed to have high potency, selectivity and reversibility. This design allows it to act throughout the body, and also to cross the blood-brain barrier into the central nervous system (CNS) targeting chronic inflammation.

About the FENhance 1 and 2 studies

FENhance 1 and 2 are two Phase III multicentre, randomised, double-blind, double-dummy, parallel-group studies to evaluate the efficacy and safety of investigational fenebrutinib compared with teriflunomide in a total of 1,497 adult patients with RMS. Eligible participants were randomised 1:1 to receive treatment with either oral fenebrutinib twice a day (and placebo matched to oral teriflunomide once a day) or oral teriflunomide once a day (and placebo matched to oral fenebrutinib twice a day) for at least 96 weeks.

The primary endpoint is annualised relapse rate (ARR). Secondary endpoints include total number of T1-gadolinium-enhancing MRI lesions, total number of new and/or enlarging T2-weighted MRI lesions, time to onset of 12-week composite confirmed disability progression (cCDP12) and 24-week cCDP (cCDP24). cCDP incorporates three measures of disability – total functional disability measured by 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).

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. 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.

Fenebrutinib is designed to have high potency and reversibility, with a selectivity for BTK 130 times greater than other kinases. This high selectivity highlights fenebrutinib's potential to bind to its intended target without interfering with other kinases. While most current BTK inhibitors are covalent and irreversible, meaning they form a permanent chemical bond with the enzyme, fenebrutinib is non-covalent and reversible, meaning it binds and then eventually releases the enzyme. These design features may help limit off-target effects.

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 are initially diagnosed with relapsing-remitting multiple sclerosis (RRMS). Relapsing forms of the disease (RMS) include RRMS and active secondary progressive MS, and people with RMS experience relapses and 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.

Despite the availability of CD20s, 30% of patients remain on low-efficacy oral therapy today. Slowing or stopping progression while simultaneously stopping relapses remains a high unmet need in MS.

About Roche in Neurology

Neurology 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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