Media & Investor Release

Roche's fenebrutinib significantly reduced relapses versus standard of care to approximately one every 17 years in RMS

- **Late-breaking Phase III FENhance 1 and 2 study results showed superiority of investigational fenebrutinib compared to teriflunomide in reducing relapses and brain lesions in relapsing multiple sclerosis (RMS)**
- **Both studies showed positive trends in reducing disability progression with fenebrutinib compared to teriflunomide**
- **Fenebrutinib could become a first-in-class BTK inhibitor and the first and only high-efficacy oral for both RMS and primary progressive multiple sclerosis (PPMS)**
- **The totality of RMS and PPMS data for fenebrutinib will be submitted to regulatory authorities**

Basel, 22 April 2026 - Roche (SIX: RO, ROP; OTCQX: RHHBY) announced today new data from the positive Phase III FENhance 1 and 2 studies, which met their primary endpoint. The studies showed that fenebrutinib, an investigational non-covalent Bruton's tyrosine kinase (BTK) inhibitor, reduced the annualised relapse rate (ARR) by 51.1% ($p<0.001$) in FENhance 1 and 58.5% ($p<0.0001$) in FENhance 2 compared with teriflunomide in patients with relapsing multiple sclerosis (RMS) over 96 weeks. This equates to patients having approximately one relapse every 17 years, more than half the relapses seen with teriflunomide in the same period of time. The results were shared today as a late-breaking presentation at the 2026 American Academy of Neurology (AAN) Annual Meeting in Chicago.

"These results underscore that fenebrutinib has potential as a high-efficacy oral treatment for RMS. Its unique mode of action may offer a differentiated profile by targeting dual drivers of MS within the central nervous system and periphery to address disease mechanisms underlying both relapsing and progressive disease biology," said Jiwon Oh, M.D., Ph.D., Medical Director of the Barlo Multiple Sclerosis Program at St. Michael's Hospital, University of Toronto. "For the first time, a BTK inhibitor has demonstrated superiority in reducing relapses and formation of new brain lesions with comparable rates of liver enzyme elevations to a long-standing first-line medication in multiple Phase III RMS trials."

"The fenebrutinib data across three pivotal studies strongly support its potential to benefit people with both RMS and PPMS," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "By more than doubling the time without relapses compared to teriflunomide, fenebrutinib may offer patients years of relapse-free living, thereby preserving both daily independence and long-term function."

The relapse rate was consistently reduced across patient subgroups. The greatest reductions were observed in patients with more inflammatory disease characteristics including active brain lesions, younger age, more recent diagnosis and less disability, which highlights the potential of fenebrutinib as a high-efficacy, oral treatment option for these patient populations, if approved.

Secondary endpoints showed that fenebrutinib significantly reduced disease activity in the brain, as evidenced by MRI scans. Fenebrutinib reduced markers of active inflammation by 70.7% ($p<0.0001$) in FENhance 1 and 77.6% ($p<0.0001$) in FENhance 2 compared with teriflunomide, as measured by new T1 gadolinium-enhancing (T1-Gd+) lesions. Chronic disease burden was reduced by 76.0% ($p<0.0001$) in FENhance 1 and 82.5% ($p<0.0001$) in FENhance 2 with fenebrutinib compared with teriflunomide, as measured by new or enlarging T2 lesions.

Additional secondary endpoints showed positive trends toward reducing disability progression with fenebrutinib. A numerical reduction in the risk of 12-week composite confirmed disability progression (cCDP12) by 20% (hazard ratio [HR] 0.80; 95% confidence interval [CI]: 0.63-1.02) in FENhance 1 and 13% (HR 0.87; 95% CI: 0.69-1.11) in FENhance 2 was observed with fenebrutinib compared with teriflunomide. 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). The greatest reductions were observed on overall disability and upper-limb disability. In a post-hoc analysis of a modified 12-week confirmed composite of the EDSS and the 9HPT, fenebrutinib reduced the risk of worsening by 26% (HR 0.74; 95% CI: 0.53-1.03) in FENhance 1 and 20% (HR 0.80; 95% CI: 0.57-1.12) in FENhance 2 compared with teriflunomide.

In both RMS studies, liver enzyme elevations above three times the upper limit of normal were comparable with teriflunomide (7.3% vs 5.7% in FENhance 1; 5.6% vs 5.6% in FENhance 2). In the FENhance 1 study, there was one Hy's Law case in the fenebrutinib arm (which occurred before biweekly liver monitoring was implemented) and one in the teriflunomide arm. Both cases were asymptomatic and resolved after study drug discontinuation.

Rates of infections were also comparable between the fenebrutinib and teriflunomide arms. Serious adverse events (AEs) were reported in 8.6% of patients receiving fenebrutinib (vs 8.9% on teriflunomide) in FENhance 1 and 11.2% (vs 6.1%) in FENhance 2.

Overall, an imbalance with respect to reported fatalities across studies was observed. In FENhance 1 and 2, there was one death (0.1%) in the teriflunomide arm and seven deaths (0.9%) in the fenebrutinib arm during the reporting period. One additional death was observed after this period. Overall in the fenebrutinib arm, deaths occurred at different timepoints and

were caused by various causes including infections (neuro cryptococcosis gattii and pneumonia), complications of type 1 diabetes, serious bleeding, suicide, injuries from accident and death of unknown cause.

Previously, the Phase III FENtrepid study in primary progressive multiple sclerosis (PPMS) showed fenebrutinib met its primary endpoint of non-inferiority compared with the current standard of care, OCREVUS, in reducing disability progression in PPMS. The collective positive results across all three pivotal studies demonstrate that fenebrutinib consistently showed a profound benefit on relapsing and progressive disease biology. The totality of data from all three Phase III fenebrutinib studies will be submitted to regulatory authorities.

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).

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.

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 diagnostics and treatments that help improve the lives of people with chronic and potentially devastating diseases globally.

Roche is investigating more than a dozen medicines for neurological conditions, including multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular dystrophy. Roche Diagnostics has developed a broad range of approved and investigational tools, including digital and blood-based tests and cerebrospinal fluid (CSF) assays, aiming to more effectively detect, diagnose and monitor neurological conditions. Together with our partners, we are committed to pushing the boundaries of scientific understanding to solve some of the most difficult challenges in neurology today.

About Roche

Roche (SIX: RO, ROP; OTCQX: RHHBY) is a healthcare company uniquely placed to prevent, stop and cure diseases by uniting leading science and technology across diagnostics, medicines and digital solutions.
Roche was founded in Basel, Switzerland in 1896 and today is a leading provider of transformative medicines and diagnostics for millions of people in over 150 countries around the world. It is dedicated to tackling healthcare challenges that place the greatest strain on patients, families, communities and healthcare systems. Across its Diagnostics and Pharmaceutical divisions, Roche focuses on areas including oncology, neurology,

cardiovascular and metabolic diseases, ophthalmology, infectious diseases and immunology with the aim of providing real and positive change for patients, the people they love and the professionals who care for them.

Genentech in the United States is a fully owned subsidiary in the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, a major innovator in the Japanese therapeutic antibody market.

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