

# Roche's fenebrutinib is the first BTK inhibitor to receive U.S. FDA filing acceptance in both relapsing and primary progressive multiple sclerosis

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**Fenebrutinib cut relapses by 51% and 58% vs teriflunomide in Phase III RMS trials (FENhance 1 & 2) while showing a consistent, positive trend in delaying disability<sup>1</sup>Fenebrutinib became the first investigational medicine in more than a decade to slow disability progression in a Phase III PPMS trial (FENTrepid), with numerical benefit vs Ocrevus<sup>2</sup>Fenebrutinib is designed to address two drivers of MS - acute inflammation causing relapses and chronic brain inflammation driving disability progression<sup>1,2</sup>If approved, fenebrutinib would become the first BTK inhibitor and first high-efficacy oral treatment for both RMS and PPMS, offering a new option for the nearly 1 million Americans living with MS<sup>3</sup>**

Basel, 30 September 2026 - Roche (SIX: RO, ROP; OTCQX: RHHBY) announced today that the United States Food and Drug Administration (FDA) has accepted the company's New Drug Application (NDA) under priority review for fenebrutinib, an investigational non-covalent Bruton's tyrosine kinase (BTK) inhibitor for the treatment of relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS). The filing acceptance is based on data from the comprehensive clinical programme, including the Phase III FENhance 1 and 2 RMS studies and the Phase III FENTrepid PPMS study.<sup>1,2</sup>

"People living with multiple sclerosis need treatments that go beyond controlling relapses to help preserve function and independence as the disease progresses," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Three Phase III studies have demonstrated the potential for fenebrutinib to address both relapsing and progressive disease, thereby bringing us closer to an oral treatment that could make a meaningful difference across the MS spectrum."

"Ocrevus transformed how we treat MS, helping more than 525,000 people live a life less defined by their disease. Yet, over a third of all people with MS still receive lower-efficacy treatment," said Teresa Graham, Roche's Chief Executive Officer, Pharma. "If approved, fenebrutinib could open a new chapter as the first high-efficacy oral therapy for both relapsing and primary progressive MS, helping to control disease activity while giving people more flexibility and choice."

Concurrently addressing the life-disrupting relapses and long-term disease progression - the slow, steady loss of physical and mental abilities over time - remains one of the greatest challenges in MS.<sup>4</sup> Fenebrutinib is designed to act throughout the body and to cross the blood-brain barrier into the central nervous system to target both the acute inflammation that causes relapses and the chronic inflammation that is thought to drive disability progression.<sup>1,2</sup>

The NDA for fenebrutinib is supported by three positive Phase III studies:

- The FENhance 1 and 2 RMS studies showed that fenebrutinib significantly reduced relapses and both active and chronic brain lesions compared with standard of care, teriflunomide.

Fenebrutinib reduced the annualised relapse rate (ARR) by 51.1% ( $p < 0.001$ ) in FENhance 1 and 58.5% ( $p < 0.00001$ ) in FENhance 2 compared with teriflunomide over 96 weeks. This equates to patients having approximately one relapse every 17 years, which is the lowest relapse rate seen in Phase III MS studies. In addition, measures of disability progression, including 12-week composite confirmed disability progression (cCDP12), showed consistent positive trends favouring fenebrutinib over teriflunomide.<sup>1</sup>

- The FENTrepid PPMS study showed fenebrutinib met its primary endpoint of non-inferiority compared with Ocrevus® (ocrelizumab), the current standard of care and only approved medicine for PPMS, in reducing disability progression. Fenebrutinib numerically reduced the risk of progression by 12% compared to Ocrevus, as measured by the time to onset of 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 disability progression was observed across patient subgroups, including those without active inflammation, and for the entire treatment duration after 24 weeks.<sup>2</sup>

The overall rate of serious adverse events for fenebrutinib and teriflunomide, respectively, was 9% and 9% in FENhance 1 and 11% and 6% in FENhance 2. The overall rate of serious adverse events in FENTrepid was 19% for fenebrutinib and 19% for Ocrevus. Liver enzyme elevations were comparable between the fenebrutinib and teriflunomide arms in the RMS studies and observed more often with fenebrutinib compared to Ocrevus in the PPMS study. While an imbalance in reported fatalities was observed across the three pivotal studies, the deaths occurred at different timepoints and had various causes.<sup>1,2</sup> Overall, fenebrutinib has shown a manageable safety profile across the three Phase III trials and earlier studies, with a large safety database including more than 2,700 study participants.<sup>1,2,5</sup>

#### 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.

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.

#### About multiple sclerosis

Multiple sclerosis is a chronic disease that affects more than 3 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.

## 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.

For more information, please visit [www.roche.com](http://www.roche.com).

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## References

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