Roche expands its multiple sclerosis portfolio with investigational BTK inhibitor fenebrutinib and initiates novel clinical trials for OCREVUS (ocrelizumab)

- **Phase III clinical trial programme initiated for investigational medicine fenebrutinib, designed to be a highly selective and reversible Bruton's tyrosine kinase (BTK) inhibitor, in relapsing multiple sclerosis (RMS) and primary progressive MS (PPMS)**
- **Phase IIIb clinical trial programme of higher-dose OCREVUS (ocrelizumab) to evaluate impact on reducing disability progression in RMS and PPMS**
- **OCREVUS CHIMES study exclusively focused on disease insights and more tailored care for minority populations with MS**

Basel, 9 September 2020 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the initiation of an innovative Phase III clinical trial programme for its investigational medicine fenebrutinib in multiple sclerosis (MS), along with a higher-dose Phase III clinical trial programme for OCREVUS® (ocrelizumab) and a distinct OCREVUS trial specifically to support African-American and Hispanic- and Latinx-American patients with MS. Overviews of clinical trials and scientific rationale will be presented at MSVirtual2020, the 8th Joint Meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) and the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) from 11-13 September 2020.

"We remain committed to advancing the science in MS by investigating potential new medicines such as fenebrutinib, with the ultimate goal of halting progression of this disease," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "In addition, over 170,000 people have been treated with OCREVUS, our first-in-class B-cell therapy, and we are incorporating years of clinical trial data and real-world evidence to optimise its potential to improve outcomes for patients with MS."

Fenebrutinib Phase III clinical trial programme

Roche is initiating a Phase III clinical trial programme for fenebrutinib, an investigational oral Bruton's tyrosine kinase (BTK) inhibitor in relapsing MS (RMS) and primary progressive MS (PPMS). Increasing evidence suggests that B cells and myeloid lineage cells contribute to disease progression in MS. Fenebrutinib is a dual inhibitor of both B-cell and myeloid lineage-cell activation, which may conceivably offer a novel approach to suppress disease activity and slow disease progression by targeting both acute and chronic inflammatory aspects of MS, which will be studied in the Phase III clinical trial programme. Pre-clinical data have shown fenebrutinib is highly selective and acts as a non-covalent agent with a slow release rate from its target.

The Phase III clinical trial programme includes two identical Phase III trials in RMS (named FENhance 1 and FENhance 2) and one Phase III trial in PPMS (named FENtrepid). All three trials are targeting clinical disability progression and have a primary endpoint of 12-week composite confirmed disability progression (cCDP-12), with the addition of a co-primary endpoint of annualised relapse rate in the RMS trials. The

PPMS study is the first study in this patient population to have an active comparator – OCREVUS – rather than placebo.

OCREVUS higher dose Phase IIIb clinical trial programme
Halting disease progression is the ultimate aim for patients and physicians, and we are acting on the needs of the MS community, informed by recent data, to optimise the potential of OCREVUS to slow progression for a broad range of patients. Roche is therefore initiating two new Phase IIIb trials, one in RMS (named MUSETTE) and one in PPMS (named GAVOTTE), which will evaluate a higher OCREVUS dose compared with the currently approved 600 mg dose, with both evaluated at the twice-yearly (six-monthly) dosing schedule. This decision was based on analyses from the pivotal RMS and PPMS studies presented at the American Academy of Neurology Annual Meeting 2019, which showed higher OCREVUS exposure was associated with lower B-cell levels and with greater control of disability progression, without impacting safety.

At the currently approved 600 mg dose, OCREVUS is the only MS treatment that has demonstrated a consistent and significant impact on slowing disability progression in both RMS and PPMS Phase III studies. The clinical trial programme will evaluate the potential benefit of higher dose OCREVUS in further reducing disability progression for people living with both RMS and PPMS.

OCREVUS CHIMES trial in minority patients
Roche recently initiated the Phase IV CHIMES (CHaracterization of ocrelizumab In Minorities with multiplE Sclerosis) trial in African-Americans and Hispanic- and Latinx-Americans with RMS. These patient populations are more likely to experience more relapses and greater disability than Caucasians, yet are vastly underrepresented in most clinical trials.

CHIMES is the first prospective trial developed in collaboration with MS patients, patient advocacy groups and investigators to exclusively focus on meeting the needs of minority patients with MS. The findings are expected to improve current understanding of MS disease biology and treatment response, among African-American and Hispanic- and Latinx-American patients with MS, with the ultimate goal of increasing high-quality standard of care to traditionally underserved communities and enhancing equality through clinical research.

All of the newly announced clinical trials are underway and anticipated to begin recruiting in the coming months.

About multiple sclerosis
Multiple sclerosis (MS) is a chronic disease that affects nearly 1 million people in the U.S. and more than 2.3 million people worldwide. MS 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 muscle weakness, fatigue and difficulty seeing, and may eventually lead to disability. Most people with MS 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 MS experience disease progression – permanent loss of nerve cells in the central nervous system and gradual worsening of disability – at the beginning of their disease even if their clinical symptoms aren't apparent or don't appear to be getting worse. Delays in diagnosis and treatment can negatively impact people with MS, both in terms of their physical, mental and financial health. An important goal of treating MS is to slow the progression of disability as early as possible.

Relapsing-remitting MS (RRMS) is the most common form of the disease and is characterised by episodes of new or worsening signs or symptoms (relapses) followed by periods of recovery. Approximately 85% of people with MS are initially diagnosed with RRMS. The majority of people who are diagnosed with RRMS will eventually transition to secondary progressive MS (SPMS), in which they experience steadily worsening disability over time. Relapsing forms of MS (RMS) include people with RRMS and people with SPMS who continue to experience relapses. Primary progressive MS (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 MS 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.

About fenebrutinib
Fenebrutinib is designed to be a highly selective small molecule and is the only reversible (non-covalent) BTK inhibitor currently in Phase III development in MS. Increasing evidence suggests that B cells and myeloid lineage cells contribute to disease progression in MS. Fenebrutinib is a dual inhibitor of both B-cell and myeloid lineage-cell activation, which may offer a novel approach to suppress disease activity and slow disease progression by targeting both acute and chronic inflammatory aspects of MS, which will be studied in our Phase III clinical trial programme. The safety profile of fenebrutinib has been studied in more than 1,200 people to date across several inflammatory diseases, and the data indicate that the high selectivity of fenebrutinib may limit off-target effects.

About OCREVUS® (ocrelizumab)
OCREVUS is the first and only therapy approved for both RMS (including clinically isolated syndrome, RRMS and active, or relapsing, SPMS, in addition to clinically isolated syndrome [CIS] in the U.S.) and PPMS. OCREVUS is a humanised monoclonal antibody designed to target CD20-positive B cells, a specific type of immune cell thought to be a key contributor to myelin (nerve cell insulation and support) and axonal (nerve cell) damage. This nerve cell damage can lead to disability in people with MS. Based on preclinical studies, OCREVUS binds to CD20 cell surface proteins expressed on certain B cells, but not on stem cells or plasma cells, suggesting that important functions of the immune system may be preserved. OCREVUS is administered by intravenous infusion every six months. The initial dose is given as two 300 mg infusions given two weeks apart. Subsequent doses are given as single 600 mg infusions.

About Roche in multiple sclerosis
Roche is following the science in an effort to ultimately stop disease progression and preserve function in people living with multiple sclerosis (MS). As a company, we continue to advance the clinical understanding of MS and progression with the aim of bringing the most benefit to people living with MS.

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, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease, Duchenne's muscular dystrophy and autism spectrum disorder. 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
Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the eleventh consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 billion. 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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