NEWS RELEASE

Genentech’s Ocrevus Twice-Yearly, 10-Minute Subcutaneous Injection Was Non-Inferior to Intravenous Infusion and Provided Near-Complete Suppression of Brain Lesions

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– Late-breaking Phase III results show subcutaneous injection was non-inferior to intravenous infusion based on Ocrevus levels in the blood over 12 weeks –

– Ocrevus subcutaneous injection was comparable to IV infusion in providing rapid and sustained depletion of B cells and near-complete suppression of MRI lesion activity in the brain over 24 weeks –

– The safety profile of Ocrevus subcutaneous injection was consistent with the well-established safety profile of Ocrevus IV infusion –

– The 10-minute subcutaneous injection has potential to improve the treatment experience and expand usage for people with multiple sclerosis (MS) in centers with IV capacity limitations –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)-- Genentech, a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), today announced late-breaking data from the Phase III OCARINA II study. Study results demonstrate the effect of Ocrevus® (ocrelizumab) as an investigational twice-yearly, 10-minute subcutaneous injection on pharmacokinetic, biomarker, and MRI measures in patients with relapsing or primary progressive multiple sclerosis (RMS or PPMS). The data will be presented in a poster at the 9th Joint ECTRIMS-ACTRIMS Meeting (European and Americas Committees for Treatment and Research in Multiple Sclerosis).

“We are pleased to share that Ocrevus 10-minute subcutaneous injection suppressed brain lesions as effectively as

the intravenous infusion," said Levi Garraway, M.D., Ph.D., Genentech's chief medical officer and head of Global Product Development. "Having this additional treatment option may improve the treatment experience for both patients and physicians, and we hope the twice-a-year dosing will offer the same high adherence and persistence."

Ocrevus subcutaneous injection was non-inferior to Ocrevus IV infusion as measured by Ocrevus levels in the blood of patients (area under the serum concentration time curve) from day 1 to 12 weeks (3500 day*µg/mL for subcutaneous injection vs. 2750 day*µg/mL for IV infusion). Peak Ocrevus blood (serum) concentrations were similar for subcutaneous injection (132 µg/mL) and IV infusion (137 µg/mL).

Ocrevus subcutaneous injection provided rapid, sustained and near-complete B-cell depletion that was similar to Ocrevus IV infusion (97% and 98% of patients respectively had B cell levels of 5 cells/µL or less when first measured at 14 days), which was sustained over 24 weeks. At the time of analysis, approximately half the patients in the study had reached 24 weeks of treatment.

Both Ocrevus subcutaneous injection and Ocrevus IV infusion resulted in rapid and near-complete suppression of MRI lesion activity by 24 weeks, with most patients having no T1 gadolinium-enhancing (T1 Gd+) lesions, which are markers of active inflammation, and no new/enlarging T2 lesions, which represent the amount of disease burden or lesion load at 24 weeks.

	T1 Gd+ lesions			New/enlarging T2 lesions		
	Average lesion number	Adjusted lesion rate		Average lesion number	Adjusted lesion rate	
	Baseline	8 weeks	24 weeks	Baseline	12 weeks	24 weeks
Ocrevus subcutaneous injection	0.54	0.11	0.00	44.48	0.04	0.00
Ocrevus IV	0.98	0.12	0.00	49.84	0.05	0.00

The safety profile of Ocrevus subcutaneous injection was consistent with the well-established safety profile of Ocrevus IV infusion. No new safety signals were identified for Ocrevus subcutaneous injection. The most common adverse events in the Ocrevus subcutaneous injection group were injection reactions (48% of all exposed patients), all of which were either mild or moderate. The most common AEs in the Ocrevus IV infusion group were infusion-related reactions (17%). A total of 4 and 7 serious AEs were experienced by 3 (2.5%) and 4 (3.4%) patients in the Ocrevus subcutaneous and IV infusion groups, respectively.

The Ocrevus twice-yearly, 10-minute subcutaneous injection is healthcare provider administered and designed to be delivered without the need for IV infrastructure, so it has the potential to expand the usage of Ocrevus in treatment centers without IV infrastructure or those with IV capacity limitations. This provides an additional delivery

option so that Ocrevus can be matched to the individual needs of people with MS and healthcare professionals.

The OCARINA II data will be submitted to health authorities around the world in the coming months. Genentech is committed to advancing innovative clinical research programs to broaden the scientific understanding of MS, further reduce disability progression in RMS and PPMS and improve the treatment experiences for those living with the disease.

About the subcutaneous formulation of Ocrevus (ocrelizumab)

The investigational subcutaneous formulation combines Ocrevus with Halozyme Therapeutics' Enhanze® drug delivery technology.

Ocrevus is a humanized 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.

The Enhanze drug delivery technology is based on a proprietary recombinant human hyaluronidase PH20 (rHuPH20), an enzyme that locally and temporarily degrades hyaluronan – a glycosaminoglycan or chain of natural sugars in the body – in the subcutaneous space. This increases the permeability of the tissue under the skin, allowing space for large molecules like Ocrevus to enter, and enables the subcutaneous formulation to be rapidly dispersed and absorbed into the bloodstream.

Ocrevus IV is the first and only therapy approved for both RMS (including relapsing-remitting MS [RRMS] and active, or relapsing secondary progressive MS [SPMS], in addition to clinically isolated syndrome [CIS] in the U.S.) and PPMS. Ocrevus IV 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 the OCARINA II study

OCARINA II is a Phase III, global, multicenter, randomized study evaluating the pharmacokinetics, safety and radiological and clinical effects of the subcutaneous formulation of Ocrevus compared with Ocrevus intravenous (IV) infusion in 236 patients with relapsing MS (RMS) or primary progressive MS (PPMS). The primary endpoint is non-inferiority in area under the serum concentration time curve (AUC) from day 1 to 12 weeks after subcutaneous injection compared to IV infusion. Secondary endpoints include maximum serum concentration (Cmax) of Ocrevus, the total number of active, gadolinium-enhancing T1 lesions at 8 and 12 weeks, and new or enlarging T2 lesions at

12 and 24 weeks, as well as safety and immunogenicity outcomes. Exploratory endpoints include patient-reported outcomes.

About multiple sclerosis

Multiple sclerosis (MS) is a chronic disease that affects more than 2.8 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 – from 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, in terms of their physical and mental health, and contribute to the negative financial impact on the individual and society. An important goal of treating MS is to slow, stop and ideally prevent disease activity and progression as early as possible.

Relapsing-remitting MS (RRMS) is the most common form of the disease and is characterized 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.

Indications and Important Safety Information

What is Ocrevus?

Ocrevus is a prescription medicine used to treat:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults.

It is not known if Ocrevus is safe or effective in children.

Who should not receive Ocrevus?

Do not receive Ocrevus if you have an active hepatitis B virus (HBV) infection.

Do not receive Ocrevus if you have had a life-threatening allergic reaction to Ocrevus. Tell your healthcare provider if you have had an allergic reaction to Ocrevus or any of its ingredients in the past.

What is the most important information I should know about Ocrevus?

Ocrevus can cause serious side effects, including:

- Infusion reactions: Infusion reactions are a common side effect of Ocrevus, which can be serious and may require you to be hospitalized. You will be monitored during your infusion and for at least 1 hour after each infusion of Ocrevus for signs and symptoms of an infusion reaction. Tell your healthcare provider or nurse if you get any of these symptoms:
    - itchy skin
    - rash
    - hives
    - tiredness
    - coughing or wheezing
    - trouble breathing
    - throat irritation or pain
    - feeling faint
    - fever
    - redness on your face (flushing)
    - nausea
    - headache
    - swelling of the throat
    - dizziness
    - shortness of breath
    - fatigue
    - fast heart beat

These infusion reactions can happen for up to 24 hours after your infusion. It is important that you call your healthcare provider right away if you get any of the signs or symptoms listed above after each

infusion.

If you get infusion reactions, your healthcare provider may need to stop or slow down the rate of your infusion.

- Infection:
  - Ocrevus increases your risk of getting upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes infections. Infections are a common side effect, which can be serious. Tell your healthcare provider if you have an infection or have any of the following signs of infection including fever, chills, or a cough that does not go away. Signs of herpes include cold sores, shingles, genital sores, skin rash, pain, and itching. Signs of more serious herpes infection include: changes in vision, eye redness or eye pain, severe or persistent headache, stiff neck, and confusion. Signs of infection can happen during treatment or after you have received your last dose of Ocrevus. Tell your healthcare provider right away if you have an infection. Your healthcare provider should delay your treatment with Ocrevus until your infection is gone.
  - Hepatitis B virus (HBV) reactivation: Before starting treatment with Ocrevus, your healthcare provider will do blood tests to check for hepatitis B viral infection. If you have ever had hepatitis B virus infection, the hepatitis B virus may become active again during or after treatment with Ocrevus. Hepatitis B virus becoming active again (called reactivation) may cause serious liver problems including liver failure or death. Your healthcare provider will monitor you if you are at risk for hepatitis B virus reactivation during treatment and after you stop receiving Ocrevus.
  - Weakened immune system: Ocrevus taken before or after other medicines that weaken the immune system could increase your risk of getting infections.
- Progressive Multifocal Leukoencephalopathy (PML): PML is a rare brain infection that usually leads to death or severe disability, and has been reported with Ocrevus. Symptoms of PML get worse over days to weeks. It is important that you call your healthcare provider right away if you have any new or worsening neurologic signs or symptoms that have lasted several days, including problems with:
  - thinking
  - eyesight
  - strength
  - balance
  - weakness on 1 side of your body
  - using your arms or legs
- Decreased immunoglobulins: Ocrevus may cause a decrease in some types of immunoglobulins. Your healthcare provider will do blood tests to check your blood immunoglobulin levels.

Before receiving Ocrevus, tell your healthcare provider about all of your medical conditions,

including if you:

- have ever taken, take, or plan to take medicines that affect your immune system, or other treatments for MS.
- have ever had hepatitis B or are a carrier of the hepatitis B virus.
- have had a recent vaccination or are scheduled to receive any vaccinations.
    - You should receive any required 'live' or 'live-attenuated' vaccines at least 4 weeks before you start treatment with Ocrevus. You should not receive 'live' or 'live-attenuated' vaccines while you are being treated with Ocrevus and until your healthcare provider tells you that your immune system is no longer weakened.
    - When possible, you should receive any 'non-live' vaccines at least 2 weeks before you start treatment with Ocrevus. If you would like to receive any non-live (inactivated) vaccines, including the seasonal flu vaccine, while you are being treated with Ocrevus, talk to your healthcare provider.
    - If you have a baby and you received Ocrevus during your pregnancy, it is important to tell your baby's healthcare provider about receiving Ocrevus so they can decide when your baby should be vaccinated.
- are pregnant, think that you might be pregnant, or plan to become pregnant. It is not known if Ocrevus will harm your unborn baby. You should use birth control (contraception) during treatment with Ocrevus and for 6 months after your last infusion of Ocrevus. Talk with your healthcare provider about what birth control method is right for you during this time.
    - Pregnancy Registry. There is a pregnancy registry for women who take Ocrevus during pregnancy. If you become pregnant while receiving Ocrevus, tell your healthcare provider right away. Talk to your healthcare provider about registering with the Ocrevus Pregnancy Registry. The purpose of this registry is to collect information about your health and your baby's health. Your healthcare provider can enroll you in this registry by calling 1-833-872-4370 or visiting **https://www.ocrevuspregnancyregistry.com**.
- are breastfeeding or plan to breastfeed. It is not known if Ocrevus passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you take Ocrevus.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of Ocrevus?

Ocrevus may cause serious side effects, including:

- Risk of cancers (malignancies) including breast cancer. Follow your healthcare provider's instructions about standard screening guidelines for breast cancer.
- Inflammation of the colon, or colitis: Tell your healthcare provider if you have any symptoms of colitis, such

as:

- Diarrhea (loose stools) or more frequent bowel movements than usual
- Stools that are black, tarry, sticky or have blood or mucus
- Severe stomach-area (abdomen) pain or tenderness

These are not all the possible side effects of Ocrevus.

Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

For more information, go to **https://www.Ocrevus.com** or call 1-844-627-3887.

Please see additional Important Safety Information throughout and click here for the full **Prescribing Information** and **Medication Guide**.

About Genentech in Neuroscience

Neuroscience is a major focus of research and development at Genentech. Our goal is to pursue groundbreaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases.

Genentech and Roche are investigating more than a dozen medicines for neurological disorders, including MS, spinal muscular atrophy (SMA), neuromyelitis optica spectrum disorder (NMOSD), Alzheimer's, Huntington's, Parkinson's, acute ischemic stroke, Duchenne muscular dystrophy and Angelman syndrome. 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 Genentech

Founded more than 40 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with serious and life-threatening medical conditions. The company, a member of the Roche Group, has headquarters in South San Francisco, California. For additional information about the company, please visit **http://www.gene.com**.

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