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FDA grants Breakthrough Therapy Designation for Roche's Hemlibra in haemophilia A without inhibitors

- **Designation based on phase III HAVEN 3 study demonstrating Hemlibra prophylaxis significantly reduced bleeds compared to no prophylaxis**
- **First medicine to show superior efficacy compared to prior factor VIII prophylaxis in an intra-patient comparison**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to Hemlibra® (emicizumab-kxwh) for people with haemophilia A without factor VIII inhibitors. Breakthrough Therapy Designation is designed to accelerate the development and review of medicines intended to treat a serious condition with preliminary evidence that indicates they may demonstrate a substantial improvement over existing therapies.

"Hemlibra is the first medicine to show superior efficacy compared to factor VIII prophylaxis, the standard of care for people with haemophilia A without inhibitors, in an intra-patient comparison," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We look forward to working with health authorities to make Hemlibra available to people without inhibitors as soon as possible, and we are excited to share this news with the community as we join in celebrating World Hemophilia Day."

This designation is based on data from the phase III HAVEN 3 study in people 12 years or older with haemophilia A without inhibitors. In the study, Hemlibra prophylaxis dosed subcutaneously every week or every two weeks showed a statistically significant and clinically meaningful reduction in treated bleeds compared to no prophylaxis. In an intra-patient comparison, once-weekly Hemlibra prophylaxis was superior to prior factor VIII prophylaxis as demonstrated by a statistically significant and clinically meaningful reduction in treated bleeds. The most common adverse events with Hemlibra were injection site reactions, and no new safety signals were observed. No thrombotic microangiopathy or thrombotic events occurred in this study.

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Hemlibra was granted its first Breakthrough Therapy Designation in September 2015 and was approved by the FDA in November 2017 for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children with haemophilia A with factor VIII inhibitors based on results from the HAVEN 1 and HAVEN 2 studies. Hemlibra was also recently approved by regulatory authorities in other countries around the world, including by the European Commission in February 2018 for routine prophylaxis of bleeding episodes in people with haemophilia A with factor VIII inhibitors.

The Hemlibra development programme reflects Roche's commitment to address clinical unmet needs in the haemophilia A community. Roche and Genentech are proud to support the World Federation of Hemophilia and the global bleeding disorders community as sponsors of World Hemophilia Day. To learn more about World Hemophilia Day and the World Federation of Hemophilia visit http://www.wfh.org/en/whd.

About HAVEN 3 (NCT02847637)

HAVEN 3 is a randomised, multicentre, open-label, phase III study evaluating the efficacy, safety and pharmacokinetics of Hemlibra prophylaxis versus no prophylaxis (episodic/on-demand factor VIII treatment) in people with haemophilia A without inhibitors to factor VIII. The study included 152 patients with haemophilia A (12 years of age or older) who were previously treated with factor VIII therapy either on-demand or for prophylaxis. Patients previously treated with on-demand factor VIII were randomised in a 2:2:1 fashion to receive subcutaneous Hemlibra prophylaxis at 3 mg/kg/wk for 4 weeks, followed by 1.5 mg/kg/wk until the end of study (Arm A), subcutaneous Hemlibra prophylaxis at 3 mg/kg/wk for 4 weeks, followed by 3 mg/kg/2wks until the end of study (Arm B), or no prophylaxis (Arm C). Patients previously treated with factor VIII prophylaxis received subcutaneous Hemlibra prophylaxis at 3 mg/kg/wk for 4 weeks, followed by 1.5 mg/kg/wk until the end of study (Arm D). Episodic treatment of breakthrough bleeds with factor VIII therapy was allowed per protocol.

About Hemlibra (emicizumab)

Hemlibra is a bispecific factor IXa- and factor X-directed antibody. It is designed to bring together factor IXa and factor X, proteins required to activate the natural coagulation cascade and restore the blood clotting process for people with haemophilia A. Hemlibra is a prophylactic (preventative) treatment that can be administered by an injection of a ready-to-use solution under the skin (subcutaneously) once-weekly.
The clinical development programme is assessing the safety and efficacy of Hemlibra and its potential to help overcome current clinical challenges: the short-lasting effects of existing treatments, the development of factor VIII inhibitors and the need for frequent venous access. Hemlibra was created by Chugai

Pharmaceutical Co., Ltd. and is being co-developed by Chugai, Roche and Genentech. It is marketed in the United States as Hemlibra (emicizumab-kxwh) for people with haemophilia A with factor VIII inhibitors, with kxwh as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the US Food and Drug Administration.

About haemophilia A

Haemophilia A is an inherited, serious disorder in which a person's blood does not clot properly, leading to uncontrolled and often spontaneous bleeding. Haemophilia A affects around 320,000 people worldwide,[1,2] approximately 50-60% of whom have a severe form of the disorder.[3] People with haemophilia A either lack or do not have enough of a clotting protein called factor VIII. In a healthy person, when a bleed occurs, factor VIII brings together the clotting factors IXa and X, which is a critical step in the formation of a blood clot to help stop bleeding. Depending on the severity of their disorder, people with haemophilia A can bleed frequently, especially into their joints or muscles.[1] These bleeds can present a significant health concern as they often cause pain and can lead to chronic swelling, deformity, reduced mobility, and long-term joint damage.[4] A serious complication of treatment is the development of inhibitors to factor VIII replacement therapies.[5] Inhibitors are antibodies developed by the body's immune system that bind to and block the efficacy of replacement factor VIII,[6] making it difficult, if not impossible to obtain a level of factor VIII sufficient to control bleeding.

About Roche in haematology

For more than 20 years, Roche has been developing medicines that redefine treatment in haematology. Today, we are investing more than ever in our effort to bring innovative treatment options to people with diseases of the blood. In addition to approved medicines MabThera®/Rituxan® (rituximab), Gazyva®/Gazyvaro® (obinutuzumab), and Venclexta®/Venclyxto™ (venetoclax) in collaboration with AbbVie, Roche's pipeline of investigational haematology medicines includes Tecentriq® (atezolizumab), an anti-CD79b antibody drug conjugate (polatuzumab vedotin/RG7596) and a small molecule antagonist of MDM2 (idasanutlin/RG7388). Roche's dedication to developing novel molecules in haematology expands beyond malignancy, with the development of Hemlibra (emicizumab), a bispecific monoclonal antibody for the treatment of haemophilia A.

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. 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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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