Basel, 5 June 2018

**FDA grants Priority Review to Roche’s Hemlibra for people with haemophilia A without factor VIII inhibitors**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has accepted the company’s supplemental Biologics License Application (sBLA) and granted Priority Review for Hemlibra* (emicizumab-kxwh) for adults and children with haemophilia A without factor VIII inhibitors. The sBLA is based on data from the phase III HAVEN 3 study. The FDA is expected to make a decision on approval by 4 October 2018.

“People with haemophilia A can face significant challenges in managing their condition and may need to adapt their daily lives to avoid bleeds and accommodate treatment,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We believe the FDA’s decision to grant Priority Review to Hemlibra underscores its potential to improve the standard of care for people without factor VIII inhibitors and to help reduce treatment burden by offering more flexible subcutaneous dosing options. We look forward to working with the FDA to hopefully bring Hemlibra to all people with haemophilia A as quickly as possible.”

In the HAVEN 3 study, adults and adolescents aged 12 years or older with haemophilia A without factor VIII inhibitors who received Hemlibra prophylaxis every week or every two weeks showed a 96% \( (p<0.0001) \) and 97% \( (p<0.0001) \) reduction in treated bleeds, respectively, compared to those who received no prophylaxis. In an additional arm of the study, people who had previously received factor VIII prophylaxis in a non-interventional study switched to Hemlibra prophylaxis, allowing for an intra-patient comparison of two prophylaxis regimens. Based on the intra-patient comparison, Hemlibra demonstrated a statistically significant reduction of 68% \( (p<0.0001) \) in treated bleeds, making it the first medicine to show superior efficacy to prior treatment with factor VIII prophylaxis, the standard of care. There were no unexpected or serious adverse events (AEs) related to Hemlibra in the HAVEN 3 study, and the most common AEs were consistent with previous studies. The most common AEs occurring in 5% or more of people in the HAVEN 3 study were injection site reactions, joint pain (arthralgia), common cold symptoms (nasopharyngitis), headache, upper respiratory tract infection and influenza. Results from the HAVEN 3 study were presented at the World Federation of Hemophilia (WFH) 2018 World Congress in May.
Priority Review designation is granted to medicines that the FDA has determined to have the potential to provide significant improvements in the treatment, prevention or diagnosis of a serious disease. The FDA granted Breakthrough Therapy Designation for Hemlibra in people with haemophilia A without factor VIII inhibitors in April 2018 based on data from the HAVEN 3 study. Breakthrough Therapy Designation is designed to expedite the development and review of medicines intended to treat a serious condition with preliminary evidence that indicates they may demonstrate substantial improvement over existing therapies. Data from the HAVEN 3 study have also been submitted for approval consideration to the European Medicines Agency. Submissions with other regulatory authorities around the world are ongoing.

Hemlibra 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.

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 factor VIII inhibitors. 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 for at least 24 weeks (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.

In the phase III HAVEN 3 study, adults and adolescents aged 12 years or older without factor VIII inhibitors who received Hemlibra prophylaxis every week or every two weeks showed a 96% (p<0.0001) and 97% (p<0.0001) reduction in treated bleeds, respectively, compared to those who received no prophylaxis.
In addition, 55.6% (95% CI: 38.1, 72.1) of people treated with Hemlibra every week and 60% (95% CI: 42.1, 76.1) of people treated with Hemlibra every two weeks experienced zero treated bleeds, compared to 0% (95% CI: 0.0; 18.5) of people treated with no prophylaxis. Importantly, in an intra-patient comparison in patients who were previously enrolled in a prospective non-interventional study (NIS), once-weekly Hemlibra prophylaxis showed superior efficacy compared to prior factor VIII prophylaxis, the standard of care for people with haemophilia A without factor VIII inhibitors, as demonstrated by a 68% reduction (p<0.0001) in treated bleeds.

There were no unexpected or serious adverse events (AEs) related to Hemlibra, and the most common AEs were consistent with previous studies. No thrombotic events or cases of thrombotic microangiopathy were observed. The most common AEs occurring in 5% or more of people in the HAVEN 3 study were injection site reactions, joint pain (arthralgia), common cold symptoms (nasopharyngitis), headache, upper respiratory tract infection and influenza.

**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, approximately 50-60% of whom have a severe form of the disorder. 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. 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. A serious complication of treatment is the development of inhibitors to factor VIII replacement therapies. Inhibitors are antibodies developed by the body’s immune system that bind to and block the efficacy of replacement factor VIII, 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. All trademarks used or mentioned in this release are protected by law.

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