Media & Investor Release

CHMP recommends expansion of EU label for Hemlibra to include people with moderate haemophilia A

- **The positive CHMP opinion is based on the results of the HAVEN 6 study, which demonstrated effective bleed control and a favourable safety profile of Hemlibra in people with moderate haemophilia A without inhibitors[1]**
- **Given that many people with moderate haemophilia A may not receive prophylaxis, they may endure a worsened clinical burden with only 15% living a bleed-free life[2]**
- **If approved, Hemlibra, already approved for severe haemophilia A in the EU, will offer an effective and convenient prophylactic treatment option with a favourable safety profile for people with moderate haemophilia A**

Basel, 16 December 2022 - Roche (SIX: RO, ROG; OTCQZ: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended expansion of the Hemlibra® (emicizumab) European Union (EU) marketing authorisation. If approved, Hemlibra would also be indicated for the routine prophylaxis of bleeding episodes in people with haemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors, who have moderate disease (FVIII ≥1% and ≤ 5%) with a severe bleeding phenotype. It is estimated that people with moderate haemophilia A make up 14% of the haemophilia A population.[3]

"We know that people with moderate haemophilia A can still have bleeds that cause irreversible joint damage and impact quality of life," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We're very pleased that the CHMP's recommendation brings us closer to potentially transforming the day-to-day lives of people in the EU living with moderate haemophilia A."

While the treatment and management of severe haemophilia A are well-established, there is less information and guidance on prophylaxis for moderate haemophilia A.[4] Additionally, the severity of haemophilia A, traditionally measured by factor VIII levels, is not always reflective of bleeding behaviour. Some people with non-severe haemophilia may experience symptoms similar to those with severe haemophilia and would benefit from prophylaxis.[5] All severities of haemophilia A may significantly reduce the quality of life for people affected, as well as their family and caregivers. [6] Given that many people with moderate haemophilia A may not receive prophylactic treatments, they may endure a worsened clinical burden, with 85% having bleeds within their lifetime. This can lead to long-term joint problems, requiring interventions and impacting quality of life.[2,4,5]

The CHMP recommendation is based on the results from the phase III HAVEN 6 study, as well as on real world data. The results from the study showed that Hemlibra demonstrated effective bleed control and a favourable safety profile in people with non-severe haemophilia A without factor VIII inhibitors, where prophylaxis was clinically indicated.[1] A final decision regarding the approval of Hemlibra is expected from the European Commission in the near future. If approved, this update will provide an effective and convenient prophylactic treatment option with a favourable safety profile, for people in the EU with moderate haemophilia A with a severe bleeding phenotype.

Hemlibra is approved as a treatment for people with haemophilia A with factor VIII inhibitors in more than 110 countries worldwide and for people without factor VIII inhibitors in more than 100 countries worldwide. It has been studied in one of the largest clinical trial programmes in people with haemophilia A with and without factor VIII inhibitors, including eight phase III studies.

About HAVEN 6

HAVEN 6 is a phase III clinical study designed to evaluate the safety, efficacy, pharmacokinetics and pharmacodynamics of Hemlibra in people with non-severe haemophilia A without factor VIII inhibitors. Data from the primary analysis of HAVEN 6 was presented at the 30th International Society on Thrombosis and Haemostasis (ISTH) Annual Congress, on 11 July 2022.[1] The analysis included data from 72 participants, including three women, 51 (70.8%) of whom had moderate haemophilia A without factor VIII inhibitors. The data indicate that Hemlibra has effective bleed control and a favourable safety profile in people with non-severe haemophilia A without factor VIII inhibitors, with no new safety signals identified. Hemlibra achieved clinically meaningful bleed control, with 66.7% of participants experiencing no bleeds that required treatment, 81.9% experiencing no spontaneous bleeds that required treatment, and 88.9% experiencing no joint bleeds that required treatment.[1]

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 involved in 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, every two weeks, or every four weeks (after an initial once-weekly dose for the first four weeks). Hemlibra was created by Chugai Pharmaceutical Co., Ltd. and is being co-developed globally by Chugai, Roche and Genentech. It is marketed in the United States by Genentech as Hemlibra (emicizumab-kxwh), with kxwh as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. 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 900,000 people worldwide,[7,8] approximately 14% of whom have a moderate form of the disorder.[3] However, the severity of haemophilia A is not always reflective of bleeding behaviour, as some people with non-severe haemophilia may experience symptoms similar to those with severe haemophilia and warrant prophylaxis.[5] All severities of haemophilia A can significantly reduce the quality of life for people affected, as well as their family and caregivers. 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 symptoms, people with haemophilia A can bleed frequently, especially into their joints or muscles.[3] 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.[9] 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.[7]

About Roche in haematology

Roche has been developing medicines for people with malignant and non-malignant blood diseases for more than 20 years; our experience and knowledge in this therapeutic area runs deep. Today, we are investing more than ever in our effort to bring innovative treatment options to patients across a wide range of haematologic diseases. Our approved medicines include MabThera®/Rituxan® (rituximab), Gazyva®/Gazyvaro® (obinutuzumab), Polivy® (polatuzumab vedotin), Venclexta®/Venclyxto® (venetoclax) in collaboration with AbbVie, Hemlibra® (emicizumab) and Lunsumio® (mosunetuzumab). Our pipeline of investigational haematology medicines includes T-cell engaging bispecific antibodies glofitamab, targeting both CD20 and CD3, and cevostamab, targeting both FcRH5 and CD3; Tecentriq® (atezolizumab), a monoclonal antibody designed to bind with PD-L1 and crovalimab, an anti-C5 antibody engineered to optimise complement inhibition. Our scientific expertise, combined with the breadth of our portfolio and pipeline, also provides a unique opportunity to develop combination regimens that aim to improve the lives of patients even further.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each

person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognizing our endeavor to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

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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