Media & Investor Release

Interim data from phase III study presented at ASH 2022 show Hemlibra achieved meaningful bleed control in infants from birth

- **The HAVEN 7 study was designed to further confirm the benefit of preventative treatment (prophylaxis) with Hemlibra from birth in previously untreated or minimally treated infants with severe haemophilia A without inhibitors**
- **In the study, 77.8% of participants had no bleeding episodes that required treatment[1]**
- **In addition, real-world efficacy and safety data from the EUHASS database and ATHN 7 study were also presented [2,3]**

Basel, 11 December 2022 – Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced interim results from the phase III HAVEN 7 study. The study shows Hemlibra® (emicizumab) achieved meaningful bleed control with a favourable safety profile in infants (up to 12 months) with severe haemophilia A, without factor VIII inhibitors: 77.8% of participants did not have any bleeds that required treatment and 42.6% did not have any treated or untreated bleeds at all.[1] These results help support the use of Hemlibra in this population, in which it is already approved in many countries around the world. The new data were presented at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition taking place in New Orleans from 10-13 December 2022.

The burden of severe haemophilia A in infants and on their parents and caregivers is significant. The World Federation of Haemophilia treatment guidelines consider the standard of care in haemophilia to be regular prophylaxis initiated at a young age, as studies have shown that early prophylaxis improves long-term outcomes, while reducing the risk of intracranial haemorrhage. [4-6] However, for many infants with haemophilia A, prophylaxis is not started until after the first year of life because of the high treatment burden.[7-11] Hemlibra provides a flexible treatment option that can be administered subcutaneously from birth at different dosing frequencies.

“These initial results support the benefit of starting Hemlibra from birth given that early preventative treatment is essential in infants,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “Haemophilia can substantially reduce quality of life for those affected, starting at infancy, which is especially distressing for parents and caregivers. We continue to explore Hemlibra's potential benefits to a broad range of people with haemophilia A.”

HAVEN 7 is a phase III, multi-centre, open-label study evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of Hemlibra in infants with severe haemophilia A without factor VIII inhibitors. The results of this interim analysis, which included data from 54

participants, showed that 77.8% of participants (n=42) did not have any bleeds which required treatment, while 42.6% (n=23) did not have any treated or untreated bleeds at all. There were no treated spontaneous bleeds in any participants, and all treated bleeds were traumatic. A total of 77 bleeds occurred in 31 participants (57.4%); 88.3% were traumatic. Mean model-based annualised bleeding rate (ABR) (95% CI) at the time of interim analysis was 0.4 (0.23–0.65) for treated bleeds. [1]

Hemlibra's safety profile was consistent with previous studies, with no new safety signals observed. Nine people (16.7%) reported a Hemlibra-related adverse event (AE), all of which were local injection site reactions. Eight participants (14.8%) reported 12 serious AEs, unrelated to Hemlibra. There were no deaths, thromboembolic events or cases of thrombotic microangiopathy, reinforcing Hemlibra's favourable safety profile. No intracranial haemorrhages occurred.[1]

Primary analysis will be conducted at 52 weeks. The study also has an additional seven-year follow-up period to collect long-term data such as safety and joint health outcomes, further building upon our understanding of the benefit of Hemlibra in this population.

EUHASS database and ATHN 7 study

Roche also presented data from the European Haemophilia Safety Surveillance (EUHASS) database and the prospective observational ATHN 7 study at ASH 2022. Data from EUHASS, which collects real-world safety data on treatments for inherited disorders, showed the safety profile of Hemlibra in people with haemophilia A was favourable and consistent with clinical trial data. [2] Data from ATHN 7, exploring the efficacy of Hemlibra in women with haemophilia A, showed two of the three female participants had no bleeds; the third had one treated bleed associated with a dental procedure and one untreated bleed associated with menses. Ongoing evaluation is vital to further understand the safety and efficacy profile of Hemlibra in this rare and under-represented population.[3]

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 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, [4,12] approximately 14% and 48% of whom have a moderate or mild form of the disorder,[13] respectively. 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.[14] 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. [13] 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.[15] 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.[4]

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 recognising 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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