

Basel, 20 November 2017

Roche's Hemlibra significantly reduced bleeds in phase III study in haemophilia A

- **HAVEN 3 study met primary endpoint and key secondary endpoints**
- **Intra-patient comparison demonstrated superiority of Hemlibra prophylaxis compared to prior factor VIII prophylaxis**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the phase III HAVEN 3 study evaluating Hemlibra® (emicizumab) in adults and adolescents (aged 12 years or older) with haemophilia A without inhibitors to factor VIII. The study met its primary endpoint, showing a statistically significant and clinically meaningful reduction in the number of treated bleeds over time in people receiving Hemlibra prophylaxis every week compared to those receiving no prophylaxis. The study also met key secondary endpoints, including a statistically significant and clinically meaningful reduction in the number of treated bleeds over time with Hemlibra prophylaxis dosed every two weeks compared to no prophylaxis. Importantly, once-weekly Hemlibra prophylaxis was superior to factor VIII prophylaxis, as demonstrated by a statistically significant and clinically meaningful reduction in treated bleeds in an intra-patient comparison of patients receiving Hemlibra prophylaxis compared to their prior factor VIII prophylaxis. The most common adverse events with Hemlibra were injection site reactions, with no new safety signals observed. No thrombotic microangiopathy or thrombotic events occurred in this study.

“Hemlibra is the first product to show superior efficacy to factor VIII prophylaxis. These results in people with haemophilia A without inhibitors represent the next step forward in our clinical trial programme, which includes the positive HAVEN 1 and interim HAVEN 2 data in people with inhibitors,” 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 this treatment available for all people with haemophilia A as soon as possible.”

“It is well established that prophylaxis is the preferred approach for treatment of haemophilia A, but this can require frequent intravenous infusions, and some patients on prophylaxis can still experience bleeds, while others prefer on-demand treatment,” said Johnny Mahlangu, Faculty of Health Sciences, University of the Witwatersrand and NHLS, Johannesburg, South Africa. “Given its potential to be dosed through subcutaneous injection only once weekly or every other week, Hemlibra may provide a further effective prophylactic treatment option for more people with haemophilia A and help alleviate some of the administration burden associated with current treatment.”

Data from the HAVEN 3 study will be presented at an upcoming medical meeting and submitted to health authorities around the world for approval consideration. These results add to the growing body of evidence shown in the inhibitor population and support that Hemlibra may benefit all people with haemophilia A regardless of inhibitor status. Data from the HAVEN 1 and HAVEN 2 studies supported the recent US Food and Drug Administration approval of Hemlibra for adults and children with haemophilia A with inhibitors, and are being reviewed under accelerated assessment by the European Medicines Agency.

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 haemophilia A patients. Hemlibra is a prophylactic (preventative) treatment that can be administered by an injection of a ready-to-use solution under the skin (subcutaneously).

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 patients with factor VIII inhibitors, with kxwh as the suffix designated in compliance 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 In addition to impacting a person's quality of life,⁵ these bleeds can be life threatening if they go into vital organs, such as the brain.^{6,7}

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 2016 employed more than 94,000 people worldwide. In 2016, Roche invested CHF 9.9 billion in R&D and posted sales of CHF 50.6 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.

Roche Group Media Relations

Phone: +41 -61 688 8888 / e-mail: media.relations@roche-global.com

- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow

References

- ¹ WFH. Guidelines for the management of hemophilia. [Internet; cited 2012]. Available from: <http://www1.wfh.org/publications/files/pdf-1472.pdf>
- ² Berntorp E, Shapiro AD. Modern haemophilia care. *The Lancet* 2012; 370:1447-1456.
- ³ Marder VJ, et al. Hemostasis and Thrombosis. Basic Principles and Clinical Practice. 6th Edition, 2013. Milwaukee, Wisconsin. Lippincott Williams and Wilkin.
- ⁴ Franchini M, Mannucci PM. Hemophilia A in the third millennium. *Blood Rev* 2013; 179-84.
- ⁵ Flood, E et al. Illustrating the impact of mild/moderate and severe haemophilia on health-related quality of life: hypothesised conceptual models. *European Journal of Haematology* 2014; 93: Suppl. 75, 9–18.
- ⁶ Young G. New challenges in hemophilia: long-term outcomes and complications. *Hematology Am Soc Hematol Educ Program* 2012. 2012; 362–8.
- ⁷ Zanon E, Iorio A, Rocino A, et al. Intracranial haemorrhage in the Italian population of haemophilia patients with and without inhibitors. *Haemophilia* 2012; 18: 39–45.