Basel, 17 April 2017

Roche announces positive interim results for emicizumab in phase III study of children with haemophilia A

- Emicizumab prophylaxis reduced the number of bleeds in children with haemophilia A and inhibitors to factor VIII
- Results build upon data for emicizumab in adults and adolescents with haemophilia A and inhibitors to factor VIII

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today interim results from the phase III HAVEN 2 study evaluating emicizumab prophylaxis in children less than 12 years of age with haemophilia A and inhibitors to factor VIII. At this interim analysis after a median of 12 weeks of treatment, emicizumab prophylaxis showed a clinically meaningful reduction in the number of bleeds over time. These findings are consistent with results from the phase III HAVEN 1 study in adults and adolescents (12 years of age or older) with haemophilia A and inhibitors to factor VIII, in which emicizumab prophylaxis showed a statistically significant and clinically meaningful reduction in the number of bleeds over time compared to no prophylaxis, as well as compared to prior prophylaxis with bypassing agents. The most common adverse events with emicizumab in the HAVEN2 study were injection site reactions and nasopharyngitis.

“Managing haemophilia A with inhibitors to factor VIII is especially challenging for children and their caregivers, because bleeding is difficult to control and current treatments require frequent intravenous infusions”, said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development.

“We are encouraged that once-weekly subcutaneous emicizumab prophylaxis showed a clinically meaningful reduction in the number of bleeds over time in children and are pleased to share these results with the community as we join in celebrating World Hemophilia Day.”
HAVEN 2 is the second phase III study in the emicizumab clinical development programme to report results. Data from both HAVEN 1 and the interim data from HAVEN 2 studies will be presented at an upcoming medical meeting and submitted to health authorities for approval consideration.

Two additional phase III studies of emicizumab are ongoing:

- HAVEN 3, evaluating emicizumab prophylaxis dosed once weekly or once every other week in people 12 years of age or older with haemophilia A without inhibitors to factor VIII.
- HAVEN 4, evaluating emicizumab prophylaxis dosed every four weeks in people 12 years of age or older with haemophilia A with or without inhibitors to factor VIII.

The development programme for emicizumab reflects Roche’s commitment to help address clinical unmet needs in the treatment of haemophilia A. As part of this commitment, 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](http://www.wfh.org/en/whd).

**About HAVEN 2 (NCT02795767)**

HAVEN 2 is a single-arm, multicentre, open-label, phase III study evaluating the efficacy, safety, and pharmacokinetics of once weekly subcutaneous administration of emicizumab. The interim analysis after a median of 12 weeks of treatment included 19 children less than 12 years of age with haemophilia A and inhibitors to factor VIII, who require treatment with bypassing agents. The objectives of the study are to evaluate the number of bleeds over time with emicizumab prophylaxis, safety, pharmacokinetics, health-related quality of life (HRQoL) and proxy HRQoL with aspects of caregiver burden. The study will enrol a total of 60 children for its final analysis planned after 52 weeks of treatment with emicizumab.

**About HAVEN 1 (NCT02622321)**

HAVEN 1 is a randomised, multicentre, open-label, phase III study evaluating the efficacy, safety, and pharmacokinetics of emicizumab prophylaxis versus no prophylaxis in people with haemophilia A and inhibitors to factor VIII. The study included 109 patients with haemophilia A (12 years of age or older) with inhibitors to factor VIII, who were previously treated with episodic or prophylactic bypassing agents. Patients previously treated with episodic bypassing agents were randomised in a 2:1 fashion to receive emicizumab prophylaxis (Arm A) or no prophylaxis (Arm B). Patients previously treated prophylactically with bypassing agents received emicizumab prophylaxis (Arm C).
Episodic treatment of breakthrough bleeds with bypassing agents was allowed per protocol. The primary endpoint of the study is the number of bleeds over time with emicizumab prophylaxis (Arm A) versus no prophylaxis (Arm B). Secondary endpoints include all bleed rate, joint bleed rate, spontaneous bleed rate, target joint bleed rate, health-related quality of life (HRQoL)/ health status, intra-patient comparison to bleed rate on their prior prophylaxis regimen with bypassing agents (Arm C) and safety. As previously reported, the study showed a statistically significant reduction in the number of bleeds over time in people treated with emicizumab prophylaxis compared to those receiving no prophylactic treatment. The study also met all secondary endpoints, including a statistically significant reduction in the number of bleeds over time with emicizumab prophylaxis treatment in an intra-patient comparison in people who had received prior bypassing agent prophylaxis treatment. The most common adverse event with emicizumab was injection site reactions, consistent with prior studies.

**About emicizumab (ACE910)**

Emicizumab is an investigational bispecific monoclonal antibody designed to bring together factors IXa and X, proteins required to activate the natural coagulation cascade and restore the blood clotting process. Emicizumab can be administered by an injection of a ready-to-use solution under the skin (subcutaneously) once weekly. Emicizumab is being evaluated in pivotal phase III studies in people 12 years of age and older, both with and without inhibitors to factor VIII, and in children under 12 years of age with factor VIII inhibitors. Additional trials are exploring less frequent dosing schedules. The clinical development programme is assessing the safety and efficacy of emicizumab 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. Emicizumab was created by Chugai Pharmaceutical Co., Ltd. and is being co-developed by Chugai, Roche and Genentech.

**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\(^1\), 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.\(^6,7\) A serious complication of treatment is the development of inhibitors to factor VIII replacement therapies.\(^8\) Inhibitors are antibodies developed by the body’s immune system that bind to and block the efficacy of replacement factor VIII\(^9\), 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 the investigational haemophilia A treatment emicizumab (ACE910).

**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 for improving patient access to medical innovations by working with all relevant stakeholders. Twenty-nine 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 eight 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.

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References