Media Release

Roche presents a broad range of data for Hemlibra demonstrating continued benefits for people with haemophilia A at the ISTH 2019 Congress

- **New analyses from phase III HAVEN studies support Hemlibra's sustained efficacy, safety and quality of life benefit in people with haemophilia A, with and without factor VIII inhibitors**
- **First data of phase IIIb STASEY study reinforces safety profile of Hemlibra seen in pivotal HAVEN 1 clinical trial**
- **New analysis of pivotal data suggests additional factor treatment may not be needed for people on Hemlibra undergoing certain minor surgeries**

Basel, 9 July 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced new data for Hemlibra® (emicizumab) across multiple pivotal studies in people with haemophilia A with and without factor VIII inhibitors at the International Society on Thrombosis and Haemostasis (ISTH) 2019 Congress on 6-10 July in Melbourne, Australia. In total, Roche presented 21 abstracts from its haemophilia programme, including five oral presentations. Further data from the four pivotal HAVEN clinical trials were presented, demonstrating the long-term safety, efficacy and quality of life benefit of Hemlibra in people with haemophilia A with and without factor VIII inhibitors. Roche also presented the first interim analysis from the phase IIIb STASEY study, reinforcing the safety profile of Hemlibra in adults and adolescents (aged 12 years or older) with haemophilia A with factor VIII inhibitors seen in the HAVEN 1 clinical trial.

"Data presented at ISTH continues to reinforce Hemlibra's potential to redefine the standard of care for people living with haemophilia A," said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. "We are particularly excited to present the first interim analysis of safety data from the STASEY study, which adds to the growing body of evidence supporting Hemlibra as an important treatment option for people with haemophilia A."

Long-term efficacy, safety and quality of life data show sustained benefit of Hemlibra
Updated data from the pooled HAVEN studies (HAVEN 1, HAVEN 2, HAVEN 3 and HAVEN 4; n=400), in people with haemophilia A of all ages with and without factor VIII inhibitors, showed that a high proportion of patients experienced zero treated bleeds on Hemlibra, and that this was maintained over a median of 83 weeks. Across all four HAVEN studies, over 87% of participants had no treated joint bleeds (either spontaneous or due to injury/trauma) and over 92% of participants experienced no spontaneous bleeds in each interval from week 25. Hemlibra's established safety and tolerability profile was maintained.

Additionally, updated data from the HAVEN 3 and HAVEN 4 studies demonstrate that Hemlibra prophylaxis offers a clinically meaningful improvement in long-term health-related quality of life, versus previous episodic or prophylactic factor VIII treatment, for people with haemophilia A with and without factor VIII inhibitors as measured by the Haem-A-QoL questionnaire. In the 28 days prior to starting treatment with Hemlibra, 76% and 79% of employed patients from HAVEN 3 and HAVEN 4 studies, respectively, reported no missed days of work. At week 25 of HAVEN 3 and HAVEN 4, 91% and 93% of

participants reported no missed workdays, respectively, with these figures remaining stable thereafter.

Interim data from the STASEY study reinforce Hemlibra's safety profile
Results from the first interim analysis of the phase IIIb STASEY study, including data from 88 patients, reinforce the safety profile of Hemlibra characterised in the pivotal HAVEN 1 study. HAVEN 1 has formed the basis of Hemlibra's approval in people with haemophilia A with factor VIII inhibitors in over 70 countries worldwide to date. In the STASEY study, in people with haemophilia A with factor VIII inhibitors, no cases of thrombotic microangiopathy or thrombotic events were reported and no new safety signals were identified. Eighteen (20.5%) patients reported a Hemlibra-related adverse event (AE), of which one was a serious AE (catheter site abscess). The most common AEs, occurring in 10% or more of people in the STASEY study were injection site reactions (14.8%), joint pain (arthralgia; 13.6%), headache (11.4%) and common cold symptoms (nasopharyngitis; 11.4%). Bleeding rates in people with haemophilia A with factor VIII inhibitors receiving Hemlibra in the STASEY study were also in line with previously reported observations from the HAVEN 1 study.

Additional factor treatment may not be needed for people on Hemlibra undergoing certain minor surgeries
A retrospective analysis of pooled data across the HAVEN studies indicates that people with haemophilia A with and without factor VIII inhibitors had a reduced need for preventative (prophylactic) coagulation factor (factor VIII replacement therapy or bypassing agents) when undergoing certain minor surgeries. The majority of minor surgeries (n=215) were performed without prophylactic coagulation factor (n=141; 65.6%), and of these, 90.8% did not result in a treated post-operative bleed. Of the 18 major surgeries, three were managed without prophylactic coagulation factor, with no post-operative bleeds. The remaining 15 major surgeries were managed with prophylactic coagulation factor, only one of which resulted in a treated post-operative bleed.

Hemlibra regulatory status
Hemlibra is approved for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in people with haemophilia A with factor VIII inhibitors in over 70 countries worldwide, based on the results of the pivotal HAVEN 1 and HAVEN 2 studies. This includes the US in November 2017, EU member states in February 2018 and Japan in March 2018. Hemlibra has also been approved in people with haemophilia A without factor VIII inhibitors in over 40 countries worldwide, based on results from the pivotal HAVEN 3 and HAVEN 4 studies. This includes the US in October 2018, EU member states in March 2019 and Japan in December 2018. Submissions to other regulatory authorities around the world are ongoing.

About the HAVEN clinical trial programme
The HAVEN clinical trial programme is one of the largest pivotal clinical trial programmes in haemophilia A, designed to assess the efficacy and safety of Hemlibra in people with and without factor VIII inhibitors, 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.

- HAVEN 1 is a randomised, multicentre, open-label, phase III study evaluating the efficacy, safety and pharmacokinetics of once-weekly subcutaneous administration of Hemlibra prophylaxis compared to no

prophylaxis in adults and adolescents (12 years of age and older) with haemophilia A with inhibitors to factor VIII, who were previously treated with bypassing agents on-demand or as prophylaxis.

- HAVEN 2 is a multicentre, open-label, clinical study in children younger than 12 years of age with haemophilia A with factor VIII inhibitors. The study is evaluating the efficacy, safety and pharmacokinetics of once weekly, every two weeks or every four weeks subcutaneous administration of Hemlibra prophylaxis.
- HAVEN 3 is a randomised, multicentre, open-label, phase III study evaluating the efficacy, safety and pharmacokinetics of Hemlibra prophylaxis once weekly or every two weeks versus no prophylaxis (episodic/on-demand factor VIII treatment) in people (12 years of age or older) with haemophilia A without factor VIII inhibitors, who were previously treated with factor VIII therapy either on-demand or as prophylaxis.
- HAVEN 4 is a single-arm, multicentre, open-label, phase III study evaluating the efficacy, safety and pharmacokinetics of subcutaneous administration of Hemlibra dosed every four weeks. The study included adults and adolescents (12 years of age or older) with haemophilia A with or without factor VIII inhibitors who were previously treated with either factor VIII or bypassing agents, on-demand or as prophylaxis.

About STASEY

STASEY is a single-arm, multicentre, open-label, phase IIIb clinical trial to evaluate the safety and tolerability of Hemlibra prophylaxis in people with haemophilia A with factor VIII inhibitors. The study included 88 patients (12 years of age or older) who had completed 24 weeks on study or discontinued, receiving subcutaneous Hemlibra 3 mg/kg/week for four weeks, followed by 1.5 mg/kg/week for the remainder of the treatment period. In the STASEY study:

- No cases of thrombotic microangiopathy or thrombotic events were reported.
- Eighteen (20.5%) patients reported a Hemlibra-related adverse event, of which one was a serious AE (catheter site abscess). The most common adverse events (AE) occurring in 10% or more of people in the STASEY study were injection site reactions (14.8%), joint pain (arthralgia; 13.6%), headache (11.4%) and common cold symptoms (nasopharyngitis; 11.4%).
- The rates of treated, all, spontaneous, joint, and target joint bleeds were low, with 71 patients experiencing zero treated bleeds (80.7%).
- Of 17 patients who received treatment for a spontaneous or traumatic bleed, 16 received recombinant factor VIIa and one received factor VIII. No thrombotic events or thrombotic microangiopathy were seen with concomitant bypassing agents or factor VIII.

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, 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 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] A serious complication of treatment is the development of inhibitors to factor VIII replacement therapies. [5] Inhibitors are antibodies developed by the body's immune system that bind to and block the efficacy of replacement factor VIII, [6] making it difficult, if not impossible to obtain a level of factor VIII sufficient to control bleeding.

About Roche in haematology

Roche has been developing medicines for people with malignant and non-malignant blood diseases for over 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-piiq), Venclexta®/Venclyxto® (venetoclax) in collaboration with AbbVie, and Hemlibra® (emicizumab). Our pipeline of investigational haematology medicines includes idasanutlin, a small molecule which inhibits the interaction of MDM2 with p53; T-cell engaging bispecific antibodies targeting both CD20 and CD3, and Tecentriq® (atezolizumab), a monoclonal antibody designed to bind with PD-L1. 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

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. Moreover, for the tenth consecutive year, Roche has been recognised as

the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 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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