Media Release

Roche announces new data at the ISTH 2020 Congress, demonstrating ongoing commitment to advancing care for people with haemophilia A

- **Spark Therapeutics will present data from the initial dose cohorts of its phase I/II SPK-8011 gene therapy study, showing stable and durable factor VIII expression, substantial improvement in annualised bleed rate for more than two years, and an acceptable safety profile after more than two years of follow-up[1]**
- **Roche will present second interim analysis results from the phase IIIb STASEY study, reinforcing the safety and efficacy profile of Hemlibra in people with haemophilia A with factor VIII inhibitors seen in phase III HAVEN studies[2,3,4]**
- **First clinical data from the phase III HAVEN 5 study in people with haemophilia A in the Asia-Pacific region, demonstrating that Hemlibra prophylaxis resulted in a statistically significant reduction in treated bleeds compared to no prophylaxis[5]**
- **Preliminary analysis from CHESS II, a socioeconomic survey, providing insights into the clinical outcomes and burdens of living with haemophilia A**

Basel, 29 June 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that new data from its haemophilia A clinical programme will be presented at the International Society on Thrombosis and Haemostasis (ISTH) 2020 Congress on 12-14 July 2020. Data will include updated safety results from the phase IIIb STASEY study of Hemlibra® (emicizumab) and new results from the phase III HAVEN 5 study of Hemlibra. Data will also include insights into the impact of living with haemophilia A. Spark Therapeutics (a member of the Roche Group) will also present data from the initial dose cohorts of its phase I/II SPK-8011 gene therapy study.

"We are excited to share updated data from our combined haemophilia A programme at this year's virtual ISTH 2020," said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. "These data exemplify our efforts to increase our knowledge and capabilities in haemophilia A, including in the context of gene therapy, with the goal of advancing care and providing innovative treatment approaches for people living with this chronic condition."

SPK-8011 data presentation

Data from the initial dose cohorts of Spark's phase I/II SPK-8011 gene therapy study in haemophilia A will be presented at the congress. Updated data from five participants in the initial dose cohorts, who are up to 142 weeks post-vector infusion, show stable and durable factor VIII expression and a 91% reduction in annualised bleed rate (ABR). There is no evidence of decline in factor VIII expression after more than two years of follow up.[1]

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These data indicate an acceptable safety profile, with no development of factor VIII inhibitors. Furthermore, they represent the longest stable expression of factor VIII following gene transfer and support the use of adeno-associated virus-mediated (AAV-mediated), liver directed gene therapy to achieve durable factor VIII expression for the treatment of haemophilia A.[1]

Key Hemlibra data presentations
Data for Hemlibra will be featured in four poster presentations at the congress. This further supports the comprehensive body of clinical evidence available for Hemlibra, including from the HAVEN studies – the most extensive clinical development programme in haemophilia A. This includes results from the second interim analysis of the phase IIIb STASEY study, evaluating the safety and tolerability of Hemlibra prophylaxis in people with haemophilia A with factor VIII inhibitors.

Further data from the STASEY study to be presented outline surgical experiences in the trial, as well as additional insights into the pharmacokinetics and pharmacodynamics profile of Hemlibra.

Roche will also share the first clinical data from the phase III HAVEN 5 study, evaluating the efficacy, safety and pharmacokinetics of Hemlibra in 70 people with haemophilia A with and without factor VIII inhibitors in the Asia-Pacific region. The study met its primary endpoint, demonstrating that Hemlibra prophylaxis dosed every week or every four weeks resulted in a statistically significant 96% ($p<0.0001$) reduction in the number of treated bleeds over time compared to those receiving no prophylaxis.[5] In addition, all secondary bleed-related endpoints were met with clinically meaningful results. Overall, this study showed that Hemlibra was effective and well tolerated in this population.[5] HAVEN 5 was conducted as part of the post-approval agreement with the Chinese health authorities to provide supportive data in people with haemophilia A in China, and was expanded to enrol patients from other Asia-Pacific countries.

Key data presentations on impact of haemophilia A
Roche will also present two analyses providing insights into clinical outcomes from the CHESS II (Cost of Haemophilia in Europe: a Socioeconomic Survey-II) study evaluating disease burden in people with haemophilia A. The first analysis examines clinical outcomes in adults with mild, moderate and severe haemophilia A without factor VIII inhibitors, focusing on bleeding episodes and joint outcomes. Results show most people with mild and moderate haemophilia A (91% and 98% respectively) did not receive prophylaxis and the majority of these experienced one or more bleeds (74% and 85% respectively).[6] These data demonstrate the potential treatment needs in these populations, and the clinical burden on those living with mild and moderate haemophilia A. Additional data from the CHESS II study explores the correlation between bleed frequency and physical activity levels in the same patient population, suggesting there is a correlation between the two.[7]

Key abstracts from Roche and Spark that will be presented at ISTH can be found in the table below.

Follow Roche and Spark on Twitter via @Roche and @Spark_tx respectively, and keep up to date with ISTH 2020 Congress news and updates by using the hashtag #ISTH2020.

Abstract title	Abstract number/Presentation details
Second Interim Analysis Results from the STASEY Trial: A Single-arm, Multicenter, Open-label, Phase III Clinical Trial to Evaluate the Safety and Tolerability of Emicizumab Prophylaxis in People with Hemophilia A (PwHA) with FVIII Inhibitors	PB0958: On-Demand Poster Session Sunday 12 July 2020, 14:00 – 15:00 EST Virtual Meeting Room 6
Surgical Experience from the Phase III STASEY Trial of Emicizumab Prophylaxis in Persons with Hemophilia A (PwHA) with FVIII Inhibitors: Data from the Second Interim Analysis	PB0939: On-Demand Poster Session Sunday 12 July 2020, 14:00 – 15:00 EST Virtual Meeting Room 6
Pharmacokinetics and Coagulation Biomarkers in Persons with Hemophilia A (PwHA) and FVIII Inhibitors Receiving Emicizumab in the Phase IIIb STASEY Study	PB0942: On-Demand Poster Session Sunday 12 July 2020, 14:00 – 15:00 EST Virtual Meeting Room 6
A Randomized, Multicenter, Open-label, Phase III Clinical Trial to Evaluate the Efficacy, Safety, and Pharmacokinetics of Prophylactic Emicizumab Versus No Prophylaxis in Persons with Hemophilia A in the Asia-Pacific region (HAVEN 5)	PB0957: On-Demand Poster Session Sunday 12 July 2020, 14:00 – 15:00 EST Virtual Meeting Room 6
An Insight into Clinical Outcomes in Mild, Moderate, and Severe Hemophilia A (HA): A Preliminary Analysis of the CHESS II Study	OC 09.3: Oral presentation Monday 13 July 2020, 10:39 - 10:51 EST Virtual Meeting Room 2
Associations Between Physical Activity Levels and Bleeding Frequency in People with Mild, Moderate, and Severe Hemophilia A (HA): A Preliminary Analysis of the CHESS II Study	PB0943: On-Demand Poster Session Sunday 12 July 2020, 14:00 – 15:00 EST Virtual Meeting Room 6
Phase I/II Trial of SPK-8011: Stable and Durable FVIII Expression for >2 Years with Significant ABR Improvements in Initial Dose Cohorts Following AAV-Mediated FVIII Gene Transfer for Hemophilia A	OC 03.5: Oral abstract presentation Sunday 12 July 2020, 11:03 - 11:15 EST Virtual Meeting Room 3
Immunogenicity of Adeno-Associated Vectors	Invited presentation delivered by Federico Mingozzi, Ph.D., Chief Scientific Officer, Spark Therapeutics Second of three presentations occurring in the session, "State of the Art Session on Hemophilia and Rare Bleeding Disorders" on Sunday 12 July 2020, 8:45 – 10:00am EST

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 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,[8,9] approximately 50-60% of whom have a severe form of the disorder.[10] 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.[8] 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.[11] A serious complication of treatment is the development of inhibitors to factor VIII replacement therapies.[12] Inhibitors are antibodies developed by the body's immune system that bind to and block the efficacy of replacement factor VIII,[13] 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), 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, glofitamab and mosunetuzumab, targeting both CD20 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 and Spark Therapeutics gene therapy research in haemophilia A
We believe gene therapy has the potential to revolutionise medicine and improve the lives of patients with genetic and other serious diseases. Pairing Roche's long-standing commitment to developing medicines in haemophilia with Spark Therapeutics' proven gene therapy expertise brings together the best team of collaborators researching gene therapies in haemophilia A.

It is our aligned objective to develop gene therapies for haemophilia A that, with the lowest effective dose and the optimal immunomodulatory regimen, demonstrate safety, predictability, efficacy, and durability for patients.

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. More than 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 eleventh consecutive year, Roche has been recognised as one of the most sustainable companies 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 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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