Roche to present new data at the ISTH 2021 Congress highlighting long-standing commitment to advancing haemophilia A standard of care

- **Roche will present the final analysis from the phase IIIb STASEY study, reinforcing the safety and efficacy profile of Hemlibra in a broad range of people with haemophilia A with factor VIII inhibitors[1]**
- **Spark Therapeutics will share updated data from the ongoing phase I/II clinical trial of investigational gene therapy SPK-8011, demonstrating that hepatocyte expression of factor VIII can be stable and durable up to four years following vector administration, with an acceptable safety profile[2]**
- **These data reinforce Roche's continued focus on advancing care for people living with haemophilia A and provide additional insights into the long-term efficacy and safety profile of Hemlibra, building on the results previously observed in the phase III HAVEN studies**

Basel, 02 July 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that new data from its haemophilia A clinical programme will be presented at the virtual International Society on Thrombosis and Haemostasis (ISTH) 2021 Congress, from 17-21 July 2021. Data will include the final analysis from the phase IIIb STASEY study of Hemlibra® (emicizumab) and updated data from the phase I/II study of SPK-8011, an AAV-based gene therapy in development by Spark Therapeutics (a member of the Roche Group).[1,2]

“We’re excited to present new data from our haemophilia A programme at the ISTH 2021 Congress,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “These data reinforce our continued commitment to developing transformational therapies for the haemophilia A community and advancing understanding of the long-term efficacy and safety profile of Hemlibra.”

Haemophilia A is a serious, inherited bleeding disorder in which a person’s blood doesn't clot properly, as they either lack or do not have enough of a clotting protein called factor VIII. This can lead to uncontrolled bleeding, either spontaneously or after minor trauma. 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.[3] The development of factor VIII inhibitors can be a significant challenge in the treatment of people with haemophilia A as they bind to and block the efficacy of replacement factor VIII.[4]

The STASEY study is one of the largest open-label studies primarily assessing the safety and tolerability of a medicine for adults and adolescents with haemophilia A with factor VIII inhibitors. Final data from the STASEY study, evaluating the safety and tolerability of Hemlibra prophylaxis in adults and adolescents with haemophilia A with factor VIII inhibitors, will be presented at the congress.[1] These results confirm the favourable safety profile of Hemlibra, as previously demonstrated in the phase III HAVEN clinical trials.[1,5,6,7]

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Spark Therapeutics will share updated data from the ongoing phase I/II clinical trial of SPK-8011, an investigational AAV-based gene therapy developed for the treatment of haemophilia A. These data demonstrate that hepatocyte expression of factor VIII can be stable and durable for up to four years following vector administration, with an acceptable safety profile.[2]

"We are looking forward to sharing data on our investigational gene therapy, SPK-8011, which is being evaluated in the largest phase I/II gene therapy trial in haemophilia A to date, and which reinforces Spark's mission to bring a novel gene therapy option to persons with haemophilia A," said Gallia Levy, M.D., Ph.D., Chief Medical Officer, Spark Therapeutics.

SPK-8011 data presentation
Updated results from Spark's ongoing phase I/II study of investigational SPK-8011 will be shared as an oral presentation during the meeting. These data highlight the safety profile and durability of SPK-8011 in 18 participants, up to four years following vector administration with SPK-8011 in four dose cohorts, ranging from $5x10^{11}$ *vg/kg* to 2×10^{12} *vg/kg*, with results showing a 93% reduction in annualised bleed rate (ABR) and a 97% reduction in annualised infusion rate.[2]

Key Hemlibra and haemophilia data presentations
Final data from the STASEY study presented at the congress demonstrate that Hemlibra is effective, with ABRs consistent with observations reported from the pivotal HAVEN studies.[1,5,6,7] Additionally, no new safety signals were identified in adults and adolescents with haemophilia A with factor VIII inhibitors, consistent with previous safety observations.[1]

Roche will also present a retrospective analysis comparing ABR and Hemlibra concentrations among obese and non-obese adults with haemophilia A from pooled data from the HAVEN 1, 3, and 4 studies.[8] These data suggest that body weight does not significantly impact the efficacy of Hemlibra, regardless of dosing regimen, demonstrating that Hemlibra offers an effective, well tolerated treatment, with flexible dosing options, in obese and non-obese people with haemophilia A.

Additionally, an analysis of data from the 2017 CHESS PAEDs (Cost of Haemophilia across Europe: a Socioeconomic Survey in the Paediatric Population) study, examining the association between physical activity levels and bleed rates in children with haemophilia A, will be presented.[9] Results from this analysis demonstrate the potential treatment needs and clinical burden in physically active children with moderate and severe haemophilia A receiving factor VIII replacement therapy.

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 2021 Congress news and updates by using the hashtag #ISTH2021.

Abstract title	**Abstract number/Presentation details**
Final Analysis of the STASEY Trial: A Single-arm, Multicenter, Open-label, Phase III Clinical Trial Evaluating the Safety and Tolerability of Emicizumab Prophylaxis in Persons with Hemophilia A (PwHA) with factor (F)VIII Inhibitors	PB0521: Poster Networking Session Saturday 17 July, 16:00-17:00 EDT Virtual Meeting Room 3
Emicizumab in Obese Adults with Hemophilia A – Pooled Data from Three Phase III Studies (HAVEN 1, 3 and 4)	PB0495: Poster Networking Session Saturday 17 July, 16:00-17:00 EDT Virtual Meeting Room 3
Association of Physical Activity with Bleeding Frequency in Children with Hemophilia A: a CHESS PAEDs Study Analysis	PB0512: Poster Networking Session Saturday 17 July, 16:00-17:00 EDT Virtual Meeting Room 3
Phase I/II trial of SPK-8011: Stable and Durable FVIII Expression After AAV Gene Transfer for Hemophilia A	OC 67.2: Oral Communication Session Wednesday 21 July, 10:12-10:24 EDT Virtual Meeting Room 8

About Hemlibra® (emicizumab)

Hemlibra is approved for routine prophylaxis of bleeding episodes in people with haemophilia A with and without factor VIII inhibitors in over 100 countries worldwide for those with inhibitors and over 80 countries for those without inhibitors, in adults and children, ages newborn and older. 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 SPK-8011 for haemophilia A

Investigational SPK-8011, a novel bio-engineered adeno-associated viral (AAV) vector utilizing the AAV-LK03 capsid, also referred to as Spark200, contains a codon-optimized human factor VIII gene under the control of a liver-specific promoter. The Food and Drug Administration (FDA) granted orphan-disease designation and breakthrough therapy designation in the U.S., while the European Commission has granted orphan designation to SPK-8011.

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,[10,11] approximately 35-39% of whom have a severe form of the disorder.[11] 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.[10] 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.[3] 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 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 Spark Therapeutics
At Spark Therapeutics, a fully integrated, commercial company committed to discovering, developing and delivering gene therapies, we challenge the inevitability of genetic diseases, including blindness, haemophilia, lysosomal storage disorders and neurodegenerative diseases. We currently have four programs in clinical trials. At Spark, a member of the Roche Group, we see the path to a world where no life is limited by genetic disease. For more information, visit www.sparktx.com, and follow us on Twitter and LinkedIn.

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 T-cell engaging bispecific antibodies, glofitamab and mosunetuzumab, targeting both CD20 and CD3, and cevostamab, targeting 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
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, as well as growing capabilities in the area of data-driven medical insights help Roche deliver truly personalised healthcare. Roche is working with partners across the healthcare sector to provide the best care for each person.

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. In recent years, Roche has invested in genomic profiling and real-world data partnerships and has become an industry-leading partner for medical insights.

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 twelfth 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 2020 employed more than 100,000 people worldwide. In 2020, Roche invested CHF 12.2 billion in R&D and posted sales of CHF 58.3 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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