

Basel, 4 September 2015

US FDA grants breakthrough therapy designation for Roche's investigational medicine ACE910 for people with haemophilia A with factor VIII inhibitors

- **First factor VIIIA-mimetic bispecific antibody to be investigated for the prophylactic treatment of haemophilia A**
- **Ninth breakthrough therapy designation for Roche's portfolio of medicines¹⁻⁶**

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the US Food and Drug Administration (FDA) has granted breakthrough therapy designation to ACE910 (RG6013, RO5534262) for the prophylactic treatment of people who are 12 years or older with haemophilia A with factor VIII inhibitors. Haemophilia A, a rare genetic disorder, occurs when an essential blood clotting protein called factor VIII is either not present in sufficient amounts or is defective.⁷ People with severe haemophilia A can be susceptible to uncontrolled or difficult to control bleeding including internal bleeding, especially into the joints, which can lead to the need for joint replacements.⁸

Breakthrough therapy designation is designed to accelerate the development and review of medicines that demonstrate early clinical evidence of a substantial improvement over current treatment options for serious diseases.

In a Phase I study,⁹ ACE910 showed promising results as a prophylactic treatment administered as a weekly subcutaneous injection in people with severe haemophilia A with and without inhibitors to factor VIII. The development of inhibitors is a serious complication of haemophilia A treatment regardless of disease severity,¹⁰ making it difficult, if not impossible, to achieve a level of factor VIII sufficient to control bleeding with traditional replacement therapies. Management of bleeding in people with haemophilia A who have inhibitors to factor VIII is a major challenge, and there remains a need for additional treatment options for these patients.¹¹

“People with haemophilia A may require regular and frequent infusions of replacement clotting factor to

reduce the risk of dangerous bleeding, and they can develop inhibitors that make replacement ineffective,” said Sandra Horning, M.D., Roche’s Chief Medical Officer and Head of Global Product Development. “We are pleased that the FDA has granted breakthrough therapy designation for ACE910, recognising an unmet need for patients with inhibitors and the promise of these early data. Roche has been developing antibody treatments for people with blood disorders for over 20 years, and we are excited to expedite the development of a potential new treatment for haemophilia A.”

Roche is preparing to initiate a Phase III trial of ACE910 in patients with haemophilia A with factor VIII inhibitors by the end of 2015 and a Phase III trial in patients without inhibitors in 2016. Additionally, a trial in paediatric patients with haemophilia A is planned to commence in 2016.

The breakthrough therapy designation for ACE910 was granted based on results of a Phase I study of ACE910 in people with severe haemophilia A presented at the annual meeting of the American Society of Hematology (ASH) in 2014, and the Phase I/II extension study of the same patients presented at the annual meeting of the International Society of Thrombosis and Haemostasis (ISTH) in 2015.

About ACE910

ACE910 is an investigational humanised bispecific monoclonal antibody engineered to simultaneously bind factors IXa and X. ACE910 thereby mimics the cofactor function of factor VIII and is designed to promote blood coagulation in haemophilia A patients, regardless of whether they have developed inhibitors to factor VIII. ACE910 is administered subcutaneously once weekly, and as it is distinct in structure from factor VIII, it is not expected to lead to the formation of inhibitors against factor VIII. The development programme of ACE910 is assessing its potential to help overcome some of the clinical challenges faced in haemophilia care, such as the development of factor VIII inhibitors and the need for frequent venous access. ACE910 was created by Chugai Pharmaceutical Co., Ltd. and is being co-developed by Roche.

About Roche in haematology

For more than 20 years, Roche has been developing medicines that redefine treatment in haematology. Today, we’re 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) and Gazyva®/Gazyvaro® (obinutuzumab), Roche’s pipeline of investigational haematology medicines includes an anti-PDL1 antibody (atezolizumab/MPDL3280A), an anti-CD79b antibody drug conjugate (RG7596/polatuzumab vedotin), a small molecule antagonist of MDM2 (RG7388/idasanutlin) and in

collaboration with AbbVie, a small molecule BCL-2 inhibitor (venetoclax/RG7601/GDC-0199/ABT-199). Roche's dedication to developing novel molecules in haematology expands beyond oncology, with the development of the investigational haemophilia A treatment ACE910.

About Roche

Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. 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 chemotherapy.

In 2014, the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss francs in R&D and posted sales of 47.5 billion Swiss francs. 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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