FDA Grants Breakthrough Therapy Designation for Genentechâ€™s HEMLIBRA (emicizumab-kxwh) in Hemophilia a Without Inhibitors

â€“ Designation based on Phase III HAVEN 3 study demonstrating HEMLIBRA prophylaxis significantly reduced bleeds compared to no prophylaxis â€“

â€“ First medicine to show superior efficacy compared to prior factor VIII prophylaxis in an intra-patient comparison â€“

Genentech, a member of the Roche Group (SIX: RO, ROG; OTCQX: RHHBY), announced today that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation to HEMLIBRAÂ® (emicizumab-kxwh) for people with hemophilia A without factor VIII inhibitors. Breakthrough Therapy Designation is designed to accelerate the development and review of medicines intended to treat a serious condition with preliminary evidence that indicates they may demonstrate a substantial improvement over existing therapies.

â€œHEMLIBRA is the first medicine to show superior efficacy compared to factor VIII prophylaxis, the standard of care for people with hemophilia A without inhibitors, in an intra-patient comparison,â€• said Sandra Horning, M.D., chief medical officer and head of Global Product Development. â€œWe look forward to working with health authorities to make HEMLIBRA available to people without inhibitors as soon as possible, and we are excited to share this news with the community as we join in celebrating World Hemophilia Day.â€•

This designation is based on data from the Phase III HAVEN 3 study in people 12 years or older with hemophilia A without inhibitors. In the study, HEMLIBRA prophylaxis dosed subcutaneously every week or every two weeks showed a statistically significant and clinically meaningful reduction in treated bleeds compared to no prophylaxis. In an intra-patient comparison, once-weekly HEMLIBRA prophylaxis was superior to prior factor VIII prophylaxis as demonstrated by a statistically significant and clinically meaningful reduction in treated bleeds. The most common adverse events with HEMLIBRA

were injection site reactions, and no new safety signals were observed. No thrombotic microangiopathy or thrombotic events occurred in this study.

HEMLIBRA was granted its first Breakthrough Therapy Designation in September 2015 and was approved by the FDA in November 2017 for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children with hemophilia A with factor VIII inhibitors based on results from the HAVEN 1 and HAVEN 2 studies.

The HEMLIBRA development program reflects Genentechâ€™s commitment to address clinical unmet needs in the hemophilia A community. 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.

About HAVEN 3 (NCT02847637)

HAVEN 3 is a randomized, multicenter, open-label, Phase III study evaluating the efficacy, safety and pharmacokinetics of HEMLIBRA prophylaxis versus no prophylaxis (episodic/on-demand factor VIII treatment) in people with hemophilia A without inhibitors to factor VIII. The study included 152 patients with hemophilia A (12 years of age or older) who were previously treated with factor VIII therapy either on-demand or for prophylaxis. Patients previously treated with on-demand factor VIII were randomized in a 2:2:1 fashion to receive subcutaneous HEMLIBRA prophylaxis at 3 mg/kg/wk for 4 weeks, followed by 1.5 mg/kg/wk until the end of study (Arm A), subcutaneous HEMLIBRA prophylaxis at 3 mg/kg/wk for 4 weeks, followed by 3 mg/kg/2wks until the end of study (Arm B), or no prophylaxis (Arm C). Patients previously treated with factor VIII prophylaxis received subcutaneous HEMLIBRA prophylaxis at 3 mg/kg/wk for 4 weeks, followed by 1.5 mg/kg/wk until the end of study (Arm D). Episodic treatment of breakthrough bleeds with factor VIII therapy was allowed per protocol.

About HEMLIBRA

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 hemophilia A patients. 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. HEMLIBRA was created by Chugai Pharmaceutical Co., Ltd. and is being co-developed by Chugai, Roche and Genentech.

HEMLIBRA U.S. Indication

HEMLIBRA is a prescription medicine used for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children with hemophiliaÂ A with factor VIII inhibitors.

Important Safety Information

HEMLIBRA increases the potential for blood to clot. Discontinue prophylactic use of bypassing agents the day before starting HEMLIBRA prophylaxis. Carefully follow the healthcare providerâ€™s instructions regarding when to use an on-demand bypassing agent, and the dose and schedule one should use. Cases of thrombotic microangiopathy and thrombotic events were reported when on average a cumulative amount of >100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) was administered for 24 hours or more to patients receiving HEMLIBRA prophylaxis.

HEMLIBRA may cause the following serious side effects when used with aPCC (FEIBAÂ®), including:

Thrombotic microangiopathy (TMA). This is a condition involving blood clots and injury to small blood vessels that may cause harm to oneâ€™s kidneys, brain, and other organs. Patients should get medical help right away if they have any of the following signs or symptoms during or after treatment with HEMLIBRA: confusion weakness swelling of arms and legs yellowing of skin and eyes stomach (abdomen) or back pain nausea or vomiting feeling sick decreased urination Blood clots (thrombotic events). Blood clots may form in blood vessels in oneâ€™s arm, leg, lung or head. Patients should get medical help right away if they have any of these signs or symptoms of blood clots during or after treatment with HEMLIBRA: swelling in arms or legs pain or redness in the arms or legs shortness of breath chest pain or tightness fast heart rate cough up blood feel faint headache

numbness in the face eye pain or swelling trouble seeing

If aPCC (FEIBAÂ®) is needed, patients should talk to their healthcare provider in case they feel they need more than 100 U/kg of aPCC (FEIBAÂ®) total.

How should patients use HEMLIBRA?

HEMLIBRA may interfere with laboratory tests that measure how well blood is clotting and may cause a false reading. Patients should talk to their healthcare provider about how this may affect their care.

What are the other possible side effects of HEMLIBRA?

The most common side effects of HEMLIBRA include: redness, tenderness, warmth, or itching at the site of injection; headache; and joint pain.

Before using HEMLIBRA, patients should tell their healthcare provider about all of their medical conditions, including if they:

are pregnant or plan to become pregnant. It is not known if HEMLIBRA may harm their unborn baby. Females who are able to become pregnant should use birth control (contraception) during treatment with HEMLIBRA. are breastfeeding or plan to breastfeed. It is not known if HEMLIBRA passes into a femaleâ€™s breast milk. These are not all of the possible side effects of HEMLIBRA. Patients should call their doctor for medical advice about side effects.

Side effects may be reported to the FDA at (800) FDA-1088 or http://www.fda.gov/medwatch. Side effects may also be reported to Genentech at (888) 835-2555.

Please see the HEMLIBRA full Prescribing Information and the Medication Guide, including Serious Side Effects, for more important safety information.

About hemophilia A

Hemophilia A is an inherited, serious disorder in which a personâ€™s blood does not clot properly,

leading to uncontrolled and often spontaneous bleeding. Hemophilia affects around 20,000 people in the United States, with hemophilia A being the most common form and approximately 50-60 percent of people living with a severe form of the disorder.

People with hemophilia 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 hemophilia A can bleed frequently, especially into their joints or muscles. 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.

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

About Genentech in hemophilia

In 1984, Genentech scientists were the first to clone recombinant factor VIII in response to the contaminated hemophilia blood supply crisis of the early 1980s. For more than 20 years, Genentech has been developing medicines to bring innovative treatment options to people with diseases of the blood within oncology, and in hemophilia A. Genentech is committed to improving treatment and care in the hemophilia community by delivering meaningful science and clinical expertise. For more information visit http://www.gene.com/hemophilia.

About Genentech

Founded more than 40 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures and commercializes medicines to treat patients with serious or life-threatening medical conditions. The company, a member of the Roche Group, has headquarters in South San Francisco, California. For additional information about the company, please visit http://www.gene.com.

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