Innovation all for the patients

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Chugai's Bispecific Antibody "ACE910" for the Treatment of Hemophilia A Designated as a Breakthrough Therapy by the US FDA

— Third Breakthrough Therapy Designation for Chugai's Drug Candidate —

September 4, 2015 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Head Office: Chuo-ku, Tokyo; Chairman & CEO: Osamu Nagayama] (hereafter, "Chugai") announced today that the US Food and Drug Administration (FDA) has granted the Breakthrough Therapy Designation to "ACE910," for the prophylactic treatment of people who are 12 years or older with hemophilia A with factor VIII inhibitors.

"We are very pleased that the FDA has granted Breakthrough Therapy Designation to ACE910," said Chugai's Director and Executive Vice President, Dr. Yutaka Tanaka. "We believe with its new mode of action, ACE910 will contribute to the patients by offering new choice of treatment options."

Hemophilia A is a disease presenting repeated severe bleeding symptoms. In this disease, the blood coagulation reaction does not proceed normally due to the deficiency or functional disorder of coagulation factor VIII. Although the regular factor VIII replacement therapy has been widely used to prevent bleeding, this intravenous treatment may develop anti-factor VIII neutralizing antibodies (inhibitors) which result in reduced effectiveness. Under these circumstances, hemophilia A is a disease with high unmet medical needs.

ACE910 is a bispecific antibody created using Chugai's proprietary antibody engineering technologies for the purpose of mimicking the function of blood coagulation factor VIII, in order to provide a novel concept for the treatment of hemophilia A. The Japanese phase I / II clinical study is currently being conducted to investigate the safety and exploratory prophylactic efficacy of ACE910 for preventing bleeding with the once-weekly subcutaneous injection of ACE910 in patients both with and without inhibitors.
(Chugai's press release dated June 23, 2015 on the interim results of this study:
http://www.chugai-pharm.co.jp/english/news/detail/20150623083000.html)

The breakthrough therapy designation was adopted as part of the FDA Safety and Innovation Act (FDASIA) enacted in July 2012 aiming at expediting the development and review of drugs for the treatment of severe or life-threatening diseases or symptoms. The designation for ACE910 was based on the domestic phase I / II clinical study conducted with Japanese and Caucasian healthy volunteers as well as Japanese hemophilia A patients. It is the third such designation for a drug candidate developed by Chugai after alectinib (for patients with ALK-

positive non-small cell lung cancer whose disease progressed on crizotinib therapy) and tocilizumab (systemic sclerosis).

Development rights for regions other than Japan, Taiwan, and Korea were licensed out to F. Hoffman-La Roche, Ltd. [Headquarters: Basel, Switzerland; CEO: Severin Schwan] (hereafter, "Roche") (Roche development code: RG6013). Chugai and Roche plan to initiate a phase III global study in patients with inhibitors by the end of 2015 and a phase III global study in patients without inhibitors in 2016. Additionally, a trial in pediatric patients with hemophilia A is planned to commence in 2016.

Based on its business philosophy of "innovation all for the patients," Chugai will work with Roche towards the marketing applications of ACE910 in countries around the world in order to provide the new treatment option to patients and healthcare professionals as soon as possible.

【Reference】

About ACE910

ACE910 is a bispecific antibody created by Chugai, and substitutes for the function of blood coagulation factor VIII, which is deficient or lowered in hemophilia A patients, by promoting factor IXa-catalyzed factor X activation as factor VIII does[1) 2)]. ACE910 is expected to prevent bleeding irrespective of the presence of inhibitors because ACE910 has a different molecular structure from FVIII, and the interim analysis of the domestic clinical studies showed the favorable results by once-a-week subcutaneous administration of ACE910.

1) Kitazawa, et al. Nature Medicine 2012;18(10):1570
2) Sampei, et al. PLoS ONE 2013;8:e57479
3) National Hemophilia Foundation

About Breakthrough Therapy

The breakthrough therapy designation was adopted as part of the FDA Safety and Innovation Act (FDASIA) enacted in July 2012 aiming at expediting the development and review of drugs for the treatment of severe or life-threatening diseases or symptoms. In order to grant breakthrough therapy designation, preliminary clinical evidence is required demonstrating that the drug may have substantial improvement on at least one clinically significant endpoint over existing therapies. Although breakthrough therapy designation differs from other FDA systems that expedite the development and review of pharmaceutical products, it is a system that conveys all of the benefits of the fast track designation.

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