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Chugai's Bispecific Antibody Emicizumab Meets Primary Endpoint in Phase lll Study

- emicizumab prophylaxis shown to reduce bleeding in patients without inhibitors -

TOKYO, November 20, 2017 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the primary endpoint has been met for the global phase lll HAVEN 3 (NCT02847637) study evaluating emicizumab (ACE910) subcutaneous injection, once a week and once every two weeks, in patients with hemophilia A (12 years of age or older) without inhibitors to factor Vlll. A statistically significant reduction in the number of bleeds was confirmed in patients treated with emicizumab prophylaxis compared to those receiving no prophylactic treatment. The study also met a secondary endpoint that once-weekly emicizumab prophylaxis was superior to factor VIII prophylaxis, as demonstrated by a statistically significant and clinically meaningful reduction in treated bleeds in an intra-patient comparison of patients receiving emicizumab prophylaxis compared to their prior factor VIII prophylaxis. The most common adverse events with emicizumab were injection site reactions, consistent with prior studies. No thrombotic events occurred in this study. Further details will be presented at a future medical meeting.

"Prophylactic factor VIII replacement therapy is a standard treatment for hemophilia A patients without inhibitors. However, some patients and their caregivers have difficulties with the frequent intravenous injections in their daily life," said Chugai's Senior Vice President, Head of Project & Lifecycle Management Unit, Dr. Yasushi Ito. "As a subcutaneous injection, emicizumab can be administered more easily. Today's results, which are consistent with data reported from patients with inhibitors earlier this year, showed that emicizumab may have the potential to become an efficacious treatment option for hemophilia A patients without inhibitors. We expect emicizumab to provide benefits to a wide range of patients with hemophilia A."

Emicizumab is an investigational bispecific monoclonal antibody, which was developed using Chugai's proprietary antibody engineering technologies. The drug is designed to bind factor IXa and factor X. In doing so, emicizumab provides the cofactor function of factor Vlll in people with hemophilia A, who either lack or have impaired coagulation function of factor Vlll[1,2]. In November this year, the drug (US product name: HEMLIBRA®; Genentech) was approved by the U.S. Food and Drug Administration "for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors". An EU marketing authorization application was submitted in June 2017 and is being reviewed under Accelerated Assessment by the European Medicines Agency. In Japan, emicizumab obtained an orphan drug designation in August 2016 from the Ministry of Health, Labour and Welfare for the prevention and reduction of bleeding episodes in patients with congenital FVIII deficiency (hemophilia A) who developed inhibitors to FVIII, followed by an application for regulatory approval filed in July 2017.

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About HAVEN 3 study (NCT02847637)

HAVEN 3 study is a randomized, multicentre, open-label phase lll study evaluating the efficacy, safety and pharmacokinetics of emicizumab prophylaxis subcutaneous injection once a week and once every two weeks. The study enrolled 152 patients with hemophilia A, 12 years of age or older without inhibitors to factor Vlll, who were previously treated with episodic or prophylactic factor Vlll therapy. The primary endpoint of the study is the number of bleeds over time with emicizumab prophylaxis (Arm A and Arm B) versus no prophylaxis (Arm C). Secondary endpoints include joint bleed rate, target joint bleed rate, health-related quality of life (HRQoL)/ health status, intra-patient comparison to bleed rate on their prior prophylaxis regimen with factor Vlll therapy (Arm D) and safety.

<Study Design>

Patients previously treated with episodic factor Vlll therapy were randomized in a 2:2:1 fashion to either Arm A, B or C.

Arm A (n=34)	Received emicizumab prophylaxis at 3mg/kg by once-weekly subcutaneous injection for 4 weeks, followed by 1.5 mg/kg once-weekly subcutaneous injection
Arm B (n=34)	Received emicizumab prophylaxis at 3mg/kg by once-weekly subcutaneous injection for 4 weeks, followed by 3 mg/kg once every two weeks subcutaneous injection
Arm C (n=17)	No prophylaxis control arm

Patients previously treated with factor Vlll prophylactic were enrolled in:

Arm D (n=40-60)	Received emicizumab prophylaxis at 3mg/kg by once-weekly subcutaneous injection for 4 weeks, followed by 1.5 mg/kg once-weekly subcutaneous injection

Episodic treatment of breakthrough bleeds with factor VIII therapy was allowed per protocol.

About emicizumab clinical development status

In addition to the HAVEN 1, HAVEN 2 and HAVEN 3 studies, a global phase lll HAVEN 4 study (NCT03020160) is currently underway by Chugai, Roche and Genentech to evaluate emicizumab prophylaxis once every four weeks by subcutaneous injection in hemophilia A patients with or without factor VIII inhibitors.

About Chugai

Chugai Pharmaceutical is one of Japan’s leading research-based pharmaceutical companies with strengths in biotechnology products. Chugai, based in Tokyo, specializes in prescription pharmaceuticals and is listed on the 1st section of the Tokyo Stock Exchange. As an important member of the Roche Group, Chugai is actively involved in R&D activities in Japan and abroad. Specifically, Chugai is working to develop innovative products which may satisfy the unmet medical needs, mainly focusing on the oncology area.

In Japan, Chugai's research facilities in Gotemba and Kamakura are collaborating to develop new pharmaceuticals, and laboratories in Ukima are conducting research for technology development for industrial production. Overseas, Chugai Pharmabody Research based in Singapore is engaged in research focusing on the generation of novel antibody drugs by utilizing Chugai's proprietary innovative antibody engineering technologies. Chugai Pharma USA and Chugai Pharma Europe are engaged in clinical development activities in the United States and Europe.
The consolidated revenue in 2016 of Chugai totaled 491.8 billion yen and the operating income was 80.6 billion yen (IFRS Core basis).
Additional information is available on the internet at https://www.chugai-pharm.co.jp/english.

References

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

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