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Primary Analysis of Japanese Phase III Clinical Trial of Hemlibra for Acquired Hemophilia A (AGEHA Study) Presented at ISTH

- Data from AGEHA Study suggested a favorable benefit-risk profile of Hemlibra in acquired hemophilia A under a dosing regimen and completion criteria determined specifically for the disease
- The data supported the Japanese regulatory approval for Hemlibra in June this year for the additional indication of acquired hemophilia A

TOKYO, July 12, 2022 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the primary analysis of a Japanese phase III clinical trial (AGEHA Study) for Chugai's anti-coagulation factor IXa/X humanized bispecific monoclonal antibody/coagulation factor VIII substitute Hemlibra® [generic name: emicizumab (genetical recombination)] in acquired hemophilia A was presented at the 30th International Society on Thrombosis and Haemostasis (ISTH) Annual Congress held in London, United Kingdom, on July 11 (local time). Hemlibra was approved in Japan for the additional indication of "routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with acquired hemophilia A" on June 20, based on the data presented.

"AGEHA study is the first prospective clinical trial to examine Hemlibra in acquired Hemophilia A. It provided new evidence in the disease where limited measures have been available to control bleeding, and supported the regulatory approval in Japan. I am pleased that the data suggested the potential of Hemlibra to control bleeding in acquired hemophilia A and to lower the treatment burden on patients as it is administered subcutaneously," said Dr. Osamu Okuda, Chugai's President and CEO. "Hemlibra is a result of our endeavor to bring a paradigm shift in the treatment of hemophilia A, and created by applying Chugai's proprietary antibody engineering technologies. We will continue to pursue innovation with our scientific and technological capabilities to create medicines that are truly needed by patients."

AGEHA study is a multicenter, single-arm, Japanese phase III clinical trial with several cohorts to investigate the safety, efficacy, pharmacokinetics, and pharmacodynamics of subcutaneous administration of Hemlibra in acquired hemophilia A. The primary analysis was conducted in 12 adults with acquired hemophilia A, who were undergoing or scheduled to start immunosuppressive therapy at the time of enrollment (cohort 1). Participants subcutaneously received Hemlibra 6 mg/kg (body weight) on day 1, 3 mg/kg (body weight) on day 2, and 1.5 mg/kg (body weight) weekly from day 8. Dosing completion criteria for Hemlibra were specified in the study. Administration of Hemlibra was discontinued if the FVIII activity was more than 50 IU/dL, and no coagulation factor product was used for treating a bleed within 72 hours.

Within the efficacy evaluation period after Hemlibra treatment (median of 44.5 days, range: 8-208 days), 2 of 12 participants (16.7%) experienced bleeds that required treatment, and no major bleeds occurred in any

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL:+81-(0)3-3273-0881 E-mail:pr@chugai-pharm.co.jp
Investor Relations Group TEL:+81-(0)3-3273-0554 E-mail:ir@chugai-pharm.co.jp

participant. Annual bleeding rates were as follows.

AGEHA Study Annual Bleeding Rates

Evaluation	Pre-treatment Period*	On-treatment Period**
Treated bleeds (times per year)	35.6 (24.91-49.42)	3.2 (0.69-9.01)
Major bleeds (times per year)	66.4 (51.41-84.44)	0.0 (NA-3.69)
All bleeds (times per year)	77.0 (60.80-96.27)	6.9 (2.76-14.30)

*median evaluation period: 68.0 (range: 17-168) days

**median evaluation period: 44.5 (range: 8-208) days

The 12 participants all experienced at least one adverse event, and the total number of adverse events was 78. Four participants experienced serious adverse events, none of which was considered related to Hemlibra. Adverse events related to Hemlibra were observed in three of 12 participants (25%). Among the three cases, one participant experienced asymptomatic deep vein thrombosis, which disappeared in one week. No new safety signals were identified.

About Hemlibra

Hemlibra is a bispecific monoclonal antibody created with Chugai's proprietary antibody engineering technologies. The drug is designed to bind factor IXa and factor X. In doing so, Hemlibra provides the cofactor function of factor VIII in people with hemophilia A, who either lack or have impaired coagulation function of factor VIII.[1,2] The product was approved by the U.S. Food and Drug Administration (FDA) in November 2017, for the first time in the world, 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. In Japan, it was first approved in March 2018, and its indication was later expanded to include congenital hemophilia A without factor VIII inhibitors. Hemlibra has been approved in more than 110 countries for congenital hemophilia A with and without factor VIII inhibitors.

About acquired hemophilia A

Acquired hemophilia A is a disease in which inhibitors of blood coagulation factor VIII are acquired. The inhibitors result in a significant decrease in factor VIII activity, leading to bleeding symptoms such as spontaneous subcutaneous bleeding and intramuscular bleeding. Serious bleeding is not rare in the disease. Acquired hemophilia A is an autoimmune disease in which autoantibodies against factor VIII are produced on the basis of collagen disease, malignant tumor, and childbirth.[3,4]

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Sources

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2. Sampei, et al. PLoS ONE 2013; 8(2): e57479

3. Franchini M, Veneri D. Acquired coagulation inhibitor-associated bleeding disorders: an update. Hematology 2005;10:443-9.
4. Cohen AJ, Kessler CM. Acquired inhibitors. Baillieres Clin Haematol 1996;9:331-54.

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