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Further Clinical Data including Long-Term Follow-up for Chugai's Hemlibra Presented at ISTH

- Long-term follow-up from four phase III studies (HAVEN studies) shows Hemlibra's sustained efficacy and safety in people with hemophilia A, with and without factor VIII inhibitors.
- The first interim analysis of phase IIIb STASEY study in hemophilia A with inhibitors reinforces safety profile of Hemlibra seen in HAVEN 1 study.
- New analysis from HAVEN studies suggests additional factor treatment may not be needed for people on Hemlibra undergoing certain minor surgeries regardless of inhibitor expression.

TOKYO, July 9, 2019 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced further clinical data for the hemophilia A treatment Hemlibra® (emicizumab) at the International Society on Thrombosis and Haemostasis (ISTH) 2019 Congress on 6-10 July in Melbourne, Australia. Long-term follow-up from four phase III HAVEN studies (HAVEN 1, HAVEN 2, HAVEN 3 and HAVEN 4), and the first interim analysis of the phase IIIb STASEY study were presented.

"At present, hemophilia A requires lifelong treatment. It is very meaningful that Hemlibra demonstrated sustained long-term safety and efficacy in people with or without factor VIII inhibitors," said Chugai's Executive Vice President, Co-Head of Project & Lifecycle Management Unit, Dr. Yasushi Ito. "We believe that Hemlibra will be recognized as a drug that can be used with more confidence in terms of both efficacy and safety by people with hemophilia A, their families and their treating physicians."

Long-term efficacy and safety from the pooled HAVEN studies

Updated data from the pooled HAVEN studies (n=400), in people with hemophilia A of all ages with and without factor VIII inhibitors, showed that a high proportion of people experienced zero treated bleeds on Hemlibra, and that this was maintained over a median of 83 weeks. Across all four HAVEN studies, over 87% of participants had no treated joint bleeds (either spontaneous or due to injury/trauma) and over 92% of participants experienced no spontaneous bleeds in each interval from week 25. Hemlibra's established safety and tolerability profile was maintained.

Safety and tolerability from the STASEY study interim analysis

STASEY study is a phase IIIb clinical trial to evaluate the safety and tolerability of Hemlibra in people with hemophilia A with factor VIII inhibitors. Results from the first interim analysis of the STASEY study, including data from 88 patients, reinforce the safety profile of Hemlibra characterized in the pivotal HAVEN 1 study. HAVEN 1 has formed the basis of Hemlibra's regulatory approval in people with hemophilia A with factor VIII inhibitors. In the STASEY study, no cases of thrombotic microangiopathy (TMA) or thrombotic events were reported and no new safety signals were identified. Eighteen patients

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(20.5%) reported a Hemlibra-related adverse event (AE), of which one was a serious AE (catheter site abscess). The most common AEs, occurring in 10% or more of people in the STASEY study were injection site reactions (14.8%), joint pain (arthralgia; 13.6%), headache (11.4%) and common cold symptoms (nasopharyngitis; 11.4%). Bleeding rates in people with hemophilia A with factor VIII inhibitors receiving Hemlibra in the STASEY study were also in line with previously reported observations from the HAVEN 1 study.

Additional factor treatment may not be needed for people on Hemlibra undergoing certain minor surgeries

A retrospective analysis of pooled data across the HAVEN studies suggest that people with hemophilia A with and without factor VIII inhibitors may not need additional preventative (prophylactic) coagulation factor (factor VIII replacement therapy or bypassing agents) when undergoing certain minor surgery. 65.6% (n=141) of minor surgeries (n=215) were performed without prophylactic coagulation factor, and of these, 90.8% did not result in a treated post-operative bleed. Of the 18 major surgeries, three were managed without prophylactic coagulation factor, with no post-operative bleeds. The remaining 15 major surgeries were managed with prophylactic coagulation factor, only one of which resulted in a treated post-operative bleed.

About the HAVEN program

The HAVEN program is one of the largest pivotal clinical trial programs in hemophilia A, designed to assess the efficacy and safety of Hemlibra in hemophilia A in people with and without factor VIII inhibitors.

- HAVEN 1 study: HAVEN 1 study is a randomized, multicenter, open-label, phase III study evaluating the efficacy, safety, and pharmacokinetics of Hemlibra once-weekly subcutaneous injection in adults and adolescents (12 years of age or older) with hemophilia A with inhibitors to factor VIII, who were previously treated with bypassing agents on-demand or as prophylaxis.

- HAVEN 2 study: HAVEN 2 study is a multicenter, open-label, phase III study in children younger than 12 years of age with hemophilia A with factor VIII inhibitors. The study is evaluating the efficacy, safety and pharmacokinetics of once weekly, every two weeks or every four weeks subcutaneous administration of Hemlibra prophylaxis.

- HAVEN 3 study: HAVEN 3 study is a randomized, multicenter, open-label, phase III study evaluating the efficacy, safety and pharmacokinetics of Hemlibra prophylaxis subcutaneous injection once a week and once every two weeks. The study enrolled people with hemophilia A, 12 years of age or older without inhibitors to factor VIII, who were previously treated with episodic or prophylactic factor VIII therapy.

- HAVEN 4 study: HAVEN 4 study is a single-arm, multicenter, open-label, phase III study evaluating the efficacy, safety, and pharmacokinetics of subcutaneous administration of Hemlibra dosed every four

weeks. The study included people (12 years of age or older) with hemophilia A with or without inhibitors to factor VIII, who were previously treated with either on-demand or prophylactic factor VIII or bypassing agents.

About the STASEY study

The STASEY study is a single-arm, multicenter, open-label, phase IIIb clinical trial to evaluate the safety and tolerability of Hemlibra prophylaxis in people with hemophilia A with factor VIII inhibitors. The study included 88 people (12 years of age or older) who had completed 24 weeks on study or discontinued, receiving subcutaneous Hemlibra 3 mg/kg/week for four weeks, followed by 1.5 mg/kg/week for the remainder of the treatment period. There is no participation from Japan.

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