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Chugai's Bispecific Antibody "Emicizumab" for Hemophilia A Meets Primary Endpoint in Phase lll Study

- emicizumab prophylaxis shown to reduce bleeding in patients with inhibitors -

TOKYO, December 22, 2016 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the primary endpoint has been met for the global phase lll HAVEN 1 study evaluating emicizumab (ACE910) prophylaxis for once-weekly subcutaneous injection with patients 12 years of age or older with hemophilia A and 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 all secondary endpoints, including a statistically significant reduction in the number of bleeds over time with emicizumab prophylaxis treatment in an intra-patient comparison in people who had received prior bypassing agent prophylaxis treatment. The most common adverse events with emicizumab were injection site reactions, consistent with prior studies.

"This result indicates that emicizumab could be a transformative advancement in the treatment for hemophilia A," said Chugai's President & COO, Tatsuro Kosaka. "We are committed to delivering emicizumab worldwide as a first-in-class biologic as early as possible, particularly to patients with inhibitors who have few treatment options."

As previously reported, two patients had thromboembolic events and two patients developed thrombotic microangiopathy (TMA). The common aspect between all cases of thromboembolic events and TMA is that they occurred in patients who were on emicizumab prophylaxis and in addition received activated prothrombin complex concentrate to treat breakthrough bleeds. Neither thromboembolic event required anti-coagulation therapy and one patient restarted emicizumab. Both cases of TMA have completely resolved, and one patient restarted emicizumab.

Emicizumab is an investigational bispecific monoclonal antibody, which was developed using Chugai's proprietary antibody engineering technologies. The drug is designed to bind factors IXa and factors X, and promotes the interaction between factors IXa and factors 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 2015, the drug was granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA) for prophylactic treatment for patients aged 12 years or older with hemophilia A with factor VIII inhibitors.

HAVEN 1 is the first global phase lll study in the emicizumab clinical development program to report results. Data from the study will be presented at an upcoming medical meeting.

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About HAVEN 1 study (NCT02622321)

HAVEN 1 study is a randomized, multicentre, open-label phase lll study evaluating the efficacy, safety and pharmacokinetics of emicizumab prophylaxis for once-weekly subcutaneous injection. The study enrolled 109 patients with hemophilia A, 12 years of age or older with inhibitors to factor Vlll, who were previously treated with episodic or prophylactic bypassing agents. The primary endpoint of the study is the number of bleeds over time with emicizumab prophylaxis (Arm A) versus no prophylaxis (Arm B). Secondary endpoints include all bleed rate, joint bleed rate, spontaneous 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 bypassing agents (Arm C) and safety.

<Study Design>

Patients previously treated with episodic bypassing agents were randomized in a 2:1 fashion to either Arm A or B.

Arm A: receive emicizumab prophylaxis for once-weekly subcutaneous injection

Arm B: receive episodic bypassing agents as same as previous treatment

Patients previously treated with prophylactic bypassing agents were enrolled in:

Arm C: receive emicizumab prophylaxis for once-weekly subcutaneous injection

Patients previously treated with episodic bypassing agents and participated in the non-interventional study (BH29768) prior to HAVEN 1 entry, and were unable to enroll in Arm A or Arm B were enrolled in:

Arm D: receive emicizumab prophylaxis for once-weekly subcutaneous injection

About emicizumab clinical development status

In addition to HAVEN 1, two pivotal clinical studies are currently underway by Chugai, Roche and Genentech.

- For children younger than 12 years of age with factor Vlll inhibitors (HAVEN 2)
- For people 12 years of age and older without factor Vlll inhibitors (HAVEN 3)

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 2015 of Chugai totalled 498.8 billion yen and the operating income

was 90.7 billion yen (IFRS Core basis).
Additional information is available on the internet at http://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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