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Chugai's Bispecific Antibody "ACE910/Emicizumab" Phase I Data in Patients with Hemophilia A Published in The New England Journal of Medicine Online

-- First NEJM Publication of Chugai's Drug Candidate --

TOKYO, May 26, 2016 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the data from hemophilia A patients who participated in a Phase I study of the bispecific antibody emicizumab (ACE001JP study) was published online in The New England Journal of Medicine (NEJM) on May 25, 2016 (EST). Emicizumab is currently under development for hemophilia A. In this first-in-patient Phase I study, a once-weekly subcutaneous injection of emicizumab demonstrated a clinically acceptable safety profile and a potential benefit for preventing bleeding in hemophilia A patients, both with and without factor VIII (FVIII) inhibitors.
http://www.nejm.org/doi/full/10.1056/NEJMoa1511769

The patient part of ACE001JP study enrolled 18 Japanese hemophilia A patients, both with and without FVIII inhibitors, to investigate the safety and to explore the potential benefit of emicizumab for preventing bleeding with regular injection. In this open-label study, patients were treated with once-weekly subcutaneous injection of emicizumab across three dosing cohorts for 12 successive weeks. The study results had been presented at the 56th American Society of Hematology (ASH) Annual Meeting held in San Francisco, CA on December 8, 2014.

"A great challenge with the current treatments for hemophilia A is that these patients need frequent intravenous injections and face the possibility of developing inhibitors to FVIII," said Chugai's Director and Executive Vice President, Dr. Yutaka Tanaka. "The study results indicated a potential for benefit from emicizumab in treating hemophilia A patients with inhibitors with once-weekly subcutaneous injection. With these findings, we expect that emicizumab may be a new treatment option to fulfill unmet medical needs of hemophilia A patients."

Emicizumab was designated as a Breakthrough Therapy by the US Food and Drug Administration in September 2015. Currently, a Phase III global study in hemophilia A patients with FVIII inhibitors is being conducted in collaboration with Roche, Chugai's strategic alliance partner. Phase III global studies in patients without FVIII inhibitors and pediatric patients are also planned for initiation in 2016.

The data of the healthy subject parts of ACE001JP study was published in *Blood* online, the journal published by ASH, on December 1, 2015.
http://dx.doi.org/10.1182/blood-2015-06-650226

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Outline of the study

Dosing group	Number of patients		Dose
	Patients with inhibitors	Patients without inhibitors	
Cohort 1	4	2	1*, 0.3** mg/kg
Cohort 2	4	2	3*, 1** mg/kg
Cohort 3	3	3	3 mg/kg

*Initial dose, **Second and subsequent doses

Study results

SAFETY

All adverse effects (AEs) observed during the 12-week course of emicizumab administration were of mild intensity, except for upper respiratory tract infection and headache of moderate intensity in 2 patients. There was no evidence of clinically relevant coagulation abnormalities as indicated by clinical findings or laboratory tests. No thromboembolic AEs were observed, even when a FVIII product or bypassing agent as hemostatic therapy for bleeding events was given during the course of emicizumab administration. One patient discontinued emicizumab administration due to injection site erythema of mild intensity. No anti-emicizumab antibodies developed during the 12 weeks.

POTENTIAL BENEFIT

A potential benefit for the prevention of bleeding with emicizumab was demonstrated during the 12-week course of administration in all cohorts irrespective of the presence of inhibitors. There was no bleeding in 13 patients during the course of emicizumab administration. The median ABRs (annualized bleeding rates) before and during emicizumab administration in each cohort were as follows:

Median ABR

Dosing group	Median ABR (events/year)	
	Six months before study entry	During emicizumab administration
Cohort 1	32.5	4.4
Cohort 2	18.3	0.0
Cohort 3	15.2	0.0

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.

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