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Translation

Positive Interim Data from Phase I/II study of Chugai's Bispecific Antibody "ACE910" Presented at the ISTH 2015 Congress

June 23, 2015 (Tokyo) - Chugai Pharmaceutical Co., Ltd. [Head office: Chuo-ku, Tokyo; Chairman & CEO: Osamu Nagayama] announced today that the long-term data of phase I/II study (ACE002JP) was presented at the ISTH 2015 Congress held in Toronto, Canada. ACE002JP is the extension study of phase I study (ACE001JP) of anti-factor IXa x anti-factor X humanized bispecific antibody "ACE910," currently being developed for the indication of hemophilia A. The presentation was made in the oral session on June 22 at 4:30 pm local time.

ACE002JP is the extension study of ACE001JP study, which is the first-in-patient phase I study to investigate safety and exploratory prophylactic efficacy profiles of ACE910 in Japanese hemophilia A patients both with and without FVIII inhibitors. Interim data of these studies showed a promising profile in terms of safety and prophylactic efficacy irrespective of the presence of inhibitors during 5.6 to 18.5 months (follow up periods).

【Outline of the study】

	Number of patients		Dose
	Patients with inhibitors	Patients without inhibitors	
C-1 cohort	4	2	1*, 0.3** mg/kg
C-2 cohort	4	2	3*, 1** mg/kg
C-3 cohort	3	3	3 mg/kg

*Initial dose, **Continuous dose

【Study results】

SAFETY

- Adverse events (AEs) were observed in 18 patients and all of them were mild or moderate in terms of intensity. Of these, side effects which cannot be ruled out as having a causal relationship with ACE910 were observed in six patients and the common symptom was injection site erythema.
- There was no evidence of clinically relevant abnormalities of coagulation indicated by clinical findings or laboratory tests in all cohorts. No thromboembolic AEs were observed, even when ACE910 was given concomitantly with FVIII products or bypassing agents as on-demand therapy for bleeding events.

- Three patients developed anti-ACE910 antibodies screened by electro-chemiluminescence immunoassay (ECLIA), which did not affect the Pharmacokinetics (PK) or Pharmacodinamics (PD) of ACE910.

EFFICACY

- Once-weekly subcutaneous injection of ACE910 demonstrated a prophylactic efficacy profile in all cohorts irrespective of the presence of inhibitors. Bleeding was completely controlled in 9 out of 18 patients during the course of ACE910 administration.
- The mean ABR (Annualized Bleeding Rate) at pre and post administration in each cohort are as follows:
  - The mean ABR

	The mean ABR (times)		follow-up period (Months) Median (Range)
	Six months prior to the study	Post ACE910 administration	
C-1 cohort (N=6)	32.5	1.7	17.8 (17.4-18.5)
C-2 cohort (N=6)	18.3	0	12.3 (8.2-13.7)
C-3 cohort (N=6)	15.2	0	6.6 (5.6-7.8)

- *Two patients in C-1 cohort increased dose from 0.3 mg/kg to 1 mg/kg, and finally 3 mg/kg due to frequent bleeding. The reduction of ABR was observed in response to dose escalation.*