NXT007: Study Session on ISTH Presentation

24 June 2025

CHUGAI PHARMACEUTICAL CO., LTD.

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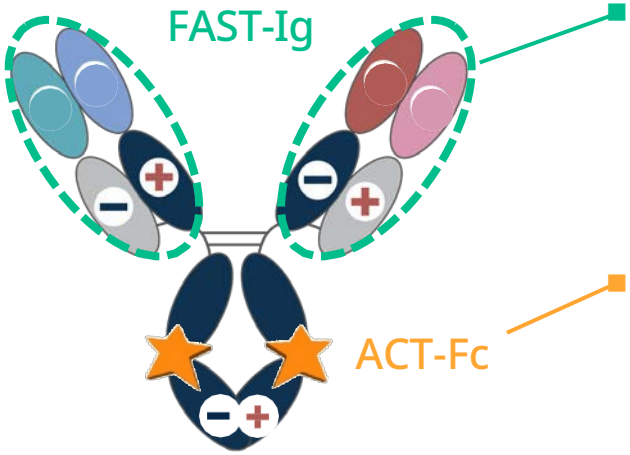
Please note that Japanese is the preferred language in expression and content, since the official language of this presentation is Japanese.

NXT007: Providing New Value to People with Hemophilia A

- **Chugai's proprietary antibody engineering technologies are applied. The ongoing Phase 2 trial results will be presented at a medical conference in 2025**
- **Three Phase 3 trials, including head to head vs. Hemlibra®, are planned to start in 2026**



Anti-coagulation factor IXa/X bispecific antibody applying FAST-Ig™: Higher efficacy is expected by optimizing the variable region of Hemlibra®

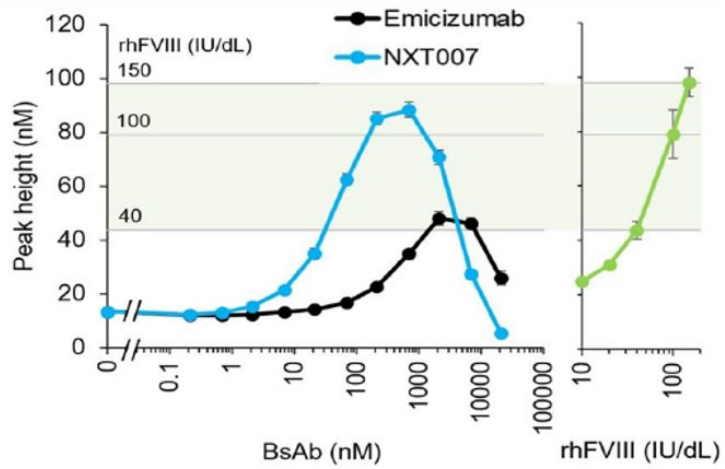
Expecting high convenience by improving antibody pharmacokinetics through the application of ACT-Fc®

P1 → P2 → P3	
P1/2	Data in 2025
vs. FVIII	P3 start exp.2026
vs. Hemlibra®	P3 start exp.2026
Pediatric patients	P3 start exp.2026

Engineered based on Hemlibra®, to enhance binding affinities, extend half-life, and allow for low volume, infrequent subcutaneous injections

- ~30-fold more potent than Hemlibra® and in vitro assay indicates that thrombin generation is within the range of people without Hemophilia A*
- High convenience in dosing (~10-week half-life** and subcutaneous injection)

in vitro Thrombin Generation Assay [1,a]



*A bispecific antibody NXT007 exerts a hemostatic activity in hemophilia A monkeys enough to keep a non-hemophiliac state (https://doi.org/10.1016/j.jtha.2023.09.034)

**Data of healthy adult part in the NXT001JG study presented at 2023 ISTH

[1] *Yuri Teranishi-Ikawa et. al Journal of Thrombosis and Haemostasis 2023* [a] tissue factor triggered

(OC 20.3)

NXT007 Prophylaxis in Emicizumab-Naive Persons with Hemophilia A without Inhibitor: Phase I/II Study (NXTAGE)

Midori Shima[1], Chur-Woo You[2], Young-Shil Park[3], Yeu-Chin Chen[4], Ming-Ching Shen[5], Jiaan-Der Wang[6], Masahiro Takeyama[7], Kagehiro Amano[8], Sheng-Chieh Chou[9], Takuya Miwa[10], Chun-An Chen[10], Takeshi Miyake[10], Keisuke Iwasaki[10], Keiji Nogami[11]

[1] Thrombosis and Hemostasis Research Center, Nara Medical University, Kashihara, Japan, [2] Department of Pediatrics, Daejeon Eulji Medical Center, Eulji University School of Medicine, Daejeon, Republic of Korea, [3] Department of Pediatrics, Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea, [4] Hemophilia Care and Research Center, Tri-Service General Hospital, Taipei, Taiwan, [5] Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan, [6] Center for Rare Disease and Hemophilia, Taichung Veterans General Hospital, Taichung, Taiwan, [7] Division of Hemophilia, National Hospital Organization Osaka National Hospital, Osaka, Japan, [8] Department of Laboratory Medicine, Tokyo Medical University, Tokyo, Japan, [9] Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [10] Chugai Pharmaceutical Co., Ltd, Tokyo, Japan; [11] Department of Pediatrics, Nara Medical University, Kashihara, Japan

Overview of NXTAGE Part B

Multiple ascending dose part in emicizumab-naïve PwHA to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics and efficacy of NXT007

Key Inclusion Criteria:
- Severe Hemophilia A
- Without FVIII inhibitors
- Ages ≥12 to <65 years

Patients received NXT007 via subcutaneous (SC) administration every 4 weeks (Q4W) in ascending dose cohorts after loading doses

(N=6-8/cohort*1)

- B-4: 4 weeks loading dose → Maintenace dose: **1.08** mg/kg **Q4W SC**
- B-3: 4 weeks loading dose → Maintenace dose: **0.7** mg/kg **Q4W SC**
- B-2: 6 weeks loading dose → Maintenace dose: **0.28** mg/kg **Q4W SC***2
- B-1: 4 weeks loading dose → Maintenace dose: **0.072** mg/kg **Q4W SC**

*1 For B-1, 10 patients were enrolled.
*2 Dosing regimen was switched from 0.14 mg/kg Q2W to reflect study protocol amendment.

Timing of the primary analysis:
- At least 6 patients completed 16 weeks of NXT007 treatment in all Part B cohorts
- First patient in: 1-Feb-2022
- Data cutoff date: 6-Nov-2024

PwHA, patients with hemophilia A; FVIII, factor VIII; Q2W, every 2 weeks

Concept of Dose Setting

- NXT007 doses were adapted by population PK simulations using the PK data from healthy volunteers who participated in NXTAGE to achieve the target FVIII-equivalent activity predicted based on FIX-NXT007-FX ternary complex concentrations.
- FVIII-equivalent activity was predicted to reach non-hemophilic level in B-2 onwards.

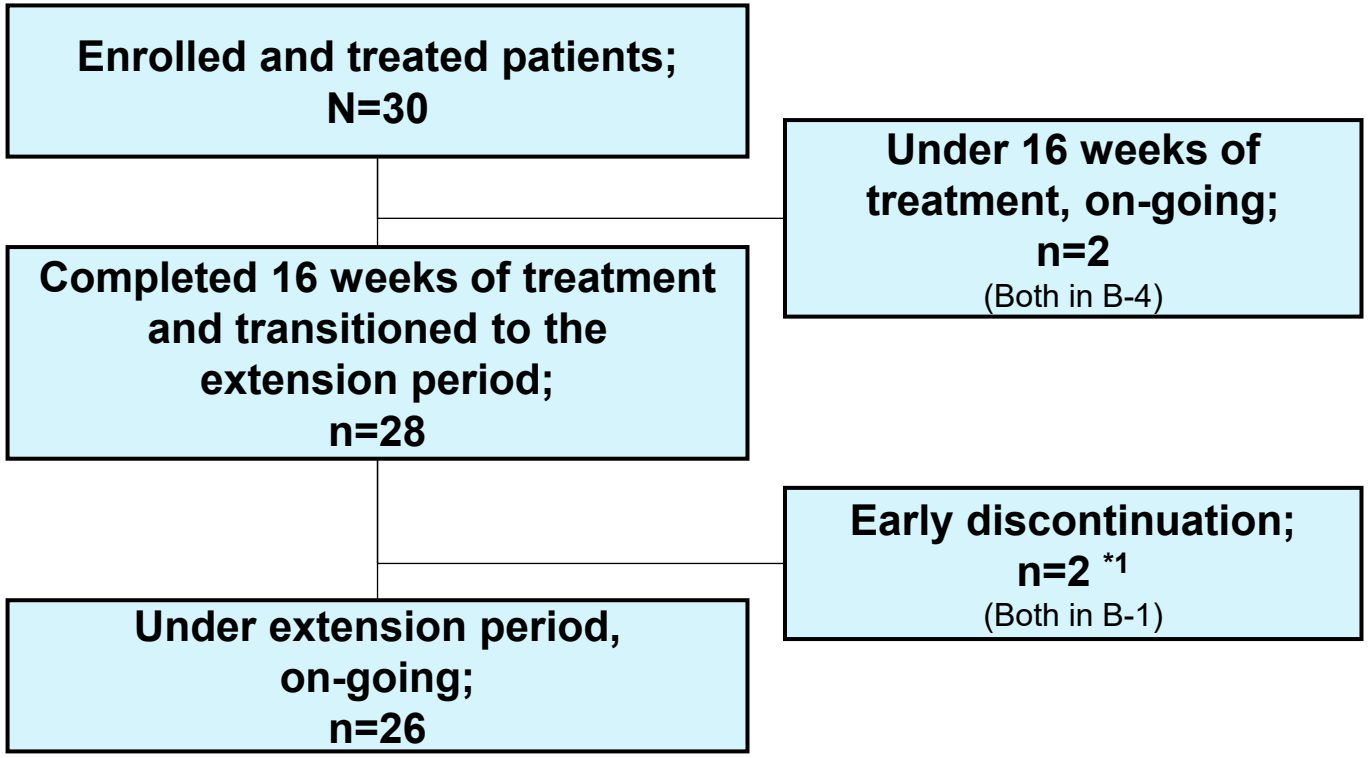
Cohort	Maintenance dose	Predicted trough levels at steady state	
		Plasma NXT007 concentration	FVIII-equivalent activity*1
B-4	1.08 mg/kg Q4W	24.8 µg/mL	**93.1 IU/dL**
B-3	0.7 mg/kg Q4W	16.1 µg/mL	**73.8 IU/dL**
B-2	0.28 mg/kg Q4W	7.27 µg/mL	**40.1 IU/dL**
B-1	0.072 mg/kg Q4W	2.29 µg/mL	**13.8 IU/dL**

*1 The FVIII-equivalent activity prediction was performed based on Yoneyama et.al., Blood (2022) 140 (Supplement 1): 11295–11296

FIX, factor IX; FVIII, factor VIII; FX, factor X; PK, pharmacokinetics; Q4W, every 4 weeks

Patient Disposition and Duration of Exposure

Patient Disposition



*1 One patient discontinued NXT007-treatments due to unrelated adverse event, lower limb fracture. Another patient discontinued NXT007-treatments due to development of anti-drug antibody (ADA) impacting PK. Both discontinued the study due to consent withdrawal thereafter.

Duration of NXT007 Exposure by Cohort

Cohort	Duration of Exposure; week (median, min-max)
B-1 (N=10)	114.1 (29-140)
B-2 (N=6)	96.4 (88-112)
B-3 (N=6)	58.1 (52-72)
B-4 (N=8)	22.2 (4-28)
Total (N=30)	**68.4 (4-140)**

PK, pharmacokinetics

Patient Demographics

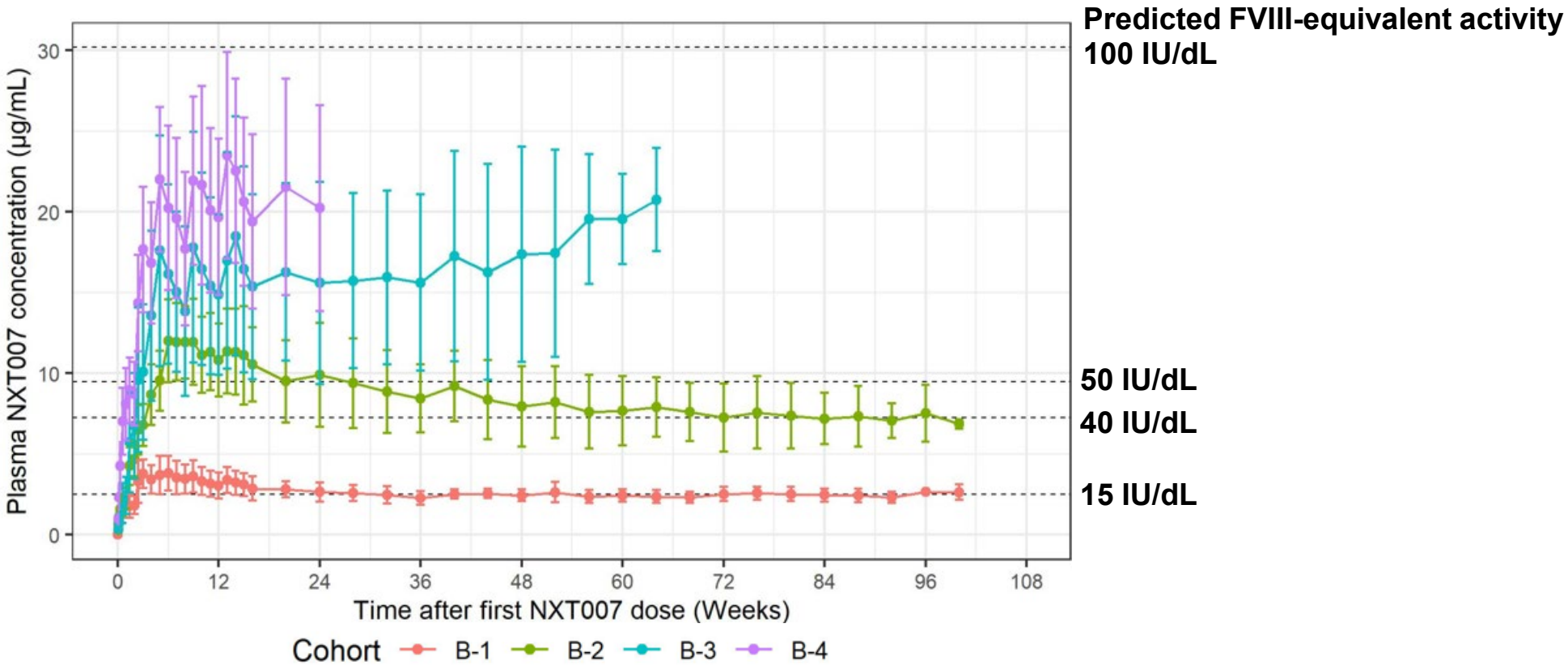
Most of the patients (96.7%) received FVIII prophylaxis before enrollment.

	B-1 (N=10)	B-2 (N=6)	B-3 (N=6)	B-4 (N=8)	Total (N=30)
Age, years, median (range)	39.5 (20 - 57)	22 (12 – 54)	37 (18 - 52)	51.0 (25 - 56)	39.5 (12-57)
Weight, kg, median (range)	68.75 (53.8 – 93.9)	78.30 (40.6 – 89.6)	60.70 (52.6 – 82.0)	70.55 (56.2 – 81.5)	69.65 (40.6-93.9)
Patients with Target joint, n (%)	3 (30.0%)	1 (16.7%)	1 (16.7%)	1 (12.5%)	6 (20.0%)
Prior treatment regimen					
Prophylaxis, n (%)	**9 (90%)**	**6 (100%)**	**6 (100%)**	**8 (100%)**	**29 (96.7%)**
Episodic, n (%)	**1 (10%)**	**0**	**0**	**0**	**1 (3.3 %)**

FVIII, factor VIII

PK and Predicted FVIII-equivalent Activity

- Dose-dependent increase of NXT007 plasma concentration was observed.
- In B-3 and B-4, plasma concentrations beyond non-hemophilic levels of FVIII-equivalent activity were maintained, consistent with the dose setting concept.

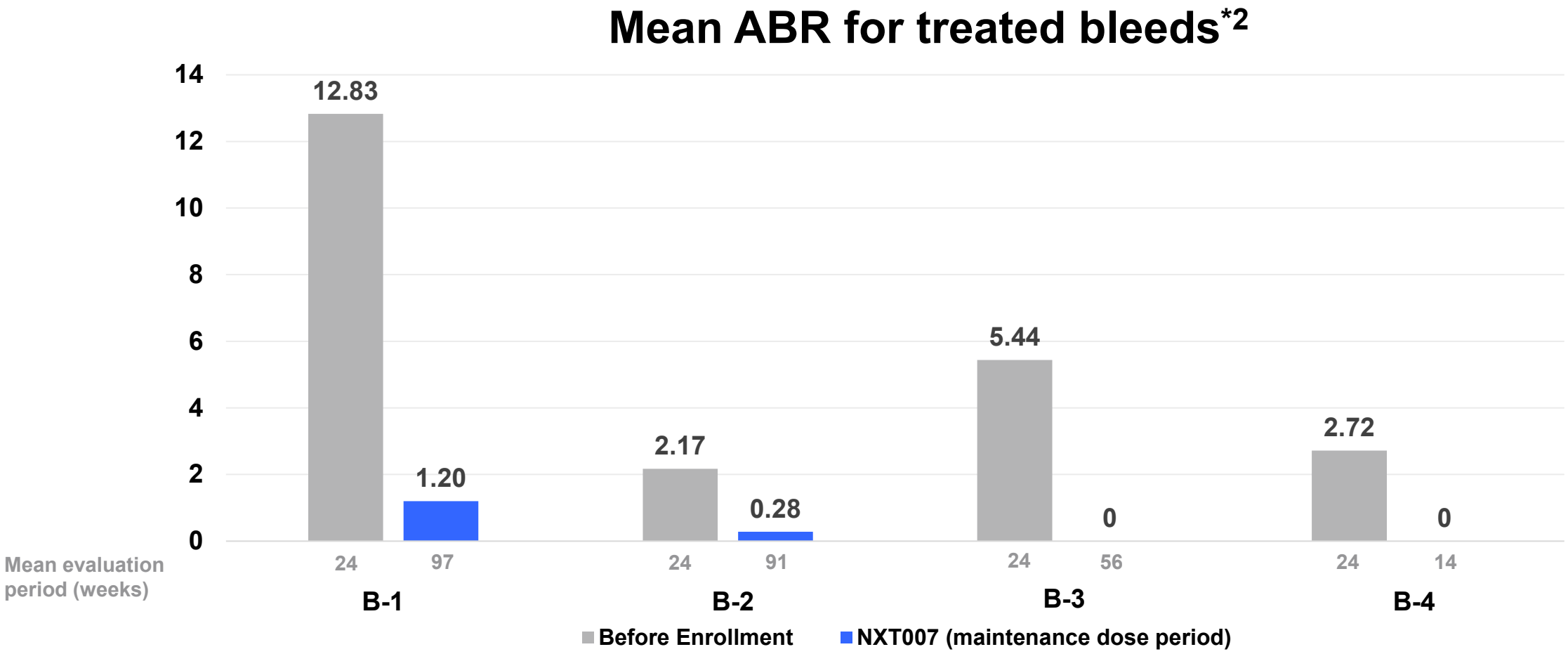


Excluding 4 PK outliers, and 2 patients with PK decrease presumably due to anti-drug antibody. The PK data after up-titration in 3 B-1 patients were also excluded. Data not shown if the number of measured values is less than two.

PK, pharmacokinetics; FVIII, factor VIII

Efficacy: Annualized Bleed Rate (ABR)

ABR decreased during NXT007 prophylaxis compared to baseline*[1].



*1 96.7% of patients received prophylactic therapy with FVIII agents.

*2 Bleeding information before study was collected from 24 weeks before the study in a retrospective manner. Calculated ABR is displayed.

FVIII, factor VIII

Safety and Tolerability

NXT007 was well tolerated:

- No dose-dependent increases in AEs were observed.
- All serious AEs were NOT related to NXT007.
- **No thromboembolic events were observed**.
- Injection site reactions were reported in 4 patients (13.3%), all of which were mild.

	B-1 (N=10)	B-2 (N=6)	B-3 (N=6)	B-4 (N=8)	Total (N=30)
Total No. of patients with at least one AE	7 (70.0%)	5 (83.3%)	3 (50.0%)	6 (75.0%)	21 (70.0%)
Total No. of AEs	17	51	10	11	89
Total No. of patients with at least one:					
Serious AE *1	3	0	0	0	3
Leaded to treatment discontinuation *1	1	0	0	0	1
NXT007-related *1	0	0	0	0	0
Thromboembolic event	0	0	0	0	0
NXT007-related AE *2	2	1	0	3	6
Injection site reactions	2	0	0	2	4

*1 Serious AEs include lower limb fracture, ankle fracture, and carbon monoxide poisoning, among which the lower limb fracture leaded to study drug discontinuation.

*2 Injection site erythema (1 event in B-1, 1 event in B-4), injection site reaction (2 events in B-1), rash (1 event in B-2) , hepatic function abnormal (1 event in B-4), and injection site rash (1 event in B-4).

AE, adverse event

Immunogenicity: Anti-Drug Antibody (ADA)

- ADA was observed in 22 out of 30 patients; the number of ADA positive patients at the final observation before the data cutoff was 10.
- ADA impacting PK was observed in 2 patients.
  - One patient in B-1 completely lost NXT007 plasma concentration due to ADA, and discontinued treatment.
  - The other patient in B-3 experienced a decrease in plasma concentration to B-1 levels, and was continuing NXT007 treatment without bleeding events.
- No ADA cross-reacting with emicizumab was observed.

	B-1 (N=10)	B-2 (N=6)	B-3 (N=6)	B-4 (N=8)	Total (N=30)
ADA post-baseline incidence *1	**7**	**6**	**4**	**5**	**22**
ADA impacting PK	1	0	1	0	2
ADA cross-reacting with emicizumab	0	0	0	0	0

*1 No patients were ADA positive at baseline.

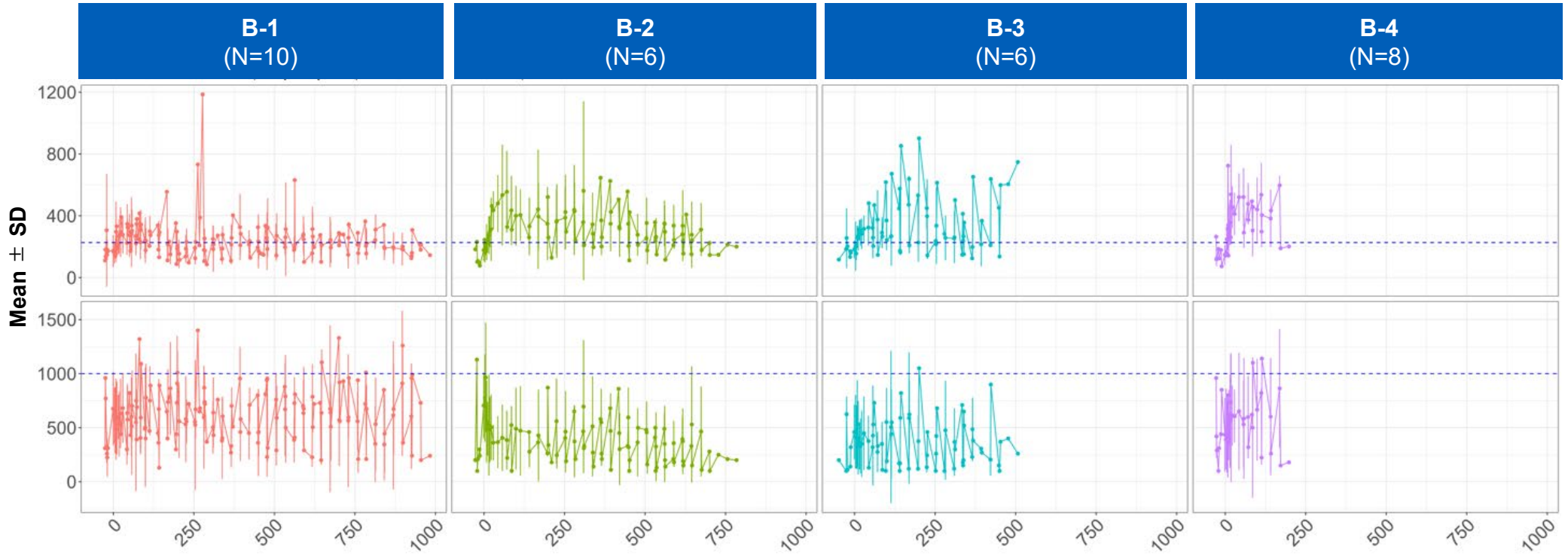
PK, pharmacokinetics

Coagulation Markers

- Prothrombin fragment 1+2 levels showed an increasing trend above the reference range, suggesting increased coagulation potential.
- No increasing trend was observed in D-dimer, suggesting no significant systemic hypercoagulability.

Prothrombin fragment 1+2

D-dimer



Blue lines represent upper limit of reference ranges

AE, adverse event

Conclusions

NXTAGE Part B examined NXT007, the emicizumab-based next generation bispecific antibody, in PwHA with Q4W SC dosing for the first time.

NXT007 prophylaxis led to a decrease in ABR compared to baseline.

No treated bleeds were observed during maintenance dose period in B-3 and B-4 with predicted FVIII-equivalent activity beyond the non-hemophilic level.

No safety concerns were observed up to the highest dose cohort (B-4).

The results suggest that NXT007 has a potential to provide a hemostatic normalization in PwHA with acceptable safety profile, supporting advancement to next phase clinical studies. The efficacy and safety of NXT007, including hypercoagulability and ADA, should be further investigated.

PwHA, patients with Hemophilia A; Q4W, every 4 weeks; SC, subcutaneous; FVIII, factor VIII

Contacts

Corporate Communications Dept.

For Investors: Investor Relations Group	
Tel：	+81 (0)3-3273-0554
E-mail：	ir@chugai-pharm.co.jp
Person in charge：	Takayuki Sakurai, Tomoyuki Shimamura, Yayoi Yamada, Yuri Ikegaya, Mari Otsuka

INNOVATION BEYOND IMAGINATION

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