First-in-human pharmacokinetic, safety, and preliminary efficacy studies of single- and multiple-dose FRSW117, a novel PEGylated recombinant factor VIII-Fc fusion protein with an extended half-life, in patients with severe hemophilia A

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Supplementary materials

Table S1. Adverse events of the phase I trial

	ADVATE®			FRSW117							Total
	PK period			PK period			Observation period			Total	(N=13)
	25 IU/kg (n=6)	50 IU/kg (n=7)	Total (N=13)	25 IU/kg (n=6)	50 IU/kg (n=7)	Total (N=13)	25 IU/kg (n=6)	50 IU/kg (n=7)	Total (N=13)	(N=13)	n (%)
TEAE	3 (50.0)	2 (28.6)	5 (38.5)	2 (33.3)	3 (42.9)	5 (38.5)	3 (50.0)	0	3 (23.1)	7 (53.8)	9 (69.2)
TEAEs related to ADVATE®	3 (50.0)	2 (28.6)	5 (38.5)	1 (16.7)	2 (28.6)	3 (23.1)	1 (16.7)	0	1 (7.7)	3 (23.1)	6 (46.2)
TEAEs related to FRSW117	0	0	0	1 (16.7)	2 (28.6)	3 (23.1)	1 (16.7)	0	1 (7.7)	3 (23.1)	3 (23.1)
SAE	0	0	0	0	0	0	0	0	0	0	0
Grade >3 TEAE	0	0	0	0	0	0	0	0	0	0	0
AESI	0	0	0	0	0	0	0	0	0	0	0
TEAE leading to early withdrawal from the study	0	0	0	0	0	0	0	0	0	0	0
TEAE leading to discontinuation of study drug	0	0	0	0	0	0	0	0	0	0	0

TEAE: treatment-emergent adverse event; SAE: serious adverse event; CTCAE: Common Terminology Criteria for Adverse Events; AESI: adverse event of special interest.

Table S2. Trough FVIIII activity of FRSW117 during multi-dose treatment period (baseline-corrected), mean ±SD

Time	**40 IU/kg (n=8)**	**50 IU/kg (n=7)**
Before ED2 administration	2.40 ±1.976	2.69 ±1.125
Before ED3 administration	3.08 ±1.482	2.23 ±0.656
Before ED4 administration	2.98 ±1.627	2.80 ±0.724
168 h after ED4 administration	3.25 ±1.596	2.88 ±0.637

ED: exposure day; SD: standard deviation.

Table S3. Adverse events of phase II trial

	40 IU/kg (n=8)			50 IU/kg (n=7)			Total (N=15)		
	PK period	**Observation period**	**Total**	**PK period**	**Observation period**	**Total**	**PK period**	**Observation period**	**Total**
TEAE	3 (37.5)	2 (25.0)	5 (62.5)	5 (71.4)	1 (14.3)	5 (71.4)	8 (53.3)	3 (20.0)	10 (66.7)
TRAE	1 (12.5)	0	1 (12.5)	1 (14.3)	0	1 (14.3)	2 (13.3)	0	2 (13.3)
SAE	0	0	0	0	0	0	0	0	0
SAE related to study drug	0	0	0	0	0	0	0	0	0
Grade >3 TEAEs	0	0	0	0	0	0	0	0	0
Grade >3 TRAE	0	0	0	0	0	0	0	0	0
AESI	0	0	0	0	0	0	0	0	0
AESI related to the study drug	0	0	0	0	0	0	0	0	0
TEAE leading to early withdrawal	0	0	0	0	0	0	0	0	0
TRAE leading to early withdrawal	0	0	0	0	0	0	0	0	0
TEAE leading to treatment discontinuation	0	0	0	0	0	0	0	0	0
TRAE leading to treatment discontinuation	0	0	0	0	0	0	0	0	0
TEAE leading to death	0	0	0	0	0	0	0	0	0
TRAE leading to death	0	0	0	0	0	0	0	0	0

TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse event; SAE: serious adverse event; CTCAE: Common Terminology Criteria for

Adverse Events; AESI: adverse event of special interest.