Clinical trial results:
A multinational, open-label, randomised, controlled trial to investigate efficacy and safety of NNC0365-3769 (Mim8) in adults and adolescents with haemophilia A with or without inhibitors.

Summary

EudraCT number	2020-001048-24
Trial protocol	IE SK DK DE BE AT LV LT FR NL PL PT IT
Global end of trial date	17 December 2024

Results information

Result version number	v1 (current)
This version publication date	03 July 2025
First version publication date	03 July 2025

Trial information

Trial identification

Sponsor protocol code	NN7769-4514

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05053139
WHO universal trial number (UTN)	U1111-1249-4378
Other trial identifiers	Japanese trial registration number: jRCT2031210643

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Alle, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002762-PIP02-20
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To confirm the haemostatic effect of Mim8 as treatment prophylaxis for adult and adolescent patients with haemophilia A with or without inhibitors. This will be done by: - Demonstrating superiority in number of bleeding episodes when treated with Mim8 once-weekly versus no prophylaxis for subjects on no prophylaxis treatment prior to enrolment (Comparing Arm 1 and Arm 2 main treatment period) - Demonstrating non-inferiority in number of bleeding episodes when treated with either Mim8 once-weekly or once-monthly versus treatment with coagulation factor prophylaxis during run-in for subjects on prophylaxis treatment prior to enrolment (Comparing Arm 3 and Arm 4 run-in with main treatment period)

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (Oct 2013) and ICH Good Clinical Practice, including archiving of essential documents (May 1996) and EN ISO 14155 Part 1 and 2 and FDA 21 CFR 312.120.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	China: 36
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	India: 12
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Japan: 12
Country: Number of subjects enrolled	Korea, Republic of: 18

Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Malaysia: 6
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	Saudi Arabia: 7
Country: Number of subjects enrolled	Serbia: 2
Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Türkiye: 11
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	United States: 20
Country: Number of subjects enrolled	South Africa: 6
Worldwide total number of subjects	281
EEA total number of subjects	114

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	87
Adults (18-64 years)	190
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 100 sites that enrolled subjects in 32 countries. The study was conducted in 2 parts: main part (26 weeks) and extension part (26 weeks), With 5 randomized arms (Arm 1, 2a, 2b, 3 and 4).

Pre-assignment

Screening details:

Subjects on coagulation factor prophylaxis entered run-in period (26 weeks) in Arm 3 and 4 to collect high-quality bleeding, treatment data and randomized to main part. Subjects with no prophylaxis (Arm 1, 2a and 2b) was randomized to main part directly. After main part of study, subjects continued in the extension part of the study.

Period 1

Period 1 title	Main Phase (26 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm1: No PPX - Mim8 PPX QW/QM

Arm description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on agreement with the investigator.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once weekly or once monthly in Arm 1 during extension phase as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing.

Arm title	Arm 2a: Mim8 PPX QW

Arm description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental

Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once weekly dose in Arm 2a as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Arm title	Arm 2b: Mim8 PPX QM

Arm description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once monthly dose in Arm 2b as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Arm title	Arm 3: PPX - Mim8 PPX QW

Arm description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once weekly dose in Arm 3 as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Arm title	Arm 4: PPX- Mim8 PPX QM

Arm description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental

Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once monthly dose in Arm 4 as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Number of subjects in period 1	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM
Started	18	22	21
Completed	18	21	21
Not completed	0	1	0
Physician decision	-	1	-
Consent withdrawn by subject	-	-	-
Withdrawal by Parent/Guardian	-	-	-

Number of subjects in period 1	Arm 3: PPX - Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM
Started	111	109
Completed	105	108
Not completed	6	1
Physician decision	2	1
Consent withdrawn by subject	3	-
Withdrawal by Parent/Guardian	1	-

Period 2

Period 2 title	Extension Phase (26 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm1: No PPX - Mim8 PPX QW/QM

Arm description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on

agreement with the investigator.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once weekly or once monthly in Arm 1 during extension phase as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing.

Arm title	Arm 2a: Mim8 PPX QW

Arm description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once weekly or once monthly in Arm 2a as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing.

Arm title	Arm 2b: Mim8 PPX QM

Arm description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once-monthly dose in Arms 2b as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Arm title	Arm 3: PPX - Mim8 PPX QW

Arm description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental

Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once weekly dose in Arm 3 as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Arm title	Arm 4: PPX- Mim8 PPX QM

Arm description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Arm type	Experimental
Investigational medicinal product name	NNC0365-3769 B (Mim8)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose was administered once, followed by once monthly dose in Arm 4 as maintenance doses. Dose amount is based on weight band of subject, whether it is a loading or maintenance dose, and the frequency of dosing

Number of subjects in period 2[1]	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM
Started	18	21	21
Arm 1: Mim8 QW	8 [2]	0 [3]	0 [4]
Arm1: Mim8 QM	10 [5]	0 [6]	0 [7]
Completed	17	21	21
Not completed	1	0	0
Consent withdrawn by subject	1	-	-
Physician decision	-	-	-

Number of subjects in period 2[1]	Arm 3: PPX - Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM
Started	104	108
Arm 1: Mim8 QW	0 [8]	0 [9]
Arm1: Mim8 QM	0 [10]	0 [11]
Completed	104	106
Not completed	0	2
Consent withdrawn by subject	-	1
Physician decision	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: As per the data this is correct, this is a bug thrown by PharmaCM

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Arm 1: Mim8 QW: The milestone is only applicable for Arm 1 (QW)

Baseline characteristics

Reporting groups

Reporting group title	Arm1: No PPX - Mim8 PPX QW/QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on agreement with the investigator.

Reporting group title	Arm 2a: Mim8 PPX QW

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 2b: Mim8 PPX QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 3: PPX - Mim8 PPX QW

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 4: PPX- Mim8 PPX QM

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM
Number of subjects	18	22	21
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0

Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	6	6	5
Adults (18-64 years)	12	16	16
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	30	31	33
standard deviation	± 13	± 16	± 16
Gender Categorical			
Units: Subjects			
Female	1	0	2
Male	17	22	19
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	12	12	12
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	4	9	7
More than one race	1	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	1	2
Not Hispanic or Latino	17	21	19
Unknown or Not Reported	1	0	0

Reporting group values	Arm 3: PPX - Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM	Total
Number of subjects	111	109	281
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	37	33	87
Adults (18-64 years)	73	73	190
From 65-84 years	1	3	4
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	31	31	
standard deviation	± 16	± 16	-

Gender Categorical Units: Subjects			
Female	0	1	4
Male	111	108	277
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	25	28	89
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	1	2	7
White	72	68	160
More than one race	7	7	15
Unknown or Not Reported	5	4	9
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	7
Not Hispanic or Latino	104	103	264
Unknown or Not Reported	5	4	10

End points reporting groups

Reporting group title	Arm1: No PPX - Mim8 PPX QW/QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on agreement with the investigator.

Reporting group title	Arm 2a: Mim8 PPX QW

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 2b: Mim8 PPX QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 3: PPX - Mim8 PPX QW

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 4: PPX- Mim8 PPX QM

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm1: No PPX - Mim8 PPX QW/QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on agreement with the investigator.

Reporting group title	Arm 2a: Mim8 PPX QW

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 2b: Mim8 PPX QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 3: PPX - Mim8 PPX QW

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 4: PPX- Mim8 PPX QM

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Subject analysis set title	Arm1: No PPX - Mim8 PPX QW/QM
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on agreement with the investigator.

Subject analysis set title	Arm 2a: Mim8 PPX QW
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Subject analysis set title	Arm 2b: Mim8 PPX QM
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Subject analysis set title	Arm 3: PPX - Mim8 PPX QW (Run-in Part)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Subject analysis set title	Arm 3: PPX - Mim8 PPX QW (Main Part)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks. Subjects entered the main part of the study, to receive loading dose of 24 mg (body weight 30-<45 kg) to 55 mg (body weight >=45 kg) Mim8 QW followed by maintenance dose of 4 mg (body weight 30 -<45 kg)-9 mg >=45 kg) subcutaneously. After the main part, subjects continued to receive the same dosing schedule of Mim8 QW subcutaneously in the extension part of the study (26 weeks).

Subject analysis set title	Arm 4: PPX- Mim8 PPX QM (Run-in Part)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Subject analysis set title	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Subject analysis set title	Arm 2a: Mim8 PPX QW
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of 24 mg (body weight 30-<45 kg) to 55 mg (body weight >=45 kg) Mim8 QW followed by maintenance dose of 4 mg (body weight 30 -<45 kg)-9 mg (body weight >=45 kg) subcutaneously. After the main part, subjects continued to receive the same dosing schedule of Mim8 QW subcutaneously in the extension part of the study (26 weeks).

Subject analysis set title	Arm 2b: Mim8 PPX QM
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of 40 mg (body weight 30-<45 kg)-92 mg (body weight ≥45 kg) Mim8 QM followed by maintenance dose 20 mg (body weight 30-<45 kg)-46 mg (body weight >=45 kg) subcutaneously. After the main part, subjects continued to receive the same dosing schedule of Mim8 QM subcutaneously in the extension part of the study (26 weeks).

Subject analysis set title	Arm 3: PPX - Mim8 PPX QW
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks. Subjects entered the main part of the study, to receive loading dose of 24 mg (body weight 30-<45 kg) to 55 mg (body weight >=45 kg) Mim8 QW

followed by maintenance dose of 4 mg (body weight 30 -<45 kg)-9 mg >=45 kg) subcutaneously. After the main part, subjects continued to receive the same dosing schedule of Mim8 QW subcutaneously in the extension part of the study (26 weeks).

Subject analysis set title	Arm 4: PPX- Mim8 PPX QM
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks. Subjects entered main part of the study, to receive loading dose of 40 mg (body weight 30-<45 kg)-92 mg (body weight ≥45 kg) Mim8 QM followed by maintenance dose 20 mg (body weight 30-<45 kg)-46 mg (body weight >=45 kg) subcutaneously. After the main part, subjects continued to receive the same dosing schedule of Mim8 QM subcutaneously in the extension part of the study (26 weeks).

Primary: No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated bleeds (Annualised Bleeding Rate)

End point title	No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated bleeds (Annualised Bleeding Rate)

End point description:

Number of treated bleeds per year (Annualised Bleeding Rate) data is reported. Annualised bleeding rate (ABR) is the number of bleeding episodes per year. Full analysis set (FAS) population included all subjects randomized.

End point type	Primary

End point timeframe:

From randomisation (week 0) to end of main part (Week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	21	20	
Units: Bleeding episodes per year				
arithmetic mean (confidence interval 95%)	15.75 (10.70 to 23.20)	0.45 (0.18 to 1.14)	0.20 (0.06 to 0.72)	

Statistical analyses

Statistical analysis title	No PPX Vs Mim8 PPX QM
Comparison groups	Arm1: No PPX - Mim8 PPX QW/QM v Arm 2b: Mim8 PPX QM
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Negative Binomial Regression
Parameter estimate	Annualised bleeding rate ratio
Point estimate	0.013
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.003
upper limit	0.048

Statistical analysis title	No PPX Vs Mim8 PPX QW
Comparison groups	Arm1: No PPX - Mim8 PPX QW/QM v Arm 2a: Mim8 PPX QW
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Negative binomial regression
Parameter estimate	Annualised bleeding rate ratio
Point estimate	0.029
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.011
upper limit	0.078

Primary: Prophylaxis treatment (Arms 3 and 4): Number of treated bleeds (Annualised Bleeding Rate)

End point title	Prophylaxis treatment (Arms 3 and 4): Number of treated bleeds (Annualised Bleeding Rate)

End point description:

Number of treated bleeds per year (Annualised Bleeding Rate) data is reported. Annualised bleeding rate(ABR) is the number of bleeding episodes per year. Full analysis set (FAS) population included all participants randomised

End point type	Primary

End point timeframe:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26)

End point values	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 3: PPX - Mim8 PPX QW (Main Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	98	98	98
Units: Bleeding episodes per year				
arithmetic mean (confidence interval 95%)	4.83 (3.59 to 6.51)	2.51 (1.42 to 4.42)	3.10 (2.23 to 4.29)	1.78 (1.17 to 2.71)

Statistical analyses

Statistical analysis title	PPX (run-in) vs Mim8 PPX QM (main)

Statistical analysis description:

The actual analyzed population is 98 subjects

Comparison groups	Arm 4: PPX- Mim8 PPX QM (Run-in Part) v Arm 4: PPX- Mim8

	PPX QM (Main Part)
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0066
Method	Negative binomial regression
Parameter estimate	Annualised bleeding rate ratio
Point estimate	0.574
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.385
upper limit	0.857

Statistical analysis title	PPX (Run-in) vs Mim8 PPX QW (Main)
Statistical analysis description:	
The actual analyzed population is 98 subjects	
Comparison groups	Arm 3: PPX - Mim8 PPX QW (Run-in Part) v Arm 3: PPX - Mim8 PPX QW (Main Part)
Number of subjects included in analysis	196
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0406
Method	Negative binomial regression
Parameter estimate	Annualised bleeding rate ratio
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.278
upper limit	0.973

Secondary: Arms 2a, 2b, 3 and 4: Number of injection site reactions	
End point title	Arms 2a, 2b, 3 and 4: Number of injection site reactions
End point description:	
Number of injection site reactions data is reported from randomisation (week 0) to end of main (week 26). Full analysis set (FAS) population included all subjects randomized.	
End point type	Secondary
End point timeframe:	
From randomisation (week 0) to end of main (week 26)	

End point values	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21	20	98	98
Units: Number of events				
number (not applicable)	2	2	86	13

Statistical analyses

No statistical analyses for this end point

Secondary: Prophylaxis treatment (Arms 3 and 4): Number of treated spontaneous bleeds

End point title	Prophylaxis treatment (Arms 3 and 4): Number of treated spontaneous bleeds

End point description:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26). Full analysis set (FAS) population included all subjects randomised

End point type	Secondary

End point timeframe:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26)

End point values	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 3: PPX - Mim8 PPX QW (Main Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	98	98	98
Units: Spontaneous bleeding episodes per year				
arithmetic mean (confidence interval 95%)	2.73 (1.94 to 3.86)	1.49 (0.65 to 3.42)	1.83 (1.10 to 3.04)	0.74 (0.42 to 1.32)

Statistical analyses

No statistical analyses for this end point

Secondary: Arms 2a, 2b, 3 and 4: Number of participants with anti-Mim8 antibodies

End point title	Arms 2a, 2b, 3 and 4: Number of participants with anti-Mim8 antibodies

End point description:

Number of participants with anti-Mim8 antibodies from randomisation (week 0) to end of extension (week 52) is reported. Safety analysis set (SAS) included all subjects randomly assigned to study treatment and who take at least 1 dose of study product.

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of extension (week 52)

End point values	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	Arm 3: PPX - Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	21	111	109
Units: Subjects	2	2	12	5

Statistical analyses

No statistical analyses for this end point

Secondary: No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated spontaneous bleeds (Annualised Bleeding Rate)

End point title	No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated spontaneous bleeds (Annualised Bleeding Rate)

End point description:

Number of treated spontaneous bleeds per year (ABR) data is reported from randomisation (week 0) to end of main (week 26). ABR is the number of bleeding episodes per year. Full analysis set (FAS) population included all subjects randomised

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of main (Week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	21	20	
Units: Spontaneous bleeding episodes per year				
arithmetic mean (confidence interval 95%)	11.78 (7.48 to 18.54)	0.09 (0.01 to 0.69)	0.24 (0.07 to 0.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Prophylaxis treatment (Arms 3 and 4): Number of treated joint bleeds

End point title	Prophylaxis treatment (Arms 3 and 4): Number of treated joint bleeds

End point description:

Number of treated joint bleeds data is reported from initiation of run-in (26-52 weeks prior to week 0) to week 0. Full analysis set (FAS) included all subjects randomized.

End point type	Secondary

End point timeframe:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomization (week 0) to end of main (Week 26)

End point values	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 3: PPX - Mim8 PPX QW (Main Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	98	98	98
Units: Spontaneous bleeding episodes per year				
arithmetic mean (confidence interval 95%)	3.60 (2.62 to 4.95)	1.80 (0.91 to 3.55)	2.06 (1.43 to 2.97)	1.09 (0.60 to 1.99)

Statistical analyses

No statistical analyses for this end point

Secondary: No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated joint bleeds

End point title	No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated joint bleeds

End point description:

Number of treated joint bleeds data is reported from randomisation (week 0) to end of main (Week 26)

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of main (Week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	21	20[1]	
Units: Joint bleeding episodes per year				
arithmetic mean (confidence interval 95%)	10.60 (6.28 to 17.89)	0.48 (0.18 to 1.29)	99999 (99999 to 99999)	

Notes:

[1] - Since number of subjects with bleeding is zero, mean and 95% CI data is not available.

Statistical analyses

No statistical analyses for this end point

Secondary: No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated traumatic bleeds

End point title	No prophylaxis treatment (Arms 1, 2a, and 2b): Number of

	treated traumatic bleeds

End point description:

Number of treated traumatic bleeds data is reported from randomisation (week 0) to end of main (Week 26)

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of main (Week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	20	21	
Units: Traumatic bleeding episodes per year				
arithmetic mean (confidence interval 95%)	1.86 (0.86 to 4.05)	0.19 (0.05 to 0.67)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Prophylaxis treatment (Arms 3 and 4): Number of treated traumatic bleeds

End point title	Prophylaxis treatment (Arms 3 and 4): Number of treated traumatic bleeds

End point description:

Number of treated traumatic bleeds data is reported From initiation of run-in (26-52 weeks prior to week 0) to week 0

End point type	Secondary

End point timeframe:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomization (week 0) to end of main (Week 26)

End point values	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 3: PPX - Mim8 PPX QW (Main Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	98	98	98
Units: Traumatic bleeding episodes per year				
arithmetic mean (confidence interval 95%)	1.95 (1.39 to 2.74)	0.89 (0.58 to 1.37)	1.28 (0.94 to 1.75)	0.88 (0.57 to 1.37)

Statistical analyses

No statistical analyses for this end point

Secondary: Prophylaxis treatment (Arms 3 and 4): Number of treated target joint bleeds

End point title	Prophylaxis treatment (Arms 3 and 4): Number of treated target joint bleeds

End point description:

Number of treated target joint bleeds data is reported From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26)

End point type	Secondary

End point timeframe:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26)

End point values	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 3: PPX - Mim8 PPX QW (Main Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	98	98	98
Units: Spontaneous bleeding episodes per year				
arithmetic mean (confidence interval 95%)	1.12 (0.62 to 2.02)	0.38 (0.14 to 1.08)	0.48 (0.21 to 1.09)	0.35 (0.11 to 1.08)

Statistical analyses

No statistical analyses for this end point

Secondary: No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated target joint bleeds

End point title	No prophylaxis treatment (Arms 1, 2a, and 2b): Number of treated target joint bleeds

End point description:

Number of treated target joint bleeds data is reported from randomisation (week 0) to end of main (Week 26)

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of main (Week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	21	20	
Units: Spontaneous bleeding episodes per year				
arithmetic mean (confidence interval 95%)	3.91 (1.96 to 7.77)	0.26 (0.07 to 0.99)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: (Arms 2a, 2b, 3 and 4): Mim8 plasma concentration

End point title	(Arms 2a, 2b, 3 and 4): Mim8 plasma concentration

End point description:

Mim8 plasma concentration data is presented from randomisation (week 0) to end of extension (week 52) in this endpoint. Data is reported in which subjects were a part of at any time from week 0 to week 52, not at specific time points assessed from week 0 to week 52. FAS included all subjects who were randomized

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of extension (week 52)

End point values	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	Arm 3: PPX - Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	21	109	108
Units: microgram per mililiter (µg/mL)				
arithmetic mean (standard deviation)	4.93 (± 1.96)	3.50 (± 1.42)	4.81 (± 1.65)	4.18 (± 1.76)

Statistical analyses

No statistical analyses for this end point

Secondary: Prophylaxis treatment (Arms 3 and 4): Consumption of factor product per bleed treatment (number of injections)

End point title	Prophylaxis treatment (Arms 3 and 4): Consumption of factor product per bleed treatment (number of injections)

End point description:

Number of injections consumed per bleed treatment data is reported from initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26). FAS included all subjects who were randomised.

End point type	Secondary

End point timeframe:

From initiation of run-in (26-52 weeks prior to week 0) to week 0 and from randomisation (week 0) to end of main (Week 26).

End point values	Arm 3: PPX - Mim8 PPX QW (Run-in Part)	Arm 3: PPX - Mim8 PPX QW (Main Part)	Arm 4: PPX- Mim8 PPX QM (Run-in Part)	Arm 4: PPX- Mim8 PPX QM (Main Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	98	98	98	98
Units: Number of injections				
arithmetic mean (standard deviation)	1.8 (± 2.6)	1.8 (± 1.6)	1.4 (± 1.0)	1.5 (± 1.2)

Statistical analyses

No statistical analyses for this end point

Secondary: No prophylaxis treatment (Arms 1, 2a, and 2b): Consumption of factor product per bleed treatment (number of injections)

End point title	No prophylaxis treatment (Arms 1, 2a, and 2b): Consumption of factor product per bleed treatment (number of injections)

End point description:

Consumption of factor product per bleed treatment (number of injections) is reported from randomisation (week 0) to end of main (Week 26). Full analysis set (FAS) included all subjects who were randomised.

End point type	Secondary

End point timeframe:

From randomisation (week 0) to end of main (Week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17	21	20	
Units: Number of injections				
arithmetic mean (standard deviation)	1.7 (± 1.9)	1.2 (± 0.4)	1.0 (± 0.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: All participants (Arms 1, 2a, 2b, 3 and 4): Change in physical function domain of PedsQLTM

End point title	All participants (Arms 1, 2a, 2b, 3 and 4): Change in physical function domain of PedsQLTM

End point description:

PedsQL measures quality of life and the physical functioning domain measures physical functioning. Higher scores indicate a better quality of life and better physical functioning. Positive change indicates

improvement and negative change indicates worsening. The score ranges from 0-100. FAS included all subjects who were randomised. Here, overall number of subjects analysed (N) = subjects with available data for this outcome measure.

End point type	Secondary

End point timeframe:

From randomisation (week 0) to the end of the main part (week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	Arm 3: PPX - Mim8 PPX QW (Run-in Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	13	15	79
Units: Score points				
arithmetic mean (standard deviation)	-5.5 (± 17.8)	14.2 (± 22.0)	20.8 (± 20.3)	1.9 (± 13.1)

End point values	Arm 4: PPX-Mim8 PPX QM (Run-in Part)			
Subject group type	Subject analysis set			
Number of subjects analysed	81			
Units: Score points				
arithmetic mean (standard deviation)	2.1 (± 10.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Arms 1, 2a, 2b, 3 and 4: Change in participant’s treatment burden using the Hemo-TEM

End point title	Arms 1, 2a, 2b, 3 and 4: Change in participant’s treatment burden using the Hemo-TEM

End point description:

Hemophilia Treatment Experience Measure (Hemo -TEM) measures treatment burden. Higher scores indicate a greater treatment burden and negative change indicates improvement. The score ranges from 0-100. FAS included all subjects who were randomised. Here, Overall number of subjects analysed (N) = subjects with available data for this outcome measure.

End point type	Secondary

End point timeframe:

From randomisation (week 0) to the end of the main part (week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	Arm 3: PPX - Mim8 PPX QW (Run-in Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	13	15	82
Units: Score points				
arithmetic mean (standard deviation)	-2.2 (± 14.1)	-9.9 (± 13.4)	-11.2 (± 11.6)	-10.8 (± 15.5)

End point values	Arm 4: PPX-Mim8 PPX QM (Run-in Part)			
Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Score points				
arithmetic mean (standard deviation)	-10.0 (± 10.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Arms 1, 2a, 2b, 3 and 4: Change in participant’s joint pain score using Joint Pain Rating Scale (JPRS)

End point title	Arms 1, 2a, 2b, 3 and 4: Change in participant’s joint pain score using Joint Pain Rating Scale (JPRS)

End point description:

JPRS measures joint pain. Higher scores indicate a higher joint pain intensity. The questionnaire asks "In the past 7 days, how would you rate your worst pain in your joints?". Positive change indicates improvement and negative change indicates worsening. The score ranges from 0-10. FAS included all subjects who were randomised. Here, Overall number of subjects analysed (N) = subjects with available data for this outcome measure.

End point type	Secondary

End point timeframe:

From randomisation (week 0) to the end of the main part (week 26)

End point values	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 2b: Mim8 PPX QM	Arm 3: PPX - Mim8 PPX QW (Run-in Part)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	13	15	82
Units: Score points				
arithmetic mean (standard deviation)	-0.8 (± 2.4)	-0.5 (± 3.4)	-1.8 (± 2.8)	-0.1 (± 2.4)

End point values	Arm 4: PPX-Mim8 PPX QM (Run-in Part)			

Subject group type	Subject analysis set			
Number of subjects analysed	85			
Units: Score points				
arithmetic mean (standard deviation)	-0.3 (± 1.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation (week 0) to end of the trial (Week 52)

Adverse event reporting additional description:

The data presented for Arm1 includes both the main period (No PPX) and the extension period (Mim8 PPX QW/QM)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Arm1: No PPX - Mim8 PPX QW/QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and continued no prophylaxis (on-demand treatment with their standard of care products) treatment in the main part of the study (26 weeks). After the main part, subjects continued in the extension part of the study (26 weeks) to receive either once-weekly (QW) loading dose of 24 milligram (mg) (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 4 mg (body weight 30-<45 kg) or 9 mg (body weight >=45 kg) respectively, or once-monthly (QM) loading dose of 40 mg (body weight 30-<45 kg) or 92 mg (body weight >=45 kg) Mim8 subcutaneously followed by maintenance dose of 20 mg (body weight 30 - <45 kg) or 46 mg (body weight >=45 kg) respectively, based on agreement with the investigator.

Reporting group title	Arm 2a: Mim8 PPX QW

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 4: PPX- Mim8 PPX QM

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered main part of the study, to receive loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 3: PPX - Mim8 PPX QW

Reporting group description:

Subjects on coagulation factor prophylaxis prior to enrolment continued with the same product type and dosing frequency in the run-in period for at least 26 weeks and up to 52 weeks. Subjects entered the main part of the study, to receive loading dose of either 24 mg (body weight 30-<45 kg) or 55 mg (body weight >=45 kg) Mim8 QW subcutaneously followed by maintenance dose of 4 mg (body weight 30 -<45 kg) or 9 mg >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QW subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Reporting group title	Arm 2b: Mim8 PPX QM

Reporting group description:

Subjects on no prophylaxis treatment did not enter the run-in period and received loading dose of wither 40 mg (body weight 30-<45 kg) or 92 mg (body weight ≥45 kg) Mim8 QM subcutaneously followed by maintenance dose of 20 mg (body weight 30-<45 kg) or 46 mg (body weight >=45 kg) respectively. After the main part, subjects continued to receive the same dosing regimen of Mim8 QM subcutaneously in the extension part of the study (26 weeks). The dose could only be changed in relation to weight band change.

Serious adverse events	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	1 / 22 (4.55%)	9 / 109 (8.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testicular teratoma benign			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

VIth nerve paralysis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 22 (4.55%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			

subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	0 / 18 (0.00%)	1 / 22 (4.55%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			

Device loosening			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm 3: PPX - Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 111 (6.31%)	0 / 21 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testicular teratoma benign			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			

subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIth nerve paralysis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Haemorrhoids			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			

subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoas abscess			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			

subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device loosening			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm1: No PPX - Mim8 PPX QW/QM	Arm 2a: Mim8 PPX QW	Arm 4: PPX- Mim8 PPX QM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 18 (55.56%)	9 / 22 (40.91%)	62 / 109 (56.88%)
Investigations			
Prothrombin fragment 1.2 increased			
subjects affected / exposed	2 / 18 (11.11%)	2 / 22 (9.09%)	9 / 109 (8.26%)
occurrences (all)	2	2	9
Surgical and medical procedures			
Intra-uterine contraceptive device removal			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 18 (5.56%)	1 / 22 (4.55%)	9 / 109 (8.26%)
occurrences (all)	1	1	16
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	1	0	1
General disorders and administration site conditions			

Injection site reaction			
subjects affected / exposed	0 / 18 (0.00%)	2 / 22 (9.09%)	3 / 109 (2.75%)
occurrences (all)	0	2	3
Pyrexia			
subjects affected / exposed	2 / 18 (11.11%)	1 / 22 (4.55%)	5 / 109 (4.59%)
occurrences (all)	2	1	6
Injection site erythema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	2 / 109 (1.83%)
occurrences (all)	1	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	4 / 109 (3.67%)
occurrences (all)	1	0	4
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	1	0	1
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	3 / 109 (2.75%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Umbilical erythema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0

Seborrhoeic dermatitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 22 (4.55%)	10 / 109 (9.17%)
occurrences (all)	0	1	15
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	1 / 22 (4.55%)	7 / 109 (6.42%)
occurrences (all)	1	1	7
Sacroiliitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 18 (0.00%)	1 / 22 (4.55%)	5 / 109 (4.59%)
occurrences (all)	0	1	6
Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	2 / 22 (9.09%)	0 / 109 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)	2 / 22 (9.09%)	17 / 109 (15.60%)
occurrences (all)	2	6	20
Body tinea			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	0 / 18 (0.00%)	1 / 22 (4.55%)	9 / 109 (8.26%)
occurrences (all)	0	1	9
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 22 (0.00%)	16 / 109 (14.68%)
occurrences (all)	0	0	23
Tooth infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			

subjects affected / exposed	2 / 18 (11.11%)	0 / 22 (0.00%)	0 / 109 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	2	0	1
Hypokalaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	1	0	1
Hyperlipidaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 22 (0.00%)	1 / 109 (0.92%)
occurrences (all)	1	0	1

Non-serious adverse events	Arm 3: PPX - Mim8 PPX QW	Arm 2b: Mim8 PPX QM	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 111 (54.05%)	6 / 21 (28.57%)	
Investigations			
Prothrombin fragment 1.2 increased			
subjects affected / exposed	14 / 111 (12.61%)	1 / 21 (4.76%)	
occurrences (all)	15	1	
Surgical and medical procedures			
Intra-uterine contraceptive device removal			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 111 (10.81%)	1 / 21 (4.76%)	
occurrences (all)	15	1	
Dizziness			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			

Injection site reaction			
subjects affected / exposed	7 / 111 (6.31%)	1 / 21 (4.76%)	
occurrences (all)	103	2	
Pyrexia			
subjects affected / exposed	3 / 111 (2.70%)	2 / 21 (9.52%)	
occurrences (all)	3	2	
Injection site erythema			
subjects affected / exposed	3 / 111 (2.70%)	0 / 21 (0.00%)	
occurrences (all)	5	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	5 / 111 (4.50%)	1 / 21 (4.76%)	
occurrences (all)	8	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	3 / 111 (2.70%)	2 / 21 (9.52%)	
occurrences (all)	4	2	
Gastritis			
subjects affected / exposed	2 / 111 (1.80%)	1 / 21 (4.76%)	
occurrences (all)	2	1	
Nausea			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 111 (5.41%)	1 / 21 (4.76%)	
occurrences (all)	6	1	
Skin and subcutaneous tissue disorders			
Umbilical erythema			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	

Seborrhoeic dermatitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 111 (5.41%)	0 / 21 (0.00%)	
occurrences (all)	6	0	
Back pain			
subjects affected / exposed	6 / 111 (5.41%)	0 / 21 (0.00%)	
occurrences (all)	6	0	
Sacroiliitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Influenza			
subjects affected / exposed	6 / 111 (5.41%)	0 / 21 (0.00%)	
occurrences (all)	8	0	
Respiratory tract infection			
subjects affected / exposed	2 / 111 (1.80%)	0 / 21 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	11 / 111 (9.91%)	3 / 21 (14.29%)	
occurrences (all)	18	4	
Body tinea			
subjects affected / exposed	0 / 111 (0.00%)	0 / 21 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	7 / 111 (6.31%)	0 / 21 (0.00%)	
occurrences (all)	7	0	
Nasopharyngitis			
subjects affected / exposed	11 / 111 (9.91%)	0 / 21 (0.00%)	
occurrences (all)	16	0	
Tooth infection			
subjects affected / exposed	1 / 111 (0.90%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			

subjects affected / exposed occurrences (all)	0 / 111 (0.00%) 0	0 / 21 (0.00%) 0	
Metabolism and nutrition disorders Hyperuricaemia subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all) Hyperlipidaemia subjects affected / exposed occurrences (all)	 0 / 111 (0.00%) 0 0 / 111 (0.00%) 0 1 / 111 (0.90%) 1	 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2021	Protocol version 5.0: Change of treatment prophylaxis to bleeding prophylaxis in the primary objective and remove subjects in the sentence; Bleeds into target joints must be treated or prescribed treatment to be a target joint bleed; The run-in period is planned to be of up to 52 weeks duration; Participants on no prophylaxis are not allowed to participate in the run-in; In total approximately 244 participants are planned to be enrolled into this study, with at least 30 adolescent (12-17 years) participants; Patients on coagulation factor prophylaxis will preferably continue the same product type; Changed that on-demand treatment will receive Standard of Care product instead of usual product.
22 November 2022	Protocol version 9.0: A new study design for participants who are on no prophylaxis/on-demand treatment prior to enrolment and a change of primary endpoint analyses for Mim8 QW and QM in treatment Arms 3 and 4 were also included based on authority feedback; Primary endpoint analyses for Mim8 QW and QM treatment arms will be performed separately in a hierarchical manner. Superiority test will be performed for Arms 3 and 4 without a non-inferiority test; The total number of participants has been updated to 267; Exclusion criterion updated regarding requirement of participation in any interventional clinical study prior to this study, regarding exposure to nonfactor haemostatic products and regarding timing of planned major surgery; In the estimand section the handling of intercurrent events has been elaborated and 'major surgery' has been removed as an intercurrent event.
29 September 2023	Protocol version 11.0: Reintroduced non-inferiority tests for Arms 3 and 4 as the first step in the statistical testing hierarchy followed by the superiority tests. The power calculation based on non inferiority and superiority are provided; Added an additional secondary endpoint related to Mim8 plasma concentration addressing health authority feedback; Extended the visit window for Visit 13 for countries and sites where participants' transfer to study NN7769-4532 is not possible either due to study not being approved or sites not being open for transfer at the time of visit; Included country-specific requirements for EU countries, United States and Russia.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported