Clinical trial results:
An Open-Label Study in Adolescent and Adult Severe (Coagulation Factor Activity <1%) Hemophilia A Participants With or Without Inhibitors or Moderately Severe to Severe Hemophilia B Participants (Coagulation Factor Activity <=2%) With or Without Inhibitors Comparing Standard Treatment to PF-06741086 Prophylaxis

Summary

EudraCT number	2018-003660-31
Trial protocol	DE FR BG GB ES IE HR IT
Global end of trial date	29 April 2025

Results information

Result version number	v1 (current)
This version publication date	05 November 2025
First version publication date	05 November 2025

Trial information

Trial identification

Sponsor protocol code	B7841005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03938792
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Boulevard East, New York, United States, NY 10001
Public contact	PfizerClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	PfizerClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002285-PIP02-19
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	29 August 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy and safety of PF-06741086 for routine prophylaxis in severe hemophilia A or moderately severe to severe hemophilia B (factor VIII [FVIII] activity <1% or factor IX [FIX] activity <=2%, respectively) participants 12 to <75 years of age with or without inhibitors.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2020
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	China: 23
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	India: 26
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Hong Kong: 14
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Oman: 16
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Saudi Arabia: 2
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Serbia: 7
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Türkiye: 32
Country: Number of subjects enrolled	United States: 4

Worldwide total number of subjects	188
EEA total number of subjects	18

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)	36
Adults (18-64 years)	149
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 188 participants were enrolled in the study: 128 in the non-inhibitor cohort (no history of inhibitors) and 60 in the inhibitor cohort (current/documented history of inhibitor). The study consisted of an observational phase (OP) and an active treatment phase (ATP).

Pre-assignment

Screening details:

Participants who were receiving prior on-demand (OD) therapy or prior routine prophylaxis treatment (RP) (administration of clotting factor or bypassing agent) in either the non-inhibitor cohort or inhibitor cohort were enrolled into the OP. Participants received the study drug during the ATP.

Period 1

Period 1 title	Observational Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No blinding, open label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP

Arm description:

Participants with no history of inhibitors who were receiving prior on-demand therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 milligrams (mg) was administered as loading dose on Day 1 followed by 150 mg once weekly (QW) subcutaneously for 12 months.

Arm type	Experimental
Investigational medicinal product name	Marstacimab
Investigational medicinal product code	PF-06741086
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. Participants who met dose escalation criteria were prescribed 300 mg subcutaneously QW.

Arm title	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP

Arm description:

Participants with no history of inhibitors who were receiving prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Arm type	Experimental
Investigational medicinal product name	Marstacimab
Investigational medicinal product code	PF-06741086
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. Participants who met dose escalation criteria were prescribed 300 mg subcutaneously QW.

Arm title	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP

Arm description:

Participants with current/documented history of inhibitors who were receiving prior on-demand or prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Arm type	Experimental
Investigational medicinal product name	Marstacimab
Investigational medicinal product code	PF-06741086
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. Participants who met dose escalation criteria were prescribed 300 mg subcutaneously QW.

Number of subjects in period 1	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP
Started	37	91	60
Completed	34	84	53
Not completed	3	7	7
Consent withdrawn by subject	-	-	2
Adverse event, non-fatal	-	-	1
Unspecified	1	-	-
No Longer Meets Eligibility Criteria	-	5	-
Protocol deviation	2	2	4

Period 2

Period 2 title	Active Treatment Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No blinding, open label.

Arms

Are arms mutually exclusive?	Yes

Arm title	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP

Arm description:

Participants with no history of inhibitors who were receiving prior on-demand therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 milligrams (mg) was administered as loading dose on Day 1 followed by 150 mg once weekly (QW) subcutaneously for 12 months.

Arm type	Experimental
Investigational medicinal product name	Marstacimab
Investigational medicinal product code	PF-06741086
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. Participants who met dose escalation criteria were prescribed 300 mg subcutaneously QW.

Arm title	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP

Arm description:

Participants with no history of inhibitors who were receiving prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Arm type	Experimental
Investigational medicinal product name	Marstacimab
Investigational medicinal product code	PF-06741086
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. Participants who met dose escalation criteria were prescribed 300 mg subcutaneously QW.

Arm title	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP

Arm description:

Participants with current/documented history of inhibitors who were receiving prior on-demand or prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Arm type	Experimental
Investigational medicinal product name	Marstacimab
Investigational medicinal product code	PF-06741086
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. Participants who met dose escalation criteria were prescribed 300 mg subcutaneously QW.

Number of subjects in period 2[1]	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP
Started	33	83	51
Completed	33	78	48
Not completed	0	5	3
Consent withdrawn by subject	-	4	-
Adverse event, non-fatal	-	1	1
Lost to follow-up	-	-	1
Protocol deviation	-	-	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: Only those who started the ATP are entered. Not all who completed OP entered ATP

Baseline characteristics

Reporting groups	
Reporting group title	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP
Reporting group description:	
Participants with no history of inhibitors who were receiving prior on-demand therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 milligrams (mg) was administered as loading dose on Day 1 followed by 150 mg once weekly (QW) subcutaneously for 12 months.	
Reporting group title	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP
Reporting group description:	
Participants with no history of inhibitors who were receiving prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.	
Reporting group title	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP
Reporting group description:	
Participants with current/documented history of inhibitors who were receiving prior on-demand or prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.	

Reporting group values	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP
Number of subjects	37	91	60
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional 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
12 - 17 years	2	18	16
Adults (18 - 64 years)	35	72	42
From 65 - 84 years	0	1	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Male	37	91	60
Female	0	0	0
Race Units: Subjects			
Black or African American	0	1	8
Asian	24	37	32
White	13	52	19
Not Reported	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	4	9	2

Not Hispanic or Latino	33	82	57
Not Reported	0	0	1

Reporting group values	Total		
Number of subjects	188		
Age categorical Units: Subjects			
In Utero	0		
Preterm newborn infants (gestional age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days - 23 months)	0		
Children (2 - 11 years)	0		
12 - 17 years	36		
Adults (18 - 64 years)	149		
From 65 - 84 years	3		
85 years and over	0		
Gender categorical Units: Subjects			
Male	188		
Female	0		
Race Units: Subjects			
Black or African American	9		
Asian	93		
White	84		
Not Reported	2		
Ethnicity Units: Subjects			
Hispanic or Latino	15		
Not Hispanic or Latino	172		
Not Reported	1		

Subject analysis sets

Subject analysis set title	Inhibitor Cohort: OD at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: OD at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior OD therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: RP at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior RP therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Inhibitor Cohort: OD at OP/ Marstacimab During ATP

Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior OD therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Inhibitor Cohort: OD or RP at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD or RP therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD or RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior OD or RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Reporting group values	Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP
Number of subjects	57	37	91
Age categorical Units: Subjects			
In Utero Preterm newborn infants (gestional age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days - 23 months) Children (2 - 11 years) 12 - 17 years Adults (18 - 64 years) From 65 - 84 years 85 years and over			
Gender categorical Units: Subjects			
Male Female			

Race Units: Subjects			
Black or African American Asian White Not Reported			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Not Reported			

Reporting group values	Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Number of subjects	48	33	83
Age categorical Units: Subjects			
In Utero Preterm newborn infants (gestional age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days - 23 months) Children (2 - 11 years) 12 - 17 years Adults (18 - 64 years) From 65 - 84 years 85 years and over			0
Gender categorical Units: Subjects			
Male Female			
Race Units: Subjects			
Black or African American Asian White Not Reported			
Ethnicity Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Not Reported			

Reporting group values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Number of subjects	60	51	116
Age categorical Units: Subjects			
In Utero	0	0	0

Preterm newborn infants (gestional 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
12 - 17 years	0	0	0
Adults (18 - 64 years)	0	0	0
From 65 - 84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Male	0	0	0
Female	0	0	0
Race Units: Subjects			
Black or African American	0	0	0
Asian	0	0	0
White	0	0	0
Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	0	0	0
Not Reported	0	0	0

End points reporting groups

Reporting group title	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP

Reporting group description:

Participants with no history of inhibitors who were receiving prior on-demand therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 milligrams (mg) was administered as loading dose on Day 1 followed by 150 mg once weekly (QW) subcutaneously for 12 months.

Reporting group title	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP

Reporting group description:

Participants with no history of inhibitors who were receiving prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Reporting group title	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP

Reporting group description:

Participants with current/documented history of inhibitors who were receiving prior on-demand or prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Reporting group title	Non-Inhibitor Cohort: OD at OP + PF-06741086 in ATP

Reporting group description:

Participants with no history of inhibitors who were receiving prior on-demand therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 milligrams (mg) was administered as loading dose on Day 1 followed by 150 mg once weekly (QW) subcutaneously for 12 months.

Reporting group title	Non-Inhibitor Cohort: Prophylaxis at OP + PF-06741086 in ATP

Reporting group description:

Participants with no history of inhibitors who were receiving prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Reporting group title	Inhibitor Cohort: OD/Prophylaxis at OP + PF-06741086 ATP

Reporting group description:

Participants with current/documented history of inhibitors who were receiving prior on-demand or prior prophylactic therapy for haemophilia (clotting factor or bypass agent) were observed for 6 months in the OP. PF-06741086 (marstacimab) 300 mg was administered as loading dose on Day 1 followed by 150 mg QW subcutaneously for 12 months.

Subject analysis set title	Inhibitor Cohort: OD at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: OD at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior OD therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: RP at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior RP therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior OD therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Inhibitor Cohort: OD or RP at OP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD or RP therapy for haemophilia were observed for 6 months in the OP. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the inhibitor cohort who had prior OD or RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Subject analysis set title	Non-Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Subject analysis set type	Full analysis

Subject analysis set description:

Participants of the non-inhibitor cohort who had prior OD or RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW. This reporting arm has been created as per the endpoint requirement.

Primary: Model-Based Annualized Bleeding Rate (ABR) of Treated Bleeding Events: Inhibitor Cohort (Participants With Prior OD Therapy at OP)

End point title	Model-Based Annualized Bleeding Rate (ABR) of Treated Bleeding Events: Inhibitor Cohort (Participants With Prior OD Therapy at OP)

End point description:

ABR: number of bleeding episodes per year. ABR was calculated as number of bleeds requiring treatments/ (days on treatment period/365.25). If a participant did not complete a treatment period, days on treatment ended at last dosing date + 6 days. Treated bleed: If a bleed was treated with factor replacement or bypass agents within 48 hours of start of bleeding, regardless of the type of treatment (preventive, prophylaxis or on-demand medication). A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. Modified Intent-to-Treat (mITT) set included all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who are treated with routine prophylaxis in the OP). Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed" signifies participants in mITT analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	48		
Units: Bleeds per year				
number (confidence interval 95%)	19.78 (16.12 to 24.27)	1.39 (0.85 to 2.29)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.042
upper limit	0.118

Notes:

[1] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and confidence intervals (CIs) for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Primary: Model-Based ABR of Treated Bleeding Events: Non-Inhibitor Cohort (Participants With Prior OD Therapy at OP)

End point title	Model-Based ABR of Treated Bleeding Events: Non-Inhibitor Cohort (Participants With Prior OD Therapy at OP)

End point description:

ABR was the number of bleeding episodes per year. ABR was calculated as the number of bleeds requiring treatments/ (days on treatment period/365.25). If a participant did not complete a treatment period, the days on treatment ended at the last dosing date + 6 days. Treated bleed: If a bleed was treated with factor replacement or bypass agents within 48 hours of start of bleeding, regardless of the type of treatment (preventive, prophylaxis or on-demand medication). A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. mITT set included all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who are treated with routine prophylaxis in the OP). Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed” signifies participants in mITT analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	33		
Units: Bleeds per year				
number (confidence interval 95%)	39.86 (33.05 to 48.07)	3.20 (2.10 to 4.88)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.057
upper limit	0.113

Notes:

[2] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Primary: Model-Based ABR of Treated Bleeding Events: Non- Inhibitor Cohort (Participants With RP at OP)

End point title	Model-Based ABR of Treated Bleeding Events: Non- Inhibitor Cohort (Participants With RP at OP)

End point description:

ABR was the number of bleeding episodes per year. ABR was calculated as the number of bleeds requiring treatments/ (days on treatment period/365.25). If a participant did not complete a treatment period, the days on treatment ended at the last dosing date + 6 days. Treated bleed: If a bleed was treated with factor replacement or bypass agents within 48 hours of start of bleeding, regardless of the type of treatment (preventive, prophylaxis or on-demand medication). A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. mITT set included all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who are treated with routine prophylaxis in the OP). Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed” signifies participants in mITT analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	83	83		
Units: Bleeds per year				
number (confidence interval 95%)	7.90 (5.14 to 10.66)	5.09 (3.40 to 6.78)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.0349
Method	Repeated negative binomial regression
Parameter estimate	Difference estimate
Point estimate	-2.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.42
upper limit	-0.2

Notes:

[3] - Difference estimate = ABR of marstacimab prophylaxis during ATP - ABR of Prior routine prophylaxis at OP. The estimated mean, difference, and CIs for ABR came from negative binomial regression model. Non-inferiority of marstacimab prophylaxis was declared when upper bound of 95% CI was below 2.5. If non-inferiority was established, subsequent testing for superiority may be conducted.

Primary: Number of Participants With Adverse Events (AEs): Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Adverse Events (AEs): Inhibitor and Non-inhibitor Cohort[4]

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. All safety set: For participants with prior prophylaxis in OP, all participants who received at least 1 prophylaxis or on-demand treatment at OP; for participants with on-demand in OP, all participants who completed any of the procedures for visit 2 (OP baseline). Participants who changed from a non-inhibitor to an inhibitor on

or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	18	25	20	66

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	21	38		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Serious Adverse Events (SAEs): Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Serious Adverse Events (SAEs): Inhibitor and Non-inhibitor Cohort[5]

End point description:

AE: any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. SAE: any untoward medical occurrence at any dose that resulted in any of the following outcomes: death; life-threatening; required inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect; or that was considered as an important medical event. All safety set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	1	2	0	7

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	5	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Thrombotic Events: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Thrombotic Events: Inhibitor and Non-inhibitor Cohort[6]

End point description:

Thrombotic events are when a blood clot (thrombus) forms in a blood vessel in the arm, leg, lung, or head and can be life-threatening. A thrombus can occur in veins (venous thrombosis) or arteries (arterial thrombosis). All safety set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	0	0	0	0

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Thrombotic Microangiopathy: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Thrombotic Microangiopathy: Inhibitor and Non-inhibitor Cohort[7]

End point description:

Thrombotic Microangiopathy: pathological state where micro-vessels are occluded by platelet rich thrombi leading to thrombocytopenia (low platelets) and microangiopathic haemolytic anaemia (red blood cell destruction) and potential end organ damage. All safety set analysed. Participants who changed from non-inhibitor to inhibitor on/before ATP Day -7 testing excluded from set. Participants were analysed according to intervention they actually received. As pre-specified in protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	0	0	0	0

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Disseminated Intravascular Coagulation/ Consumption Coagulopathy: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Disseminated Intravascular Coagulation/ Consumption Coagulopathy: Inhibitor and Non-inhibitor Cohort[8]

End point description:

Disseminated Intravascular Coagulation is characterized by widespread clotting in small blood vessels, and consumption of platelets and clotting factors by the clots, leading to bleeding. All safety set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	0	0	0	0

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		

Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Transient and Persistent ADA and NAb Against Marstacimab/ PF-06741086: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Transient and Persistent ADA and NAb Against Marstacimab/ PF-06741086: Inhibitor and Non-inhibitor Cohort[9]

End point description:

Persistent ADA: participant with treatment-induced or treatment-boosted ADA detected at >=2 sampling time points (TP) during treatment including any follow-up, where first and last ADA positive samples separated by period of >=16 weeks. Transient ADA: treatment-induced/treatment-boosted ADA detected only at 1 sampling TP during treatment/follow-up. Persistent NAb: NAb-positive participant with first and last positive NAb samples detected over period of >=16 weeks posttreatment, irrespective of any negative samples in between. Transient NAb: NAb-positive participant with (1) treatment-induced/treatment-boosted NAb sample detected only at 1 sampling time post-treatment or (2) treatment-induced or treatment-boosted NAb samples detected at >=2 TP where first and last positive samples are separated by <16 weeks, and participant's last sample was NAb negative/ADA negative. Marstacimab safety set analysed. Here, "Subjects Analyzed" signifies participants in marstacimab safety analysis set.

End point type	Primary

End point timeframe:

During prophylaxis treatment in ATP (12 months)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	10	23		
Units: Participants				
Persistent ADA (n=10, 23)	1	9		
Transient ADA (n=10, 23)	9	14		
Persistent Nab (n=2, 6)	1	0		
Transient Nab (n=2, 6)	1	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Anti-drug Antibodies (ADA) and Neutralizing Antibodies (NAb) Against Marstacimab/ PF-06741086: Inhibitor and Non-inhibitor

Cohort

End point title	Number of Participants With Anti-drug Antibodies (ADA) and Neutralizing Antibodies (NAb) Against Marstacimab/ PF-06741086: Inhibitor and Non-inhibitor Cohort[10]

End point description:

ADA positive: A participant with >=1 treatment induced or treatment-boosted ADA response. NAb positive: An ADA positive participant with >=1 treatment-induced or treatment-boosted NAb response. Marstacimab safety set included all participants who received at least 1 dose of marstacimab in ATP. Here, "Subjects Analyzed" signifies participants in marstacimab safety analysis set.

End point type	Primary

End point timeframe:

During prophylaxis treatment in ATP (12 months)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	51	116		
Units: Participants				
ADA	10	23		
NAb	2	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Injection Site Reactions (ISRs): Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Injection Site Reactions (ISRs): Inhibitor and Non-inhibitor Cohort[11]

End point description:

ISR included: injection site haematoma, injection site pain, injection site bruising, injection site erythema, injection site induration, injection site oedema, Injection site pruritus and Injection site swelling. ISR were graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 where grade 1: tenderness with or without associated symptoms (eg, warmth, erythema, itching), grade 2: pain, lipodystrophy, edema, phlebitis, grade 3: ulceration or necrosis, severe tissue damage, operative intervention indicated, grade 4: life-threatening consequences, urgent intervention indicated and grade 5: death. In this endpoint only the categories with non-zero values were reported. Marstacimab safety set analysed. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all marstacimab safety set.

End point type	Primary

End point timeframe:

During prophylaxis treatment in ATP (12 months)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	83	51	
Units: Participants				
Grade 1	2	8	3	
Grade 2	0	1	1	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Changes in Physical Examinations: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Clinically Significant Changes in Physical Examinations: Inhibitor and Non-inhibitor Cohort[12]

End point description:

Physical examination included assessments of the head, ears, eyes, nose, mouth, skin, heart and lung examinations, lymph nodes, gastrointestinal, musculoskeletal, and neurological systems. Height and weight were also measured and recorded. Clinical significance in physical examinations was determined by investigator. All Safety set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	0	2	0	2

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		

Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Changes in Vital Signs: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Clinically Significant Changes in Vital Signs: Inhibitor and Non-inhibitor Cohort[13]

End point description:

Vital signs included temperature, pulse rate, respiratory rate, and blood pressure Blood pressure and pulse rate were measured in a supine position using completely automated device after at least 5 minutes of rest for the participant in a quiet setting without distractions. Respiratory rate was measured by observing and counting the respirations of the participant for 30 seconds and multiplied by 2. Clinical significance of vital signs was determined by investigator. All safety set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	0	0	0	0

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Abnormalities in Laboratory Parameters: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Clinically Significant Abnormalities in Laboratory Parameters: Inhibitor and Non-inhibitor Cohort[14]

End point description:

Hematology: Hemoglobin; leukocytes; neutrophils; and Platelets. Chemistry: Potassium; aspartate aminotransferase; creatinine; alkaline phosphatase; total bilirubin; albumin; calcium corrected, estimated decreased; sodium; and calcium. All safety set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from this set. Participants were analysed according to the intervention they actually received. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in all safety analysis set. Clinical significance was judged by Investigator.

End point type	Primary

End point timeframe:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	37	91	33	83
Units: Participants	0	0	0	0

End point values	Inhibitor Cohort: OD or RP at OP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	60	51		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Severe/ Systematic Hypersensitivity and Anaphylactic Reactions: Inhibitor and Non-inhibitor Cohort

End point title	Number of Participants With Severe/ Systematic Hypersensitivity and Anaphylactic Reactions: Inhibitor and Non-inhibitor Cohort[15]

End point description:

Systemic hypersensitivity is a complex immune response where the immune system reacts excessively to an antigen, often leading to severe allergic reactions, including widespread symptoms (which may affect multiple organs), such as rash, swelling of your face, lips, mouth, or tongue, trouble breathing, wheezing, dizziness, fainting, fast heartbeat, pounding in your chest or sweating. Anaphylaxis is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy causing substance. Marstacimab safety set included all participants who received at least 1 dose of marstacimab. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined. Here, "Subjects Analyzed" signifies participants in marstacimab safety set.

End point type	Primary

End point timeframe:

During prophylaxis treatment in ATP (12 months)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analyzed for this endpoint.

End point values	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	33	83	51	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Model-Based ABR of Joint Bleeds: Inhibitor and Non-inhibitor Cohort

End point title	Model-Based ABR of Joint Bleeds: Inhibitor and Non-inhibitor Cohort

End point description:

ABR: number of bleeding episodes per year. ABR was calculated as number of bleeds requiring treatments/ (days on treatment period/365.25). If a participant did not complete a treatment period, days on treatment ended at last dosing date + 6 days. Joint bleed: bleeding episode characterized by rapid loss of range of motion as compared with baseline that was associated with any combination of the following: pain or an unusual sensation in the joint, palpable swelling, and warmth of the skin over the joint. A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. mITT set included all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in the OP). Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here," Subjects Analyzed" signifies participants in mITT analysis set.

End point type	Secondary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	33	83	48
Units: Bleeds per year				
number (confidence interval 95%)	15.15 (11.87 to 19.34)	34.52 (27.84 to 42.79)	5.69 (3.36 to 8.02)	1.10 (0.59 to 2.04)

End point values	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	83		
Units: Bleeds per year				
number (confidence interval 95%)	2.85 (1.82 to 4.46)	4.13 (2.59 to 5.67)		

Statistical analyses

Statistical analysis title	Non-Inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.083
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.057
upper limit	0.119

Notes:

[16] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Statistical analysis title	Non-Inhibitor: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	= 0.1612
Method	Repeated negative binomial regression
Parameter estimate	Difference Estimate
Point estimate	-1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.73
upper limit	0.62

Notes:

[17] - Difference estimate = ABR of marstacimab prophylaxis during ATP - ABR of Prior routine prophylaxis at OP. The estimated mean, difference, and CIs for ABR came from negative binomial regression model. Non-inferiority of marstacimab prophylaxis was declared when upper bound of 95% CI was below 2.5. If non-inferiority was established, subsequent testing for superiority may be conducted.

Statistical analysis title	Inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio Estimate
Point estimate	0.072
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.038
upper limit	0.138

Notes:

[18] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Secondary: Model-Based ABR of Spontaneous Bleeds: Inhibitor and Non-inhibitor Cohort

End point title	Model-Based ABR of Spontaneous Bleeds: Inhibitor and Non-inhibitor Cohort

End point description:

ABR: number of bleeding episodes per year. ABR was calculated as the number of bleeds requiring treatments/ (days on treatment period/365.25). If a participant did not complete a treatment period, the days on treatment ended at the last dosing date + 6 days. Spontaneous bleed: Bleeding for no apparent/known reason particularly into the joints, muscles, and soft tissues. A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. mITT set included all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who are treated with routine prophylaxis in the OP). Participants who

changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here," Subjects Analyzed" signifies participants in mITT analysis set.

End point type	Secondary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	33	83	48
Units: Bleeds per year				
number (confidence interval 95%)	15.27 (12.07 to 19.31)	32.63 (25.79 to 41.28)	5.89 (3.57 to 8.22)	0.87 (0.53 to 1.43)

End point values	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	83		
Units: Bleeds per year				
number (confidence interval 95%)	2.45 (1.62 to 3.72)	3.78 (2.25 to 5.31)		

Statistical analyses

Statistical analysis title	Non-inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.075
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.053
upper limit	0.107

Notes:

[19] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Statistical analysis title	Non-inhibitor: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
P-value	= 0.0537
Method	Repeated negative binomial regression
Parameter estimate	Difference estimate
Point estimate	-2.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.26
upper limit	0.03

Notes:

[20] - Difference estimate = ABR of marstacimab prophylaxis during ATP - ABR of Prior routine prophylaxis at OP. The estimated mean, difference, and CIs for ABR came from negative binomial regression model. Non-inferiority of marstacimab prophylaxis declared when upper bound of 95% CI was below 2.5. If non-inferiority was established, subsequent testing for superiority may be conducted.

Statistical analysis title	Inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.035
upper limit	0.092

Notes:

[21] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Secondary: Model-Based ABR of Target Joint Bleeds: Inhibitor and Non-inhibitor Cohort

End point title	Model-Based ABR of Target Joint Bleeds: Inhibitor and Non-inhibitor Cohort

End point description:

ABR: number of bleeding episodes per year. ABR was calculated as number of bleeds requiring treatments/ (days on treatment period/365.25). If participant did not complete a treatment period, days on treatment ended at last dosing date + 6 days. Target joint: a major joint into which repeated bleeds occurred. Joint bleed: bleeding episode characterized by rapid loss of range of motion as compared with baseline that was associated with any combination of following: pain or unusual sensation in joint, palpable swelling, and warmth of the skin over joint. A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. mITT set analysed. Participants who changed from a non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed" signifies participants in mITT analysis set.

End point type	Secondary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	33	83	48
Units: Bleeds per year				
number (confidence interval 95%)	6.42 (4.42 to 9.33)	24.38 (18.27 to 32.35)	3.37 (1.60 to 5.15)	0.79 (0.36 to 1.74)

End point values	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	83		
Units: Bleeds per year				
number (confidence interval 95%)	1.84 (1.07 to 3.18)	2.51 (1.26 to 3.76)		

Statistical analyses

Statistical analysis title	Non-inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.076
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.048
upper limit	0.119

Notes:

[22] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Statistical analysis title	Non-inhibitor: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
P-value	= 0.2761
Method	Repeated negative binomial regression
Parameter estimate	Difference estimate
Point estimate	-0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.42
upper limit	0.69

Notes:

[23] - Difference estimate = ABR of marstacimab prophylaxis during ATP - ABR of Prior routine prophylaxis at OP. The estimated mean, difference, and CIs for ABR came from negative binomial regression model. Non-inferiority of marstacimab prophylaxis declared when upper bound of 95% CI was below 1.2. If non-inferiority was established, subsequent testing for superiority may be conducted.

Statistical analysis title	Inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	= 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.124

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.061
upper limit	0.251

Notes:

[24] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Secondary: Model-Based ABR of Total Bleeds: Inhibitor and Non-inhibitor Cohort

End point title	Model-Based ABR of Total Bleeds: Inhibitor and Non-inhibitor Cohort

End point description:

ABR: number of bleeding episodes per year. ABR was calculated as number of bleeds requiring treatments/ (days on treatment period/365.25). If participant did not complete treatment period, days on treatment ended at last dosing date + 6 days. Treated bleed: If a bleed was treated with factor replacement or bypass agents within 48 hours of start of bleeding, regardless of the type of treatment (preventive, prophylaxis or on-demand medication). Untreated bleed: If a bleed was untreated with factor replacement or bypass agents within 48 hours of start of bleeding, regardless of the type of treatment (preventive, prophylaxis or on-demand medication), it was considered as an untreated bleed. Total Bleeds: Treated bleeds + untreated bleeds. A model-based ABR using a repeated measures negative binomial model is reported for this endpoint. mITT set analysed. Here, "Subjects Analyzed" signifies participants in mITT analysis set.

End point type	Secondary

End point timeframe:

Up to 6 months for OP; up to 12 months for ATP

End point values	Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	33	83	48
Units: Bleeds per year				
number (confidence interval 95%)	27.29 (22.54 to 33.03)	49.97 (42.09 to 59.32)	8.90 (6.02 to 11.77)	4.36 (2.65 to 7.18)

End point values	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	33	83		
Units: Bleeds per year				
number (confidence interval 95%)	7.41 (5.10 to 10.75)	5.98 (4.14 to 7.82)		

Statistical analyses

Statistical analysis title	Non-inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.148
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.111
upper limit	0.198

Notes:

[25] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Statistical analysis title	Inhibitor: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	< 0.0001
Method	Repeated negative binomial regression
Parameter estimate	Ratio estimate
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.102
upper limit	0.249

Notes:

[26] - Ratio estimate = ABR of marstacimab prophylaxis during ATP to ABR of Prior on-demand therapy at OP. The estimated mean, ratio, and CIs for the ABR came from negative binomial regression model. Superiority of marstacimab prophylaxis was declared when the upper bound of the 95% CI was below 0.5.

Statistical analysis title	Non-inhibitor: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
P-value	= 0.0374
Method	Repeated negative binomial regression
Parameter estimate	Difference estimate
Point estimate	-2.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.66
upper limit	-0.17

Notes:

[27] - Difference estimate = ABR of marstacimab prophylaxis during ATP - ABR of Prior routine prophylaxis at OP. The estimated mean, difference, and CIs for ABR came from negative binomial regression model. Non-inferiority of marstacimab prophylaxis declared when upper bound of 95% CI was below 2.9. If non-inferiority was established, subsequent testing for superiority may be conducted.

Secondary: Change From Baseline in Hemophilia Joint Health Score (HJHS) at Month 6: Non-Inhibitor Cohort

End point title	Change From Baseline in Hemophilia Joint Health Score (HJHS) at Month 6: Non-Inhibitor Cohort

End point description:

HJHS evaluated total joint score for 6 joints (left ankle, right ankle, left elbow, right elbow, left knee, right knee) and global gait score. Joint total score per joint ranged from 0 to 20 (evaluated: swelling [0-3], duration of swelling [0-1], muscle atrophy [0-2], crepitus on motion [0-2], flexion loss [0-3], extension loss [0-3], joint pain [0-2], and strength [0-4]). Global gait score ranged from 0 to 4 based on walking, stairs, running, and hopping on 1 leg. HJHS total Score was sum of total joint score for 6 joints and global gait score, ranged from 0 to 124, higher score indicated worse joint health. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed" signifies participants in the mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	83	33	83
Units: Units on a scale				
median (confidence interval 95%)	-2.6 (-5.7 to 0.5)	1.3 (-0.7 to 3.3)	-5.2 (-8.7 to -1.8)	-0.6 (-2.2 to 1.0)

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0.266
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	2.1

Notes:

[28] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on missing at random (MAR) assumption.

Statistical analysis title	Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.0835
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	0.3

Notes:

[29] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in HJHS at Month 6: Inhibitor Cohort

End point title	Change From Baseline in HJHS at Month 6: Inhibitor Cohort

End point description:

HJHS evaluated total joint score for 6 joints (left ankle, right ankle, left elbow, right elbow, left knee, right knee) and global gait score. Joint total score per joint ranged from 0 to 20 (evaluated: swelling [0-3], duration of swelling [0-1], muscle atrophy [0-2], crepitus on motion [0-2], flexion loss [0-3], extension loss [0-3], joint pain [0-2], and strength [0-4]). Global gait score ranged from 0 to 4 based on walking, stairs, running, and hopping on 1 leg. HJHS total Score was sum of total joint score for 6 joints and global gait score, ranged from 0 to 124, higher score indicated worse joint health. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed" signifies participants in the mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	48		
Units: Units on a scale				
median (confidence interval 95%)	-1.1 (-4.0 to 1.9)	-3.9 (-6.1 to -1.7)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0.2341
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	1.4

Notes:

[30] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in Hemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL) Total Score and Physical Health Domain at Month 6: Non-inhibitor Cohort, Participants >=17 Years

End point title	Change From Baseline in Hemophilia Quality of Life Questionnaire for Adults (Haem-A-QoL) Total Score and Physical Health Domain at Month 6: Non-inhibitor Cohort, Participants >=17 Years

End point description:

Haem-A-QoL assessed health-related quality of life (QoL) in adult participants with hemophilia. It contained 46 items with 10 domains that assessed health in the following areas: physical health; feelings; view of self; sports and leisure; work and school; dealing with haemophilia; treatment; future; family planning; partnership and sexuality. All items were based on 5-point Likert type scale (1= never, 2= rarely, 3= sometimes, 4= often, 5= all the time). Scoring was performed by averaging non-missing item responses for each domain, then rescaled from 0 to 100, lower scores signified higher QoL. Total Haem-A-QoL score= was averaged across the 46 items values and then rescaled from 0 to 100, lower scores signified better QoL. mITT set analysed. "Subjects Analyzed" signifies participants of age >=17 years in mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	63	31	63
Units: Units on a scale				
median (confidence interval 95%)				
Total Score	-1.5 (-5.5 to 2.5)	-1.2 (-3.5 to 1.1)	-4.8 (-7.9 to -1.7)	-3.7 (-6.8 to -0.6)
Physical Health Score	-1.1 (-12.2 to 10.0)	-3.0 (-8.2 to 2.2)	-12.4 (-19.6 to -5.1)	-6.1 (-12.6 to 0.4)

Statistical analyses

Statistical analysis title	Total Score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 31 not 62; 62 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.3458
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	2.3

Notes:

[31] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was upper bound of 95% CI <0.

Statistical analysis title	Physical Health Score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 31 not 62; 62 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.1161
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24
upper limit	2.6

Notes:

[32] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was upper bound of 95% CI <0.

Statistical analysis title	Physical Health Score: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 63 not 126; 126 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP

Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
P-value	= 0.5223
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	4.6

Notes:

[33] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Non-inferiority criterion was upper bound of 95%CI <10. If non-inferiority was established, subsequent testing for superiority may be conducted.

Statistical analysis title	Total Score: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 63 not 126; 126 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
P-value	= 0.1493
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	1

Notes:

[34] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Non-inferiority criterion was upper bound of 95% CI <7. If non-inferiority was established, subsequent testing for superiority may be conducted.

Secondary: Change From Baseline in Haem-A-QoL Total Score and Physical Health Domain at Month 6: Inhibitor Cohort, Participants >=17 Years

End point title	Change From Baseline in Haem-A-QoL Total Score and Physical Health Domain at Month 6: Inhibitor Cohort, Participants >=17 Years

End point description:

Haem-A-QoL assessed health-related quality of life (QoL) in adult participants with hemophilia. It contained 46 items with 10 domains that assessed health in the following areas: physical health; feelings; view of self; sports and leisure; work and school; dealing with haemophilia; treatment; future; family planning; partnership and sexuality. All items were based on 5-point Likert type scale (1= never, 2= rarely, 3= sometimes, 4= often, 5= all the time). Scoring was performed by averaging non-missing item responses for each domain, then rescaled from 0 to 100, lower scores signified higher QoL. Total Haem-A-QoL score= was averaged across the 46 items values and then rescaled from 0 to 100, lower scores signified better QoL. mITT set analysed. "Subjects Analyzed" signifies participants of age >=17 years in mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	35	35		
Units: Units on a scale				
median (confidence interval 95%)				
Total Score	1.5 (-2.4 to 5.5)	-12.0 (-18.3 to -5.7)		
Physical Health Score	2.2 (-6.6 to 11.0)	-20.8 (-29.7 to -11.9)		

Statistical analyses

Statistical analysis title	Physical Health Score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 35 not 70; 70 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	< 0.0001
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-25.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.5
upper limit	-14.2

Notes:

[35] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was upper bound of 95% CI <0.

Statistical analysis title	Total Score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 35 not 70; 70 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	< 0.0001
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.8
upper limit	-7.2

Notes:

[36] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was upper bound of 95% CI <0.

Secondary: Change From Baseline in Hemophilia Quality of Life Questionnaire for Children (Haemo-QoL) Total Score at Month 6: Non-inhibitor Cohort, Participants 12 to <17 years

End point title	Change From Baseline in Hemophilia Quality of Life Questionnaire for Children (Haemo-QoL) Total Score at Month 6: Non-inhibitor Cohort, Participants 12 to <17 years

End point description:

Haemo-QoL assessed health-related QoL in adolescent participants with hemophilia. It contains 12 items with 77 domains that assesses health in the following areas: physical health; feelings; attitude/view; family; friends; other people; sport and school; coping/dealing; treatment; perceived support; future and relationship. All items were based on 5-point Likert type scale (1= never, 2= rarely, 3= sometimes, 4= often, 5= all the time). Scoring was performed by averaging non-missing item responses for each domain, then rescaled from 0 to 100, lower scores signified higher QoL. Total Haem-A-QoL score= was averaged across the 77 items values and then rescaled from 0 to 100, lower scores signified better QoL. mITT set analysed. Here, "Subjects Analyzed" signifies participants of age 12 to <17 years in mITT set. 99999= There were insufficient number of participants to enable the model based analysis.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	20	2	20
Units: Units on a scale				
median (confidence interval 95%)	99999 (-99999 to 99999)	0.8 (-6.2 to 7.8)	-99999 (-99999 to 99999)	-5.0 (-10.5 to 0.4)

Statistical analyses

Statistical analysis title	Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 20 not 40; 40 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	= 0.1418
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.2
upper limit	2.2

Notes:

[37] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in Haemo-QoL Total Score at Month 6: Inhibitor Cohort, Participants 12 to <17 years

End point title	Change From Baseline in Haemo-QoL Total Score at Month 6: Inhibitor Cohort, Participants 12 to <17 years

End point description:

Haemo-QoL assessed health-related QoL in adolescent participants with hemophilia. It contains 12 items with 77 domains that assesses health in the following areas: physical health; feelings; attitude/view; family; friends; other people; sport and school; coping/dealing; treatment; perceived support; future and relationship. All items were based on 5-point Likert type scale (1= never, 2= rarely, 3= sometimes, 4= often, 5= all the time). Scoring was performed by averaging non-missing item responses for each domain, then rescaled from 0 to 100, lower scores signified higher QoL. Total Haem-A-QoL score= was averaged across the 77 items values and then rescaled from 0 to 100, lower scores signified better QoL. mITT set analysed. Here, "Subjects Analyzed" signifies participants of age 12 to <17 years in mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: Units on a scale				
median (confidence interval 95%)	-0.1 (-9.1 to 9.0)	-7.9 (-13.7 to -2.2)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 13 not 26; 26 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other[38]
P-value	= 0.1
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	1.6

Notes:

[38] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in Hemophilia Activities List (HAL) Total Score at Month 6: Non-inhibitor Cohort, Participants >=17 Years

End point title	Change From Baseline in Hemophilia Activities List (HAL) Total Score at Month 6: Non-inhibitor Cohort, Participants >=17 Years

End point description:

The HAL was a multiple domain measure of the impact of hemophilia on functional abilities in adults. The 7 domains of this instrument contained 42 items in total, as follows: lying/sitting/kneeling/standing; lower (leg) functioning; upper (arm) functioning; transportation; self-care; household tasks; and sports/leisure. Items were rated on 6-point scale 1 (impossible) to 6 (never) that described difficulty due to hemophilia. HAL total score was sum of all items and scored 42 to 252, which were transformed to 0-100 where higher scores indicated better functional status. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. "Subjects Analyzed" signifies participants of age >=17 years in mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	31	63	31	63
Units: Units on a scale				
median (confidence interval 95%)	2.0 (-1.3 to 5.2)	-0.6 (-3.0 to 1.8)	1.1 (-2.8 to 5.1)	2.1 (-1.0 to 5.1)

Statistical analyses

Statistical analysis title	Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 63 not 126; 126 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	= 0.3002
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	5.7

Notes:

[39] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 31 not 62; 62 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other[40]
P-value	= 0.7307
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	4.8

Notes:

[40] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in HAL Total Score at Month 6: Inhibitor Cohort,

Participants >=17 Years	
End point title	Change From Baseline in HAL Total Score at Month 6: Inhibitor Cohort, Participants >=17 Years

End point description:

The HAL was a multiple domain measure of the impact of hemophilia on functional abilities in adults. The 7 domains of this instrument contained 42 items in total, as follows: lying/sitting/kneeling/standing; lower (leg) functioning; upper (arm) functioning; transportation; self-care; household tasks; and sports/leisure. Items were rated on 6-point scale 1 (impossible) to 6 (never) that described difficulty due to hemophilia. HAL total score was sum of all items and scored 42 to 252, which were transformed to 0-100 where higher scores indicated better functional status. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. "Subjects Analyzed" signifies participants of age >=17 years in mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	35	35		
Units: Units on a scale				
median (confidence interval 95%)	0.4 (-5.2 to 5.9)	10.6 (4.8 to 16.4)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 35 not 70; 70 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other[41]
P-value	= 0.0085
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	18.2

Notes:

[41] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in Pediatric Hemophilia Activities List (pedHAL) Total Score at Month 6: Non-inhibitor Cohort, Participants 12 to <17 years

End point title	Change From Baseline in Pediatric Hemophilia Activities List (pedHAL) Total Score at Month 6: Non-inhibitor Cohort, Participants 12 to <17 years

End point description:

The pedHAL was a multiple domain measure of the impact of hemophilia on functional abilities in adolescents. The 7 domains of this instrument contained 53 items in total, as follows: sitting/kneeling/standing; functions of the legs; functions of the arms; use of transportation; self-care; household tasks; leisure activities and sports. Items were rated on 6-point scale 1 (impossible) to 6 (never) that described difficulty due to hemophilia. pedHAL total score was normalized in a range of 0-100 where higher scores indicated better functional status. mITT set analysed. Here, "Subjects Analyzed" signifies participants of age 12 to <17 years in mITT set. 99999= there were insufficient number of participants to enable the model based analysis.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	20	2	20
Units: Units on a scale				
median (confidence interval 95%)	99999 (-99999 to 99999)	-1.7 (-9.8 to 6.3)	99999 (-99999 to 99999)	5.3 (-4.7 to 15.3)

Statistical analyses

Statistical analysis title	Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 20 not 40; 40 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[42]
P-value	= 0.4129
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	6.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.3
upper limit	22.7

Notes:

[42] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in pedHAL Total Score at Month 6: Inhibitor Cohort, Participants 12 to <17 years

End point title	Change From Baseline in pedHAL Total Score at Month 6: Inhibitor Cohort, Participants 12 to <17 years

End point description:

The pedHAL was a multiple domain measure of the impact of hemophilia on functional abilities in adolescents. The 7 domains of this instrument contained 53 items in total, as follows: sitting/kneeling/standing; functions of the legs; functions of the arms; use of transportation; self-care; household tasks; leisure activities and sports. Items were rated on 6-point scale 1 (impossible) to 6 (never) that described difficulty due to hemophilia. pedHAL total score was normalized in a range of 0-100 where higher scores indicated better functional status. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed" signifies participants of age 12 to <17 years in mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	13		
Units: Units on a scale				
median (confidence interval 95%)	-4.4 (-20.9 to 12.1)	14.4 (1.1 to 27.8)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 13 not 26; 26 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other[43]
P-value	= 0.076
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	20.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	43.3

Notes:

[43] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in Patient Global Impression of Change-Hemophilia (PGIC-H) at Month 6: Non-inhibitor Cohort

End point title	Change From Baseline in Patient Global Impression of Change-Hemophilia (PGIC-H) at Month 6: Non-inhibitor Cohort

End point description:

The PGIC-H was a single item assessment of the participant's overall impression of change in their life with hemophilia. The response scale was a 7-point categorical response1: greatly improved, 2: moderately improved, 3: slightly improved, 4: no change, 5: slightly worsened, 6: moderately worsened, and 7: greatly worsened. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, "Subjects Analyzed" signifies participants in the mITT set.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	83	33	83
Units: Units on a scale				
median (confidence interval 95%)	3.1 (2.4 to 3.8)	3.5 (3.0 to 3.9)	1.9 (1.3 to 2.4)	1.8 (1.4 to 2.3)

Statistical analyses

Statistical analysis title	Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP

Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	other[44]
P-value	= 0
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1.4

Notes:

[44] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[45]
P-value	= 0
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-1

Notes:

[45] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in PGIC-H at Month 6: Inhibitor Cohort

End point title	Change From Baseline in PGIC-H at Month 6: Inhibitor Cohort

End point description:

The PGIC-H was a single item assessment of the participant’s overall impression of change in their life with hemophilia. The response scale was a 7-point categorical response1: greatly improved, 2: moderately improved, 3: slightly improved, 4: no change, 5: slightly worsened, 6: moderately worsened, and 7: greatly worsened. mITT set: all participants who completed OP and received at least 1 dose of PF-06741086 in ATP (excluding participants with inhibitors who were treated with routine prophylaxis in OP). Participants who changed from non-inhibitor to an inhibitor on or before ATP Day -7 testing were excluded from mITT. Here, “Subjects Analyzed” signifies participants in the mITT set. 99999= Due to excessive ties the median and 95%CI were not estimable for the ATP phase.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	48		
Units: Units on a scale				
median (confidence interval 95%)	3.0 (2.5 to 3.4)	99999 (-99999 to 99999)		

Statistical analyses

Statistical analysis title	Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other[46]
P-value	< 0.0001
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.5

Notes:

[46] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption.

Secondary: Change From Baseline in EuroQol 5 Dimensions 5 Level (EQ-5D-5L) Index and VAS Scores at Month 6:Non-inhibitor Cohort

End point title	Change From Baseline in EuroQol 5 Dimensions 5 Level (EQ-5D-5L) Index and VAS Scores at Month 6:Non-inhibitor Cohort

End point description:

EQ-5D-5L: participant completed questionnaire with 2 components: health state profile index and VAS. EQ-5D health state profile index has 5 domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with 5 levels (1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, 5= extreme problems). Responses to 5 dimensions comprised health state index value. E.g. if a participant responds "no problems" for each 5 dimensions, then health state was coded as "11111" with predefined index value to it. EQ-5D-5L index score ranged from -0.594 to 1, UK look-up value was applied to all participants, higher scores = better health states. The EQ- VAS measured participant's self-rated health state on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state) by VAS. mITT set used. Participants who changed from non-inhibitor to inhibitor on or before ATP Day -7 testing excluded from mITT. Subjects Analyzed: participants in mITT.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: RP at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	83	33	83
Units: Units on a scale				
median (confidence interval 95%)				
EQ-5D-5L index score	-0.0116 (-0.0799 to 0.0566)	0.0300 (-0.0140 to 0.0740)	0.0122 (-0.0627 to 0.0872)	0.0752 (0.0178 to 0.1325)
EQ-VAS score	-0.2 (-6.7 to 6.2)	3.0 (-0.6 to 6.6)	4.2 (-0.1 to 8.5)	4.5 (1.4 to 7.7)

Statistical analyses

Statistical analysis title	EQ-5D-5L Index score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	= 0.7279
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	0.0139
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0645
upper limit	0.0923

Notes:

[47] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was lower bound of 95%CI >0.

Statistical analysis title	EQ-VAS score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 33 not 66; 66 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: OD at OP

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[48]
P-value	= 0.4231
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	11.8

Notes:

[48] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was lower bound of 95%CI >0.

Statistical analysis title	EQ-5D-5L index score: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
P-value	= 0.505
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	0.0223
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0432
upper limit	0.0877

Notes:

[49] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Non-inferiority criterion was lower bound of 95%CI > -0.1. If non-inferiority was established, subsequent testing for superiority may be conducted.

Statistical analysis title	EQ-VAS score: Marstacimab ATP vs RP at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 83 not 166; 166 is auto populated from database.

Comparison groups	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP v Non-Inhibitor Cohort: RP at OP
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
P-value	= 0.8006
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	5.1

Notes:

[50] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Non-inferiority criterion was lower bound of 95%CI > -9.5. If non-inferiority was established, subsequent testing for superiority may be conducted.

Secondary: Change From Baseline in EQ-5D-5L Index and VAS Scores at Month 6: Inhibitor Cohort

End point title	Change From Baseline in EQ-5D-5L Index and VAS Scores at Month 6: Inhibitor Cohort

End point description:

EQ-5D-5L: participant completed questionnaire with 2 components: health state profile index and VAS. EQ-5D health state profile index has 5 domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with 5 levels (1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, 5= extreme problems). Responses to 5 dimensions comprised health state index value. E.g. if a participant responds "no problems" for each 5 dimensions, then health state was coded as "11111" with predefined index value to it. EQ-5D-5L index score ranged from -0.594 to 1, UK look-up value was applied to all participants, higher scores = better health states. The EQ- VAS measured participant's self-rated health state on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state) by VAS. mITT set used. Participants who changed from non-inhibitor to inhibitor on or before ATP Day -7 testing excluded from mITT. Subjects Analyzed: participants in mITT.

End point type	Secondary

End point timeframe:

OP: Baseline (Day 1, day of study enrolment), Month 6; ATP: Baseline (before dose on Day 1 of ATP), Month 6

End point values	Inhibitor Cohort: OD at OP	Inhibitor Cohort: OD at OP/ Marstacimab During ATP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	48		
Units: Units on a scale				
median (confidence interval 95%)				
EQ-5D-5L index score	0.0026 (-0.0669 to 0.0721)	0.1687 (0.0718 to 0.2657)		
EQ-VAS score	1.5 (-6.2 to 9.3)	10.2 (4.2 to 16.2)		

Statistical analyses

Statistical analysis title	EQ-VAS score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[51]
P-value	= 0.1184
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	17

Notes:

[51] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was lower bound of 95%CI >0.

Statistical analysis title	EQ-5D-5L Index score: Marstacimab ATP vs OD at OP

Statistical analysis description:

Actual number of participants contributing to statistical data are only 48 not 96; 96 is auto populated from database.

Comparison groups	Inhibitor Cohort: OD at OP/ Marstacimab During ATP v Inhibitor Cohort: OD at OP
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority[52]
P-value	= 0.0377
Method	Wilcoxon Signed Rank test
Parameter estimate	Estimated Median Difference
Point estimate	0.1043
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.006
upper limit	0.2027

Notes:

[52] - Exact confidence interval using Walsh averages, p-value from Wilcoxon Signed Rank test. Missing values were imputed using multiple imputation methods based on MAR assumption. Superiority criterion was lower bound of 95%CI >0.

Adverse events information

Timeframe for reporting adverse events:

Up to 6 months for OP; up to approximately 13 months for ATP (includes 28-35 days of safety follow-up)

Adverse event reporting additional description:

Same event may appear as both non-SAE and SAE but what is presented are distinct events. All-safety set. MedDRA version 25.1 for non-inhibitor and 28.0 for inhibitor cohort. As pre-specified in the protocol, participants in inhibitor cohort receiving RP contributed to safety evaluation; therefore, the OD and RP therapy groups were combined.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1, 28.0

Reporting groups

Reporting group title	Non-Inhibitor Cohort: OD at OP

Reporting group description:

Participants of the non-inhibitor cohort who had prior OD therapy for haemophilia were observed for 6 months in the OP.

Reporting group title	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP

Reporting group description:

Participants of the non-inhibitor cohort who had prior OD therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW.

Reporting group title	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP

Reporting group description:

Participants of the inhibitor cohort who had prior OD or RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW.

Reporting group title	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP

Reporting group description:

Participants of the non-inhibitor cohort who had prior RP therapy during OP, received marstacimab at a loading dose of 300 mg on Day 1 of ATP followed by a maintenance dose of 150 mg subcutaneously QW.

Reporting group title	Inhibitor Cohort: OD or RP at OP

Reporting group description:

Participants of the inhibitor cohort who had prior OD or RP therapy for haemophilia were observed for 6 months in the OP.

Reporting group title	Non-Inhibitor Cohort: RP at OP

Reporting group description:

Participants of the non-inhibitor cohort who had prior RP therapy for haemophilia were observed for 6 months in the OP.

Serious adverse events	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 37 (2.70%)	0 / 33 (0.00%)	1 / 51 (1.96%)
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)			
Meningioma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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			
Traumatic haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Chest pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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			
Gastric haemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	0 / 33 (0.00%)	0 / 51 (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
Oesophagitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Vomiting			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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			
Haemarthrosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Muscle haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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 occlusion			

subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Infections and infestations			
Tonsillitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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
Device related infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (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	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP	Inhibitor Cohort: OD or RP at OP	Non-Inhibitor Cohort: RP at OP
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 83 (8.43%)	5 / 60 (8.33%)	2 / 91 (2.20%)
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)			
Meningioma			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (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
Injury, poisoning and procedural complications			
Traumatic haemorrhage			
subjects affected / exposed	1 / 83 (1.20%)	1 / 60 (1.67%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (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
Cardiac disorders			

Coronary artery disease			
subjects affected / exposed	0 / 83 (0.00%)	1 / 60 (1.67%)	0 / 91 (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
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (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
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (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
Gastrointestinal disorders			
Gastric haemorrhage			
subjects affected / exposed	0 / 83 (0.00%)	0 / 60 (0.00%)	0 / 91 (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
Oesophagitis			
subjects affected / exposed	0 / 83 (0.00%)	0 / 60 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 83 (0.00%)	1 / 60 (1.67%)	0 / 91 (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
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	0 / 83 (0.00%)	0 / 60 (0.00%)	0 / 91 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 83 (0.00%)	1 / 60 (1.67%)	0 / 91 (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
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	1 / 83 (1.20%)	1 / 60 (1.67%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle haemorrhage			
subjects affected / exposed	0 / 83 (0.00%)	1 / 60 (1.67%)	0 / 91 (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
Product issues			
Device occlusion			
subjects affected / exposed	0 / 83 (0.00%)	0 / 60 (0.00%)	1 / 91 (1.10%)
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			
Tonsillitis			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (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
Device related infection			
subjects affected / exposed	0 / 83 (0.00%)	1 / 60 (1.67%)	0 / 91 (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

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

Non-serious adverse events	Non-Inhibitor Cohort: OD at OP	Non-Inhibitor Cohort: OD at OP/ Marstacimab During ATP	Inhibitor Cohort: OD or RP at OP/ Marstacimab During ATP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)	9 / 33 (27.27%)	30 / 51 (58.82%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	4
Fibrin D dimer increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	5 / 51 (9.80%)
occurrences (all)	0	0	8
Protein urine present			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	4 / 51 (7.84%)
occurrences (all)	0	0	5
Prothrombin fragment 1.2 increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	3
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 33 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 37 (0.00%)	1 / 33 (3.03%)	5 / 51 (9.80%)
occurrences (all)	0	1	5
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 33 (0.00%)	4 / 51 (7.84%)
occurrences (all)	1	0	5
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	2 / 37 (5.41%)	0 / 33 (0.00%)	4 / 51 (7.84%)
occurrences (all)	3	0	5
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 37 (0.00%)	2 / 33 (6.06%)	1 / 51 (1.96%)
occurrences (all)	0	3	1

Musculoskeletal and connective tissue disorders			
Joint range of motion decreased			
subjects affected / exposed	1 / 37 (2.70%)	2 / 33 (6.06%)	0 / 51 (0.00%)
occurrences (all)	1	2	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 37 (0.00%)	2 / 33 (6.06%)	11 / 51 (21.57%)
occurrences (all)	0	2	11
Upper respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	2 / 33 (6.06%)	8 / 51 (15.69%)
occurrences (all)	0	2	9

Non-serious adverse events	Non-Inhibitor Cohort: RP at OP/ Marstacimab During ATP	Inhibitor Cohort: OD or RP at OP	Non-Inhibitor Cohort: RP at OP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 83 (37.35%)	7 / 60 (11.67%)	4 / 91 (4.40%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	0 / 91 (0.00%)
occurrences (all)	1	0	0
Fibrin D dimer increased			
subjects affected / exposed	3 / 83 (3.61%)	3 / 60 (5.00%)	0 / 91 (0.00%)
occurrences (all)	3	3	0
Protein urine present			
subjects affected / exposed	0 / 83 (0.00%)	1 / 60 (1.67%)	0 / 91 (0.00%)
occurrences (all)	0	1	0
Prothrombin fragment 1.2 increased			
subjects affected / exposed	3 / 83 (3.61%)	0 / 60 (0.00%)	0 / 91 (0.00%)
occurrences (all)	3	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	5 / 83 (6.02%)	0 / 60 (0.00%)	0 / 91 (0.00%)
occurrences (all)	8	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 83 (7.23%)	1 / 60 (1.67%)	0 / 91 (0.00%)
occurrences (all)	7	1	0

General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 83 (2.41%)	1 / 60 (1.67%)	0 / 91 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	4 / 83 (4.82%)	1 / 60 (1.67%)	0 / 91 (0.00%)
occurrences (all)	4	1	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 83 (2.41%)	0 / 60 (0.00%)	0 / 91 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Joint range of motion decreased			
subjects affected / exposed	0 / 83 (0.00%)	0 / 60 (0.00%)	0 / 91 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	18 / 83 (21.69%)	0 / 60 (0.00%)	3 / 91 (3.30%)
occurrences (all)	19	0	3
Upper respiratory tract infection			
subjects affected / exposed	1 / 83 (1.20%)	0 / 60 (0.00%)	1 / 91 (1.10%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2019	Protocol Amendment 1: a) Immunogenicity sampling on Day 7 was moved to Day 28. b) Active Treatment Phase (ATP) Day 30 Phone Call was modified to ATP Day 28 Visit and additional assessments added. c) Assessment of prior treatment was removed. d) Exclusion of bleeding data for decisions on dose modification was revised to from 30 days to 72 hours. e) Individual level stopping and dose adjustment and study level stopping rules were added. f) Blood volumes were modified based on additional PF-06741086 and immunogenicity sampling. g) Assessment of intensity was updated to the Common Terminology Criteria for Adverse Events.
08 June 2020	Protocol Amendment 4: The protocol was amended based on feedback received from Health Canada, Italian Medicines Agency (AIFA), Paul Ehrlich Institute (PEI), Germany and The Health Products Regulatory Authority (HPRA) Ireland. Additional edits resulted from internal review to simplify protocol procedures, correct errors, and include alternative study procedures information during the COVID-19 pandemic.
20 November 2020	Protocol Amendment 5: The protocol was amended based on feedback received by the Ministry of Food and Drug Safety (S. Korea) and the Polish regulatory authority to allow more flexibility to conduct safety assessments during the COVID-19 pandemic. Changes were made with regards to the estimated total blood volume and maximum allowed blood volume collection from the adolescent population based on the EMA guidance and following a request from the Italian Medicines Agency (AIFA) on this matter. Changes were also made to address feedback received from clinical study sites. Additional edits resulted from internal review to simplify protocol procedures, to clarify instructions, and to correct errors.
13 July 2021	Protocol Amendment 6: a) added a country-specific amendment to enable China to meet center for drug evaluation (CDE) registration enrollment requirements by an allowance to continue to enroll participants in China after global enrollment was completed; b) to allow additional participants (approximately 20%) in order to provide sufficient enrollment into regions which had experienced delays created by the COVID-19 global pandemic; c) changes made to reflect the change of inclusion criteria for hemophilia B to include participants with factor IX levels <=2%, in line with the currently available EMA guideline (clinical investigation of recombinant and human plasma-derived factor IX products) and to enable recruitment of hemophilia B participants and participants with inhibitors based on recruitment challenges and feedback received from clinical study sites; d) added edits based on a unanimous external data monitoring committee (eDMC) recommendation that treatment with study intervention is to be suspended if a participant develops a presumed or confirmed symptomatic COVID-19 infection due to the potential for thrombotic events; e) added changes to the estimated total blood volume and maximum allowed blood volume collection following central laboratory specification revisions; f) Adverse event of special interest (AESIs), injection site reactions, and thrombotic events were added to protocol Section 8.3.8 Adverse Events of Special Interest. These were not previously included due to edits resulting from internal review to simplify protocol procedures, to clarify instructions, and to correct errors. Editorial updates were made throughout the document.

24 March 2022	Protocol Amendment 7: a) removed the Interim Analysis (IA) for futility within each participant population of interest (i.e., Inhibitor Cohort with prior on-demand therapy; Non-Inhibitor Cohort with prior ondemand therapy; Non-Inhibitor Cohort with prior prophylaxis) planned after 50% of participants within each population of interest have completed the study as the IA data cut time would be very close to the non-inhibitor cohort completions. b) Moved the secondary endpoint of "Total coagulation factor or bypass product consumption" from secondary endpoints to tertiary/exploratory endpoints as there was no uniform unit of measure between factor-replacement products and bypass agent products and in agreement with Paediatric Committee (PDCO), a European Medicines Agency scientific committee. c) Removed "Percentage of participants with no treated bleeding episodes" from secondary endpoints. This will be presented as part of descriptive analysis for the primary endpoint (i.e., ABR of treated bleeding episodes), following agreement reached with FDA. d) incorporated the recently issued global Protocol Administrative Change Letter (PACL) dated 31 January 2022, issued primarily to reintroduce the collection of hematology and serum chemistry samples from adolescents at Visit 20/Study Completion. The collection of dilute prothrombin time samples at Visit 20/Study Completion from adolescent participants was removed in this amendment, to offset the additional blood volume required by reintroducing the collection of hematology and serum chemistry at the same study visit, included a change in local regulation for the informed consent requirements in Japan, where participants usually considered adults when reaching the age of 20 years, were considered adults when reaching the age of 18 years instead, as of 01 April 2022.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported