Clinical trial results:
A Multicenter, Open-Label, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Efficacy of Subcutaneous or Intravenous PF-06741086 in Subjects With Severe Hemophilia

Summary

EudraCT number	2016-001885-27
Trial protocol	PL ES FR BG HR
Global end of trial date	03 December 2018

Results information

Result version number	v1 (current)
This version publication date	02 December 2019
First version publication date	02 December 2019

Trial information

Trial identification

Sponsor protocol code	B7841002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02974855
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer,Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer,Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer,Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 May 2019

Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2018
Global end of trial reached?	Yes
Global end of trial date	03 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the safety and tolerability of multiple doses of PF-06741086 administered to severe hemophilia A and B subjects with and without inhibitors to Factor VIII (FVIII) or Factor IX (FIX).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 March 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	South Africa: 10
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Chile: 10
Country: Number of subjects enrolled	Croatia: 2
Country: Number of subjects enrolled	Poland: 1
Worldwide total number of subjects	26
EEA total number of subjects	3

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)	0

Adults (18-64 years)	26
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 27 subjects were enrolled in the study and assigned to 1 of 4 cohorts. Only 26 subjects received the study treatment and 1 subject withdrew after randomization but prior to dosing.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-06741086 300 mg SC QW Non-Inhibitor

Arm description:

Subjects without inhibitors to Factor VIII (FVIII) or Factor IX (FIX) in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78.

Arm type	Experimental
Investigational medicinal product name	PF-06741086 Solution for Injection, 100 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06741086 300 mg was administered subcutaneously every week.

Arm title	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor

Arm description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78.

Arm type	Experimental
Investigational medicinal product name	PF-06741086 Solution for Injection, 100 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06741086 300 mg loading dose, PF-06741086 150 mg was administered subcutaneously every week.

Arm title	PF-06741086 450 mg SC QW Non-Inhibitor

Arm description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78.

Arm type	Experimental

Investigational medicinal product name	PF-06741086 Solution for Injection, 100 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06741086 450 mg was administered subcutaneously every week.

Arm title	PF-06741086 300 mg SC QW Inhibitor

Arm description:

Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78.

Arm type	Experimental
Investigational medicinal product name	PF-06741086 Solution for Injection, 100 mg/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

PF-06741086 300 mg was administered subcutaneously every week.

Number of subjects in period 1	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor
Started	7	6	6
Completed	7	5	6
Not completed	0	1	0
Adverse event, non-fatal	-	1	-

Number of subjects in period 1	PF-06741086 300 mg SC QW Inhibitor
Started	7
Completed	6
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	PF-06741086 300 mg SC QW Non-Inhibitor
Reporting group description:	
Subjects without inhibitors to Factor VIII (FVIII) or Factor IX (FIX) in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78.	
Reporting group title	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor
Reporting group description:	
Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78.	
Reporting group title	PF-06741086 450 mg SC QW Non-Inhibitor
Reporting group description:	
Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78.	
Reporting group title	PF-06741086 300 mg SC QW Inhibitor
Reporting group description:	
Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78.	

Reporting group values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor
Number of subjects	7	6	6
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	7	6	6
>=65 years	0	0	0
Age Continuous Units: Years			
arithmetic mean	31.9	28.7	41.7
standard deviation	± 8.17	± 8.31	± 15.87
Sex: Female, Male Units: Subjects			
Female	0	0	0
Male	7	6	6
Race (NIH/OMB) Units: Subjects			
White	3	2	6
Black or African American	4	4	0
Other	0	0	0

Reporting group values	PF-06741086 300 mg SC QW Inhibitor	Total	
Number of subjects	7	26	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	7	26	

>=65 years	0	0	

Age Continuous Units: Years			
arithmetic mean	44.1		
standard deviation	± 9.44	-	
Sex: Female, Male Units: Subjects			
Female	0	0	
Male	7	26	
Race (NIH/OMB) Units: Subjects			
White	3	14	
Black or African American	4	12	
Other	0	0	

Subject analysis sets

Subject analysis set title	Overall PF-06741086 300 mg SC
Subject analysis set type	Full analysis

Subject analysis set description:

The overall PF-06741086 300 mg SC group combined subjects from both the PF-06741086 300 mg SC QW non-inhibitor and inhibitor dose cohorts.

Subject analysis set title	Total
Subject analysis set type	Full analysis

Subject analysis set description:

The total group combined subjects from all PF-06741086 cohorts in this study.

Reporting group values	Overall PF-06741086 300 mg SC	Total	
Number of subjects	14	26	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	14	26	
>=65 years	0	0	
Age Continuous Units: Years			
arithmetic mean	38.0	36.7	
standard deviation	± 10.61	± 12.05	
Sex: Female, Male Units: Subjects			
Female	0	0	
Male	14	26	
Race (NIH/OMB) Units: Subjects			
White	6	14	
Black or African American	8	12	
Other	0	0	

End points

End points reporting groups

Reporting group title	PF-06741086 300 mg SC QW Non-Inhibitor
Reporting group description:	
Subjects without inhibitors to Factor VIII (FVIII) or Factor IX (FIX) in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78.	
Reporting group title	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor
Reporting group description:	
Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78.	
Reporting group title	PF-06741086 450 mg SC QW Non-Inhibitor
Reporting group description:	
Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78.	
Reporting group title	PF-06741086 300 mg SC QW Inhibitor
Reporting group description:	
Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78.	
Subject analysis set title	Overall PF-06741086 300 mg SC
Subject analysis set type	Full analysis
Subject analysis set description:	
The overall PF-06741086 300 mg SC group combined subjects from both the PF-06741086 300 mg SC QW non-inhibitor and inhibitor dose cohorts.	
Subject analysis set title	Total
Subject analysis set type	Full analysis
Subject analysis set description:	
The total group combined subjects from all PF-06741086 cohorts in this study.	

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)[1]
End point description:	
An adverse event (AE) was any untoward medical occurrence in a clinical investigation participant administered a product; the event did not need to have a causal relationship with the treatment. A serious adverse event (SAE) was any untoward medical occurrence at any dose that resulted in death; was life threatening; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; resulted in congenital anomaly/birth defect. AEs included both SAEs and AEs. TEAEs were AEs occurred following the start of treatment or AEs increasing in severity during treatment. Severe TEAEs were TEAEs that interfered significantly with participants' usual function. Treatment-related TEAEs were determined by the investigator.	
End point type	Primary
End point timeframe:	
Study Day 1 to Day 113 Visit	

Notes:

[1] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects				
All-causalities TEAE	7	4	6	4
Treatment-related TEAE	4	4	3	3
All-causalities serious TEAE	1	1	1	1
Treatment-related serious TEAE	0	0	0	0
All-causalities Grade 3 or 4 TEAE	0	0	2	2
Treatment-related Grade 3 or 4 TEAE	0	0	2	2

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects				
All-causalities TEAE	11	21		
Treatment-related TEAE	7	14		
All-causalities serious TEAE	2	4		
Treatment-related serious TEAE	0	0		
All-causalities Grade 3 or 4 TEAE	2	4		
Treatment-related Grade 3 or 4 TEAE	2	4		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Discontinued From Study due to TEAEs

End point title	Number of Subjects Discontinued From Study due to TEAEs[2]

End point description:

An AE was any untoward medical occurrence in a clinical investigation participant administered a product; the event did not need to have a causal relationship with the treatment. TEAEs were AEs occurred following the start of treatment or AEs increasing in severity during treatment. Treatment-related TEAEs were determined by the investigator.

End point type	Primary

End point timeframe:

Study Day 1 to Day 113 Visit

Notes:

[2] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects				
All-causalities TEAE	0	1	0	1
Treatment-related TEAE	0	1	0	1

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects				
All-causalities TEAE	1	2		
Treatment-related TEAE	1	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Laboratory Findings-Hematology

End point title	Number of Subjects With Abnormal Laboratory Findings-Hematology[3]

End point description:

Hematology evaluation included: hemoglobin, hematocrit, erythrocytes, platelets, leukocytes, lymphocytes, neutrophils, basophils, eosinophils and monocytes. Pre-defined criteria for hemoglobin and hematocrit: <0.8*lower limit of normal (LLN) or <0.8*Baseline(Baseline <1.0*LLN); for platelets: <100,000 *10^3/mm^3 or <= 0.77*Baseline (Baseline <1.0*LLN).

End point type	Primary

End point timeframe:

Baseline to Study Day 113 Visit

Notes:

[3] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects				
Hemoglobin meeting pre-defined criteria	0	0	0	0
Hematocrit meeting pre-defined criteria	0	0	0	0
Erythrocytes <0.8*LLN	0	0	0	0

Platelets meeting pre-defined criteria	0	0	0	0
Leukocytes <0.6*LLN	0	0	0	0
Leukocytes >1.5*upper limit of normal (ULN)	0	0	0	0
Lymphocytes <0.8*LLN	0	1	0	0
Lymphocytes >1.2*ULN	0	0	0	0
Neutrophils <0.8*LLN	1	2	0	0
Neutrophils >1.2*ULN	0	0	0	0
Basophils >1.2*ULN	0	0	0	0
Eosinophils >1.2*ULN	0	0	0	0
Monocytes >1.2*ULN	0	0	0	0

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects				
Hemoglobin meeting pre-defined criteria	0	0		
Hematocrit meeting pre-defined criteria	0	0		
Erythrocytes <0.8*LLN	0	0		
Platelets meeting pre-defined criteria	0	0		
Leukocytes <0.6*LLN	0	0		
Leukocytes >1.5*upper limit of normal (ULN)	0	0		
Lymphocytes <0.8*LLN	0	1		
Lymphocytes >1.2*ULN	0	0		
Neutrophils <0.8*LLN	1	3		
Neutrophils >1.2*ULN	0	0		
Basophils >1.2*ULN	0	0		
Eosinophils >1.2*ULN	0	0		
Monocytes >1.2*ULN	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Laboratory Findings-Clinical Chemistry

End point title	Number of Subjects With Abnormal Laboratory Findings-Clinical Chemistry[4]

End point description:

Clinical chemistry evaluation included bilirubin, direct and indirect bilirubin, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase, alkaline phosphatase, protein, albumin, urea nitrogen, creatinine, urate, triglycerides, sodium, potassium, chloride, calcium, bicarbonate, glucose, creatine kinase, troponin I, cholesterol and fibrinogen.

End point type	Primary

End point timeframe:

Baseline to Study Day 113

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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[5]	6[6]	6[7]	7[8]
Units: Subjects				
Bilirubin >1.5*ULN	0	0	0	0
Direct Bilirubin >1.5*ULN	0	0	0	0
Indirect Bilirubin >1.5*ULN	0	0	0	0
Aspartate Aminotransferase >3.0*ULN	0	0	1	0
Alanine Aminotransferase >3.0* ULN	1	1	1	0
Gamma Glutamyl Transferase >3.0*ULN	0	1	0	0
Alkaline Phosphatase|	0	0	0	0
Protein <0.8*LLN	0	0	0	0
Protein >1.2*ULN	0	0	0	0
Albumin <0.8*LLN	0	0	0	0
Albumin >1.2*ULN	0	0	0	0
Urea Nitrogen >1.3*ULN	0	0	0	0
Creatinine >1.3*ULN	0	0	0	0
Urate >1.2*ULN	0	0	0	2
Triglycerides >1.3*ULN	0	0	0	0
Sodium <0.95*LLN	0	0	0	0
Sodium >1.05*ULN	0	0	0	0
Potassium <0.9*LLN	1	0	0	0
Potassium >1.1*ULN	0	0	0	0
Chloride <0.9*LLN	0	0	0	0
Chloride >1.1*ULN	0	0	0	0
Calcium <0.9*LLN	0	0	0	0
Calcium >1.1*ULN	0	0	0	0
Bicarbonate <0.9*LLN	2	1	0	0
Bicarbonate >1.1*ULN	0	0	0	0
Glucose <0.6*LLN	0	0	0	0
Glucose >1.5*ULN	0	0	2	1
Creatine Kinase >2.0*ULN	0	0	0	0
Troponin I >1.0*ULN	1	1	0	2
Cholesterol >1.3*ULN	0	0	0	0
Fibrinogen <=0.5*LLN	0	0	0	1

Notes:

[5] - Not all subjects had data for some specific categories.

[6] - Not all subjects had data for some specific categories.

[7] - Not all subjects had data for some specific categories.

[8] - Not all subjects had data for some specific categories.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		

Number of subjects analysed	14[9]	26[10]		
Units: Subjects				
Bilirubin >1.5*ULN	0	0		
Direct Bilirubin >1.5*ULN	0	0		
Indirect Bilirubin >1.5*ULN	0	0		
Aspartate Aminotransferase >3.0*ULN	0	1		
Alanine Aminotransferase >3.0* ULN	1	3		
Gamma Glutamyl Transferase >3.0*ULN	0	1		
Alkaline Phosphatase|	0	0		
Protein <0.8*LLN	0	0		
Protein >1.2*ULN	0	0		
Albumin <0.8*LLN	0	0		
Albumin >1.2*ULN	0	0		
Urea Nitrogen >1.3*ULN	0	0		
Creatinine >1.3*ULN	0	0		
Urate >1.2*ULN	2	2		
Triglycerides >1.3*ULN	0	0		
Sodium <0.95*LLN	0	0		
Sodium >1.05*ULN	0	0		
Potassium <0.9*LLN	1	1		
Potassium >1.1*ULN	0	0		
Chloride <0.9*LLN	0	0		
Chloride >1.1*ULN	0	0		
Calcium <0.9*LLN	0	0		
Calcium >1.1*ULN	0	0		
Bicarbonate <0.9*LLN	2	3		
Bicarbonate >1.1*ULN	0	0		
Glucose <0.6*LLN	0	0		
Glucose >1.5*ULN	1	3		
Creatine Kinase >2.0*ULN	0	0		
Troponin I >1.0*ULN	3	4		
Cholesterol >1.3*ULN	0	0		
Fibrinogen <=0.5*LLN	1	1		

Notes:

[9] - Not all subjects had data for some specific categories.

[10] - Not all subjects had data for some specific categories.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal Laboratory Findings-Urinalysis

End point title	Number of Subjects With Abnormal Laboratory Findings-Urinalysis[11]

End point description:

Urinalysis included: pH, urine glucose, ketones, urine protein, urine hemoglobin, urobilinogen, urine bilirubin, nitrite, leukocyte esterase, urine erythrocytes, urine leukocytes and bacteria.

End point type	Primary

End point timeframe:

Baseline to Study Day 113 Visit

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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[12]	6[13]	6[14]	7[15]
Units: Subjects				
pH (Scalar) <4.5	0	0	0	0
pH (Scalar) >8	0	0	0	0
Urine glucose >=1	0	0	1	0
Ketones (Scalar) >=1	0	0	1	1
Urine protein >=1	0	0	0	1
Urine hemoglobin (Scalar) >=1	0	0	0	0
Urobilinogen >=1	0	0	0	0
Urine bilirubin (Scalar) >=1	0	0	0	0
Nitrite (Scalar) >=1	0	0	0	0
Leukocyte esterase (Scalar) >=1	1	1	0	1
Urine erythrocytes (/HPF) >=20	0	0	0	0
Urine leukocytes (/HPF) >=20	0	1	0	1
Bacteria (/HPF) >20	0	0	0	0

Notes:

[12] - Not all subjects had data for some specific categories.

[13] - Not all subjects had data for some specific categories.

[14] - Not all subjects had data for some specific categories.

[15] - Not all subjects had data for some specific categories.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[16]	26[17]		
Units: Subjects				
pH (Scalar) <4.5	0	0		
pH (Scalar) >8	0	0		
Urine glucose >=1	0	1		
Ketones (Scalar) >=1	1	2		
Urine protein >=1	1	1		
Urine hemoglobin (Scalar) >=1	0	0		
Urobilinogen >=1	0	0		
Urine bilirubin (Scalar) >=1	0	0		
Nitrite (Scalar) >=1	0	0		
Leukocyte esterase (Scalar) >=1	2	3		
Urine erythrocytes (/HPF) >=20	0	0		
Urine leukocytes (/HPF) >=20	1	2		
Bacteria (/HPF) >20	0	0		

Notes:

[16] - Not all subjects had data for some specific categories.

[17] - Not all subjects had data for some specific categories.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Globulin by Dose Cohort

End point title	Change From Baseline for Globulin by Dose Cohort[18]

End point description:

Blood samples were obtained to determine globulin level in serum, total globulin was derived as total protein other than albumin.

End point type	Primary

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[18] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[19]	6[20]	6[21]	7[22]
Units: gram/liter				
arithmetic mean (standard deviation)				
Globulin, Change at Day 8	-0.3 (± 3.04)	-1.7 (± 3.93)	-1.3 (± 2.73)	0.4 (± 2.51)
Globulin, Change at Day 15	-0.7 (± 2.06)	-0.8 (± 2.32)	-1.3 (± 2.50)	-1.3 (± 3.35)
Globulin, Change at Day 22	-1.6 (± 2.82)	-0.5 (± 1.52)	-1.5 (± 3.08)	-0.6 (± 4.12)
Globulin, Change at Day 29	-0.3 (± 3.27)	-0.3 (± 3.08)	0.2 (± 1.10)	-1.3 (± 2.75)
Globulin, Change at Day 57	0.7 (± 3.72)	1.8 (± 2.99)	-0.3 (± 1.63)	-0.7 (± 2.94)
Globulin, Change at Day 85	1.3 (± 3.15)	-1.4 (± 4.77)	-0.5 (± 3.02)	1.0 (± 2.61)
Globulin, Change at Day 113	-0.3 (± 3.15)	-1.2 (± 4.67)	0.5 (± 2.65)	-0.8 (± 3.06)

Notes:

[19] - Not all subjects had data for some specific rows of time points.

[20] - Not all subjects had data for some specific rows of time points.

[21] - Not all subjects had data for some specific rows of time points.

[22] - Not all subjects had data for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[23]	26[24]		
Units: gram/liter				
arithmetic mean (standard deviation)				
Globulin, Change at Day 8	0.1 (± 2.70)	-0.7 (± 3.01)		
Globulin, Change at Day 15	-1.0 (± 2.69)	-1.0 (± 2.47)		
Globulin, Change at Day 22	-1.1 (± 3.43)	-1.0 (± 2.93)		
Globulin, Change at Day 29	-0.8 (± 2.91)	-0.5 (± 2.62)		
Globulin, Change at Day 57	0.0 (± 3.28)	0.4 (± 2.90)		
Globulin, Change at Day 85	1.2 (± 2.79)	0.2 (± 3.35)		
Globulin, Change at Day 113	-0.5 (± 2.99)	-0.5 (± 3.33)		

Notes:

[23] - Not all subjects had data for some specific rows of time points.

[24] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Prothrombin International Normalized Ratio (PT/INR) by Dose Cohort

End point title	Change From Baseline for Prothrombin International Normalized Ratio (PT/INR) by Dose Cohort[25]

End point description:

Blood samples were obtained to evaluate this ratio. The prothrombin time (PT) is a test that helps evaluate your ability to appropriately form blood clots. The international normalized ratio (INR) is a calculation based on results of a PT that is used to monitor individuals who are being treated with the blood-thinning medication (anticoagulant) warfarin (Coumadin®).

End point type	Primary

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[25] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[26]	6[27]	6[28]	7[29]
Units: Ratio				
arithmetic mean (standard deviation)				
PT/INR, Change at Day 8	-0.03 (± 0.049)	-0.02 (± 0.041)	0.05 (± 0.138)	0.03 (± 0.138)
PT/INR, Change at Day 15	0.03 (± 0.076)	0.00 (± 0.063)	0.02 (± 0.041)	0.00 (± 0.082)
PT/INR, Change at Day 22	0.03 (± 0.095)	0.00 (± 0.063)	-0.02 (± 0.041)	-0.01 (± 0.069)
PT/INR, Change at Day 29	0.03 (± 0.082)	-0.02 (± 0.041)	0.00 (± 0.063)	0.00 (± 0.115)
PT/INR, Change at Day 57	0.00 (± 0.126)	-0.03 (± 0.052)	0.00 (± 0.063)	-0.02 (± 0.075)
PT/INR, Change at Day 85	-0.01 (± 0.107)	0.04 (± 0.152)	-0.02 (± 0.075)	-0.03 (± 0.082)
PT/INR, Change at Day 113	0.06 (± 0.127)	-0.03 (± 0.052)	-0.05 (± 0.058)	0.07 (± 0.052)

Notes:

[26] - Not all subjects had data for some specific rows of time points.

[27] - Not all subjects had data for some specific rows of time points.

[28] - Not all subjects had data for some specific rows of time points.

[29] - Not all subjects had data for some specific rows of time points.

End point values	Overall PF-	Total		

	06741086 300 mg SC			
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[30]	26[31]		
Units: Ratio				
arithmetic mean (standard deviation)				
PT/INR, Change at Day 8	0.00 (± 0.104)	0.01 (± 0.102)		
PT/INR, Change at Day 15	0.01 (± 0.077)	0.01 (± 0.065)		
PT/INR, Change at Day 22	0.01 (± 0.083)	0.00 (± 0.069)		
PT/INR, Change at Day 29	0.02 (± 0.099)	0.00 (± 0.079)		
PT/INR, Change at Day 57	-0.01 (± 0.100)	-0.01 (± 0.080)		
PT/INR, Change at Day 85	-0.02 (± 0.093)	-0.01 (± 0.102)		
PT/INR, Change at Day 113	0.06 (± 0.096)	0.02 (± 0.094)		

Notes:

[30] - Not all subjects had data for some specific rows of time points.

[31] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Activated Partial Thromboplastin Time (aPTT) by Dose Cohort

End point title	Change From Baseline for Activated Partial Thromboplastin Time (aPTT) by Dose Cohort[32]

End point description:

The activated partial thromboplastin time (aPTT) is a screening test that helps evaluate a person's ability to appropriately form blood clots. It measures the number of seconds it takes for a clot to form in a sample of blood after substances (reagents) are added. Blood sample were obtained to evaluate aPTT.

End point type	Primary

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[32] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[33]	6[34]	6[35]	7[36]
Units: seconds				
arithmetic mean (standard deviation)				
aPTT, Change at Day 8	8.49 (± 17.017)	10.63 (± 11.634)	11.03 (± 15.467)	-12.26 (± 7.082)
aPTT, Change at Day 15	9.50 (± 10.907)	12.50 (± 15.303)	1.20 (± 20.075)	-10.26 (± 6.757)
aPTT, Change at Day 22	14.79 (± 10.799)	12.15 (± 15.232)	4.50 (± 9.765)	-11.77 (± 11.247)
aPTT, Change at Day 29	13.42 (± 11.102)	9.85 (± 15.999)	10.13 (± 10.250)	-12.87 (± 11.390)

aPTT, Change at Day 57	13.65 (± 13.378)	14.25 (± 14.061)	7.82 (± 11.580)	-9.13 (± 8.390)
aPTT, Change at Day 85	9.00 (± 10.928)	3.84 (± 18.089)	7.68 (± 14.733)	-7.57 (± 10.124)
aPTT, Change at Day 113	8.46 (± 23.391)	0.78 (± 16.332)	-0.97 (± 26.633)	9.37 (± 20.265)

Notes:

[33] - Not all subjects had data for some specific rows of time points.

[34] - Not all subjects had data for some specific rows of time points.

[35] - Not all subjects had data for some specific rows of time points.

[36] - Not all subjects had data for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[37]	26[38]		
Units: seconds				
arithmetic mean (standard deviation)				
aPTT, Change at Day 8	-1.89 (± 16.512)	3.98 (± 16.079)		
aPTT, Change at Day 15	-0.38 (± 13.457)	2.96 (± 15.825)		
aPTT, Change at Day 22	1.51 (± 17.381)	4.65 (± 15.543)		
aPTT, Change at Day 29	-0.74 (± 17.386)	4.41 (± 16.009)		
aPTT, Change at Day 57	2.26 (± 15.966)	6.65 (± 14.817)		
aPTT, Change at Day 85	1.35 (± 13.278)	3.45 (± 14.257)		
aPTT, Change at Day 113	8.88 (± 21.093)	5.05 (± 20.500)		

Notes:

[37] - Not all subjects had data for some specific rows of time points.

[38] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Fibrinogen by Dose Cohort

End point title	Change From Baseline for Fibrinogen by Dose Cohort[39]

End point description:

Fibrinogen is a protein, specifically a clotting factor (factor I), that is essential for proper blood clot formation. Blood samples were obtained to evaluate the amount of fibrinogen.

End point type	Primary

End point timeframe:

Baseline, Study Day 8, 15, 22, 29, 57, 85 and 113.

Notes:

[39] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[40]	6[41]	6[42]	7[43]
Units: milligram/deciliter				
arithmetic mean (standard deviation)				
Fibrinogen, Change at Day 8	-49.7 (± 28.72)	-59.7 (± 38.20)	-3.5 (± 24.16)	-54.4 (± 59.58)
Fibrinogen, Change at Day 15	-59.4 (± 41.28)	-51.0 (± 31.84)	-8.3 (± 25.96)	-85.6 (± 94.86)
Fibrinogen, Change at Day 22	-72.0 (± 40.76)	-36.8 (± 44.93)	-33.2 (± 32.41)	-87.9 (± 115.49)
Fibrinogen, Change at Day 29	-84.7 (± 43.53)	-40.0 (± 26.57)	-40.3 (± 20.99)	-99.9 (± 106.59)
Fibrinogen, Change at Day 57	-33.5 (± 85.81)	10.0 (± 79.34)	-21.3 (± 24.23)	-58.7 (± 71.81)
Fibrinogen, Change at Day 85	-49.9 (± 47.93)	-39.4 (± 63.27)	-10.5 (± 44.94)	-40.8 (± 74.28)
Fibrinogen, Change at Day 113	-38.6 (± 44.48)	-5.2 (± 29.34)	23.5 (± 26.80)	-61.7 (± 126.18)

Notes:

[40] - Not all subjects had data for some specific rows of time points.

[41] - Not all subjects had data for some specific rows of time points.

[42] - Not all subjects had data for some specific rows of time points.

[43] - Not all subjects had data for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[44]	26[45]		
Units: milligram/deciliter				
arithmetic mean (standard deviation)				
Fibrinogen, Change at Day 8	-52.1 (± 45.00)	-42.6 (± 44.14)		
Fibrinogen, Change at Day 15	-72.5 (± 71.58)	-52.7 (± 60.78)		
Fibrinogen, Change at Day 22	-79.9 (± 83.61)	-59.2 (± 69.08)		
Fibrinogen, Change at Day 29	-92.8 (± 80.82)	-67.6 (± 65.01)		
Fibrinogen, Change at Day 57	-46.1 (± 76.57)	-25.9 (± 69.68)		
Fibrinogen, Change at Day 85	-45.7 (± 58.91)	-35.6 (± 56.31)		
Fibrinogen, Change at Day 113	-49.2 (± 88.13)	-25.1 (± 73.56)		

Notes:

[44] - Not all subjects had data for some specific rows of time points.

[45] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Antithrombin III by Dose Cohort

End point title	Change From Baseline for Antithrombin III by Dose Cohort[46]

End point description:

Antithrombin (AT) is a protein produced by the liver that helps regulate blood clot formation (i.e., a naturally-occurring mild blood thinner). Blood samples were collected to measure the activity (function) and the amount (quantity) of antithrombin in an individual's blood is used to evaluate the person for excessive blood clotting.

End point type	Primary

End point timeframe:

Baseline, Study Day 8, 15, 22 and 29.

Notes:

[46] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[47]	6	6	7
Units: Percentage of activity of AT in plasma				
arithmetic mean (standard deviation)				
Antithrombin III, Change at Day 8	2.1 (± 5.18)	-1.8 (± 7.05)	3.7 (± 7.58)	-7.3 (± 9.32)
Antithrombin III, Change at Day 15	2.4 (± 16.96)	0.5 (± 8.14)	-15.3 (± 16.45)	-6.9 (± 6.74)
Antithrombin III, Change at Day 22	-7.6 (± 17.55)	5.2 (± 12.69)	-5.3 (± 9.97)	-4.4 (± 17.61)
Antithrombin III, Change at Day 29	-0.8 (± 8.04)	-4.3 (± 11.55)	-10.3 (± 15.45)	-12.7 (± 12.96)

Notes:

[47] - Not all subjects had data at Day 29.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[48]	26[49]		
Units: Percentage of activity of AT in plasma				
arithmetic mean (standard deviation)				
Antithrombin III, Change at Day 8	-2.6 (± 8.74)	-1.0 (± 8.24)		
Antithrombin III, Change at Day 15	-2.2 (± 13.30)	-4.6 (± 14.02)		
Antithrombin III, Change at Day 22	-6.0 (± 16.97)	-3.3 (± 14.97)		
Antithrombin III, Change at Day 29	-7.2 (± 12.20)	-7.3 (± 12.51)		

Notes:

[48] - Not all subjects had data at Day 29.

[49] - Not all subjects had data at Day 29.

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline for Troponin I by Dose Cohort

End point title	Change From Baseline for Troponin I by Dose Cohort[50]

End point description:

Blood samples were collected to measure the level of cardiac-specific troponin I in the blood to help detect heart injury.

End point type	Primary

End point timeframe:

Baseline, Study Day 22 and 29

Notes:

[50] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[51]	6[52]	6[53]	7[54]
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
Troponin I, Change at Day 22	0.0042 (± 0.01021)	0 (± 0)	0 (± 0)	0.0142 (± 0.03470)
Troponin I, Change at Day 29	0 (± 0)	0.0113 (± 0.02250)	0 (± 0)	0.0121 (± 0.03213)

Notes:

[51] - Not all subjects had data for each row of time point.

[52] - Not all subjects had data for each row of time point.

[53] - Not all subjects had data for each row of time point.

[54] - Not all subjects had data for each row of time point.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[55]	26[56]		
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
Troponin I, Change at Day 22	0.0092 (± 0.02494)	0.0052 (± 0.01907)		
Troponin I, Change at Day 29	0.0065 (± 0.02357)	0.0059 (± 0.02010)		

Notes:

[55] - Not all subjects had data for each row of time point.

[56] - Not all subjects had data for each row of time point.

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Vital Signs Data Meeting Pre-specified Criteria

End point title	Number of Subjects With Vital Signs Data Meeting Pre-specified Criteria[57]

End point description:

Criteria for potentially clinically important findings in vital signs data were defined as: 1) supine systolic blood pressure (BP): value <90 mm Hg or change >=30 mm Hg increase; 2) Supine diastolic BP: value <50 mm Hg or change >=20 mm Hg increase; 3) Supine pulse rate: value <40 beats/min or >120

beats/min.

End point type	Primary

End point timeframe:

Baseline to Study Day 113 Visit

Notes:

[57] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects				
Supine systolic BP value <90 mm Hg	0	0	0	0
Supine systolic BP change >=30 mm Hg increase	0	1	1	0
Supine diastolic BP value <50 mm Hg	0	0	0	0
Supine diastolic BP change >=20 mm Hg increase	0	1	0	0
Supine pulse rate value <40 beats/min	0	0	0	0
Supine pulse rate value >120 beats/min	0	0	0	0

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects				
Supine systolic BP value <90 mm Hg	0	0		
Supine systolic BP change >=30 mm Hg increase	0	2		
Supine diastolic BP value <50 mm Hg	0	0		
Supine diastolic BP change >=20 mm Hg increase	0	1		
Supine pulse rate value <40 beats/min	0	0		
Supine pulse rate value >120 beats/min	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Electrocardiogram (ECG) Change Meeting Pre-specified Criteria

End point title	Number of Subjects With Electrocardiogram (ECG) Change Meeting Pre-specified Criteria[58]

End point description:

Criteria for potentially clinically important changes in ECG were defined as: PR interval baseline >200 msec and increase of >=25%; PR interval baseline <=200 msec and increase of >=50%; QRS interval increase of >=50%. Only the number of subjects meeting pre-defined criteria was reported below.

End point type	Primary

End point timeframe:

Baseline to Study Day 29 Visit.

Notes:

[58] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects	0	0	0	0

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Physical Examination Findings

End point title	Number of Subjects With Clinically Significant Changes in Physical Examination Findings[59]

End point description:

Physical examination included head, ears, eyes, nose, mouth, skin, heart and lung examinations, lymph nodes, gastrointestinal, musculoskeletal, and neurological systems. Clinical significance was judged by the investigator.

End point type	Primary

End point timeframe:

Baseline to Study Day 113 Visit

Notes:

[59] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects	0	0	0	0

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Infusion and Injection Site Reactions

End point title	Number of Subjects With Infusion and Injection Site

End point description:

Infusion and injection site reactions included: injection site bruising, injection site erythema, injection site haemorrhage, injection site induration, injection site pain, injection site pruritus, injection site swelling and injection site warmth. Grade of severity was defined as follows: Mild: Transient or mild discomfort (< 48 hours); no medical intervention/therapy required. Moderate: Mild to moderate limitation in activity - some assistance may be needed; no or minimal medical intervention/therapy required. Severe: Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible.

End point type	Primary

End point timeframe:

Baseline to Study Day 113 Visit

Notes:

[60] - 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: No statistical analysis was planned for this endpoint

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects				
All-causality Mild	3	1	0	1
Treatment-related Mild	3	1	0	1
All-causality Moderate	0	0	0	1
Treatment-related Moderate	0	0	0	1
All-causality Severe	0	0	2	0

Treatment-related Severe	0	0	2	0

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects				
All-causality Mild	4	5		
Treatment-related Mild	4	5		
All-causality Moderate	1	1		
Treatment-related Moderate	1	1		
All-causality Severe	0	2		
Treatment-related Severe	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Bleeding Rate (ABR)

End point title	Annualized Bleeding Rate (ABR)

End point description:

Pre-treatment ABR = number of bleeding episodes within 6 months prior to study enrollment (total number of bleeding episodes in hemophilia history CRF) × 2; On-study ABR = number of bleeding episodes occurred within 9 days after the last dose / ([last dose date + 9 - first dose date + 1] / 365.25)

End point type	Secondary

End point timeframe:

Pre-treatment: within 6 months prior to study enrollment; On-study: Day 1 to 9 days after the last dose (Day 78)

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: Bleeding episodes per year				
arithmetic mean (standard deviation)				
Pre-Treatment	23.00 (± 7.457)	14.67 (± 1.633)	20.33 (± 10.838)	17.33 (± 3.011)
On-Study	4.22 (± 3.799)	1.62 (± 2.533)	4.17 (± 6.467)	0.65 (± 1.603)

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	24		
Units: Bleeding episodes per year				
arithmetic mean (standard deviation)				
Pre-Treatment	20.17 (± 6.177)	18.83 (± 7.100)		
On-Study	2.43 (± 3.345)	2.67 (± 4.092)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma PF-06741086 concentrations

End point title	Plasma PF-06741086 concentrations

End point description:

Plasma PF-06741086 concentrations were analyzed using a validated, sensitive and specific electrochemiluminescence (ECL) method. Not all subjects had data at each visit.

End point type	Secondary

End point timeframe:

pre-dose on Study Day 1, 24hours (h), 72h post Study Day 1 dosing, pre-dose on Study Day 8, 15 and 22, pre-dose on Study Day 29, 24h, 96h post Study Day 29 dosing, pre-dose on Study Day 57, 168h, 840h post Study Day 57 dosing

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[61]	6[62]	6[63]	7[64]
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
Pre-dose on Day 1	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
24h post Day 1 dosing	12180 (± 8500.2)	15620 (± 8055.3)	11640 (± 4670.6)	18130 (± 9111.3)
72h post Day 1 dosing	17560 (± 10637)	20850 (± 8433.7)	24270 (± 8018.9)	20640 (± 8978.4)
Pre-dose on Day 8	11290 (± 10019)	14060 (± 6201.2)	16700 (± 5689.1)	11940 (± 4981.7)
Pre-dose on Day 15	22850 (± 15142)	16680 (± 7668.8)	28180 (± 10163)	24870 (± 5726.8)
Pre-dose on Day 22	33010 (± 19724)	17900 (± 10509)	41200 (± 17504)	36450 (± 10432)
Pre-dose on Day 29	46180 (± 21357)	16780 (± 7939.7)	59950 (± 30625)	41500 (± 13884)
24h post Day 29 dosing	66500 (± 27135)	23530 (± 8548.4)	73780 (± 22425)	69920 (± 27902)

96h post Day 29 dosing	69130 (± 30459)	20680 (± 11580)	74950 (± 27538)	58150 (± 18753)
Pre-dose on Day 57	54580 (± 29022)	18260 (± 15062)	66480 (± 45529)	59140 (± 24377)
168h post Day 57 dosing	53890 (± 43483)	24800 (± 2994.4)	87500 (± 37163)	66700 (± 28971)
840h post Day 57 dosing	586.6 (± 1318.4)	99999 (± 99999)	99999 (± 99999)	90.00 (± 180.00)

Notes:

[61] - Not all subjects had data for some specific rows of time points.

[62] - Not all subjects had data for some specific rows of time points.

[63] - Not all subjects had data for some specific rows of time points.

[64] - Not all subjects had data for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[65]			
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
Pre-dose on Day 1	99999 (± 99999)			
24h post Day 1 dosing	15150 (± 9011.0)			
72h post Day 1 dosing	19100 (± 9591.3)			
Pre-dose on Day 8	11610 (± 7609.2)			
Pre-dose on Day 15	23860 (± 11048)			
Pre-dose on Day 22	34600 (± 15590)			
Pre-dose on Day 29	43840 (± 17161)			
24h post Day 29 dosing	68210 (± 26010)			
96h post Day 29 dosing	62860 (± 22794)			
Pre-dose on Day 57	56860 (± 25382)			
168h post Day 57 dosing	60300 (± 35481)			
840h post Day 57 dosing	406.0 (± 1056.1)			

Notes:

[65] - Not all subjects had data for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of PF-06741086

End point title	Area Under the Concentration-time Profile From Time Zero to the Time of the Last Quantifiable Concentration (AUClast) of PF-06741086

End point description:

AUClast was calculated by linear/Log trapezoidal method.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1, 24 and 96 hours post Day 1 dosing

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: nanogram*hour/milliliter				
geometric mean (geometric coefficient of variation)	1818000 (± 79)	2675000 (± 41)	2806000 (± 37)	2495000 (± 40)

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: nanogram*hour/milliliter				
geometric mean (geometric coefficient of variation)	2130000 (± 61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of PF-06741086

End point title	Maximum Plasma Concentration (Cmax) of PF-06741086

End point description:

Cmax was observed directly from data. Not all subjects had data at Day 29.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1, 24 and 96 hours post Day 1 dosing, pre-dose on Day 29, 24 and 96 hours post Day 29 dosing

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[66]	6	6[67]	7[68]
Units: nanogram/milliliter				
geometric mean (geometric coefficient of variation)				
Cmax, Day 1	14880 (± 70)	19480 (± 42)	23070 (± 37)	19680 (± 51)
Cmax, Day 29	61850 (± 47)	24150 (± 44)	73490 (± 38)	66070 (± 44)

Notes:

[66] - Not all subjects had data for some specific time points.

[67] - Not all subjects had data for some specific time points.

[68] - Not all subjects had data for some specific time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[69]			
Units: nanogram/milliliter				
geometric mean (geometric coefficient of variation)				
Cmax, Day 1	17110 (± 61)			
Cmax, Day 29	63930 (± 43)			

Notes:

[69] - Not all subjects had data for some specific time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Lowest Concentration Observed During the Dosing Interval (Cmin) of PF-06741086

End point title	Lowest Concentration Observed During the Dosing Interval (Cmin) of PF-06741086

End point description:

Cmin was observed directly from data. Not all subjects had data at Day 29.

End point type	Secondary

End point timeframe:

Post-dose on Day 2 (-6 hours/+1 day), Day 4 (-6 hours/+1 day), Day 30 (-6 hours/+1 day) and Day 33 (-6 hours/+1 day).

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[70]	6	6[71]	7[72]
Units: nanogram/milliliter				

geometric mean (geometric coefficient of variation)				
Cmin, Day 1	7980 (± 112)	13040 (± 43)	15660 (± 44)	11140 (± 41)
Cmin, Day 29	42120 (± 52)	15000 (± 59)	53630 (± 61)	39490 (± 37)

Notes:

[70] - Not all subjects had data for some specific time points.

[71] - Not all subjects had data for some specific time points.

[72] - Not all subjects had data for some specific time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[73]			
Units: nanogram/milliliter				
geometric mean (geometric coefficient of variation)				
Cmin, Day 1	9429 (± 78)			
Cmin, Day 29	40790 (± 42)			

Notes:

[73] - Not all subjects had data for some specific time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Plasma Concentration (Tmax) of PF-06741086

End point title	Time to Reach Maximum Plasma Concentration (Tmax) of PF-06741086

End point description:

Tmax was observed directly from data as time of first occurrence. Not all subjects had data at Day 29.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1, 24 and 96 hours post Day 1 dosing, pre-dose on Day 29, 24 and 96 hours post Day 29 dosing

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[74]	6	6[75]	7[76]
Units: hours				
median (full range (min-max))				
Tmax, Day 1	70.0 (69.1 to 72.8)	69.7 (68.2 to 71.1)	71.6 (67.6 to 72.3)	70.7 (22.8 to 167)
Tmax, Day 29	23.7 (23.1 to 94.2)	23.7 (22.0 to 71.7)	58.5 (23.3 to 97.0)	22.8 (22.1 to 94.7)

Notes:

[74] - Not all subjects had data for some specific time points.

[75] - Not all subjects had data for some specific time points.

[76] - Not all subjects had data for some specific time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[77]			
Units: hours				
median (full range (min-max))				
Tmax, Day 1	70.1 (22.8 to 167)			
Tmax, Day 29	23.3 (22.1 to 94.7)			

Notes:

[77] - Not all subjects had data for some specific time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration-time Curve Over the Dosing Interval tau (AUCtau) of PF-06741086

End point title	Area Under the Serum Concentration-time Curve Over the Dosing Interval tau (AUCtau) of PF-06741086

End point description:

The dosing interval tau was 1 week. AUCtau was obtained by linear/log trapezoidal method.

End point type	Secondary

End point timeframe:

Pre-dose on Day 29, 24 and 96 hours post Day 29 dosing

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	4	5
Units: nanogram*hour/milliliter				
geometric mean (geometric coefficient of variation)	9045000 (± 49)	3309000 (± 50)	11090000 (± 43)	9248000 (± 38)

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: nanogram*hour/milliliter				
geometric mean (geometric coefficient	9146000 (±			

of variation)	41)

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance After Oral Dose (CL/F) of PF-06741086

End point title	Apparent Clearance After Oral Dose (CL/F) of PF-06741086
End point description: CL/F was calculated by dose/AUCtau.	
End point type	Secondary
End point timeframe: Pre-dose on Day 29, 24 and 96 hours post Day 29 dosing	

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	4	5
Units: milliliter/hour				
geometric mean (geometric coefficient of variation)	33.16 (± 49)	45.34 (± 50)	40.60 (± 43)	32.43 (± 38)

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: milliliter/hour				
geometric mean (geometric coefficient of variation)	32.79 (± 41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Tissue Factor Pathway Inhibitor (TFPI)

End point title	Change From Baseline in Total Tissue Factor Pathway Inhibitor (TFPI)
End point description:	

Total amount of tissue factor pathway inhibitor (TFPI) (bound and unbound) in plasma. TFPI is a protease inhibitor which acts as an antagonist of the extrinsic coagulation pathway via inhibition of tissue factor activated coagulation factor VII (FVIIa) and activated factor X (FXa). Human plasma samples were analyzed for total TFPI concentrations using a validated, sensitive and specific high-performance liquid chromatography tandem mass spectrometric method (LC-MS/MS). Mixed model repeated measures (MMRM) was used to analyze the change from baseline on TFPI.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[78]	6[79]	6[80]	7[81]
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
TFPI, Change at Day 2	3.9 (± 31.43)	-13.4 (± 17.17)	8.2 (± 19.83)	0.4 (± 46.81)
TFPI, Change at Day 4	39.4 (± 46.10)	43.2 (± 25.76)	74.0 (± 22.03)	86.0 (± 29.71)
TFPI, Change at Day 8	42.7 (± 82.52)	72.4 (± 10.81)	120.5 (± 34.41)	55.9 (± 69.84)
TFPI, Change at Day 15	143.9 (± 107.56)	78.8 (± 43.36)	186.5 (± 52.80)	156.1 (± 83.87)
TFPI, Change at Day 22	256.1 (± 137.09)	110.0 (± 80.96)	301.5 (± 84.39)	223.3 (± 128.08)
TFPI, Change at Day 29	324.2 (± 127.46)	106.6 (± 77.56)	334.7 (± 120.67)	222.1 (± 135.29)
TFPI, Change at Day 30	363.8 (± 156.87)	115.6 (± 86.41)	347.8 (± 170.70)	286.7 (± 103.72)
TFPI, Change at Day 33	337.7 (± 129.05)	165.8 (± 35.20)	351.0 (± 161.54)	296.3 (± 112.30)
TFPI, Change at Day 57	383.3 (± 137.17)	140.0 (± 126.96)	460.5 (± 247.37)	371.0 (± 178.73)
TFPI, Change at Day 85	396.7 (± 216.54)	246.7 (± 51.81)	492.2 (± 308.46)	425.0 (± 266.57)
TFPI, Change at Day 113	30.0 (± 72.30)	41.5 (± 28.99)	39.0 (± 16.15)	-14.0 (± 33.17)

Notes:

[78] - Number of subjects analyzed was 6 at Day 29.

[79] - Not all subjects were analyzed for some specific rows of time points.

[80] - Not all subjects were analyzed for some specific rows of time points.

[81] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[82]			
Units: nanogram/milliliter				
arithmetic mean (standard deviation)				
TFPI, Change at Day 2	2.1 (± 38.35)			
TFPI, Change at Day 4	62.7 (± 44.41)			

TFPI, Change at Day 8	49.3 (± 73.76)			
TFPI, Change at Day 15	150.0 (± 92.88)			
TFPI, Change at Day 22	239.7 (± 128.59)			
TFPI, Change at Day 29	269.2 (± 136.83)			
TFPI, Change at Day 30	325.3 (± 133.04)			
TFPI, Change at Day 33	317.0 (± 117.34)			
TFPI, Change at Day 57	377.2 (± 152.03)			
TFPI, Change at Day 85	409.8 (± 230.80)			
TFPI, Change at Day 113	9.7 (± 59.94)			

Notes:

[82] - Not all subjects were analyzed for some specific rows of time points

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Thrombin Generation (TGA) Lag Time

End point title	Change From Baseline in Thrombin Generation (TGA) Lag Time

End point description:

An ex vivo pharmacodynamic measure of thrombin generation (initiation of thrombin generation), the lag time is the time needed to form the first traces of thrombin.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[83]	6[84]	6[85]	7[86]
Units: minutes				
arithmetic mean (standard deviation)				
TGA lag time, Change at Day 2	-7.16 (± 5.865)	-2.77 (± 1.517)	-3.93 (± 1.919)	-4.13 (± 1.238)
TGA lag time, Change at Day 4	-6.80 (± 6.079)	-2.80 (± 1.399)	-3.48 (± 1.957)	-4.17 (± 1.501)
TGA lag time, Change at Day 8	-6.94 (± 5.882)	-2.88 (± 1.292)	-3.57 (± 2.018)	-4.43 (± 1.506)
TGA lag time, Change at Day 15	-6.90 (± 5.897)	-3.07 (± 1.221)	-3.27 (± 1.870)	-4.29 (± 1.342)
TGA lag time, Change at Day 22	-6.94 (± 5.978)	-2.80 (± 1.585)	-3.12 (± 2.097)	-4.34 (± 1.638)
TGA lag time, Change at Day 29	-5.33 (± 4.871)	-2.77 (± 1.392)	-3.43 (± 2.016)	-4.32 (± 1.781)

TGA lag time, Change at Day 30	-5.22 (± 4.893)	-2.77 (± 1.372)	-3.50 (± 2.082)	-4.48 (± 1.681)
TGA lag time, Change at Day 33	-5.08 (± 4.414)	-2.40 (± 1.568)	-3.35 (± 2.261)	-4.52 (± 1.771)
TGA lag time, Change at Day 57	-4.73 (± 4.711)	-2.28 (± 2.020)	-3.42 (± 1.962)	-3.78 (± 1.376)
TGA lag time, Change at Day 85	-6.34 (± 5.745)	-3.10 (± 1.344)	-3.27 (± 2.014)	-3.33 (± 1.755)
TGA lag time, Change at Day 113	-0.79 (± 7.428)	0.80 (± 0.283)	1.53 (± 5.306)	0.78 (± 5.251)

Notes:

[83] - Not all subjects were analyzed for some specific rows of time points.

[84] - Not all subjects were analyzed for some specific rows of time points.

[85] - Not all subjects were analyzed for some specific rows of time points.

[86] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[87]			
Units: minutes				
arithmetic mean (standard deviation)				
TGA lag time, Change at Day 2	-5.64 (± 4.365)			
TGA lag time, Change at Day 4	-5.49 (± 4.467)			
TGA lag time, Change at Day 8	-5.69 (± 4.327)			
TGA lag time, Change at Day 15	-5.59 (± 4.327)			
TGA lag time, Change at Day 22	-5.64 (± 4.422)			
TGA lag time, Change at Day 29	-4.83 (± 3.537)			
TGA lag time, Change at Day 30	-4.88 (± 3.640)			
TGA lag time, Change at Day 33	-4.83 (± 3.329)			
TGA lag time, Change at Day 57	-4.26 (± 3.346)			
TGA lag time, Change at Day 85	-4.95 (± 4.497)			
TGA lag time, Change at Day 113	-0.06 (± 6.304)			

Notes:

[87] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Thrombin Generation (TGA) Peak

End point title	Change From Baseline in Thrombin Generation (TGA) Peak

End point description:

An ex vivo pharmacodynamic measure of thrombin generation (initiation of thrombin generation). The peak represents the highest thrombin concentration that can be generated. There may be patients who reach the peak faster or slower than others and this may represent hyper- or hypocoagulability,

respectively.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[88]	6[89]	6[90]	7[91]
Units: nanomole				
arithmetic mean (standard deviation)				
TGA peak, Change at Day 2	72.93 (± 35.734)	70.92 (± 23.721)	68.18 (± 15.693)	63.41 (± 9.743)
TGA peak, Change at Day 4	60.00 (± 30.196)	59.28 (± 30.156)	50.87 (± 20.687)	51.79 (± 14.929)
TGA peak, Change at Day 8	49.36 (± 32.033)	56.00 (± 33.636)	50.30 (± 14.019)	54.36 (± 15.007)
TGA peak, Change at Day 15	49.01 (± 23.471)	52.57 (± 28.440)	46.40 (± 22.985)	40.90 (± 7.886)
TGA peak, Change at Day 22	44.50 (± 27.260)	52.07 (± 33.558)	38.15 (± 16.313)	44.41 (± 22.567)
TGA peak, Change at Day 29	42.95 (± 24.026)	49.72 (± 29.316)	38.23 (± 21.808)	42.48 (± 23.057)
TGA peak, Change at Day 30	35.93 (± 26.177)	51.75 (± 29.276)	37.72 (± 24.136)	48.62 (± 21.427)
TGA peak, Change at Day 33	76.68 (± 69.887)	46.83 (± 37.084)	36.25 (± 21.955)	54.10 (± 28.276)
TGA peak, Change at Day 57	37.13 (± 21.866)	32.57 (± 20.368)	34.67 (± 20.584)	33.93 (± 7.688)
TGA peak, Change at Day 85	37.60 (± 21.142)	69.92 (± 40.250)	30.15 (± 18.614)	30.15 (± 22.743)
TGA peak, Change at Day 113	24.37 (± 33.703)	16.05 (± 36.557)	43.33 (± 68.794)	6.93 (± 15.334)

Notes:

[88] - Not all subjects were analyzed for some specific rows of time points.

[89] - Not all subjects were analyzed for some specific rows of time points.

[90] - Not all subjects were analyzed for some specific rows of time points.

[91] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[92]			
Units: nanomole				
arithmetic mean (standard deviation)				
TGA peak, Change at Day 2	68.17 (± 25.642)			
TGA peak, Change at Day 4	55.89 (± 23.278)			
TGA peak, Change at Day 8	51.86 (± 24.171)			

TGA peak, Change at Day 15	44.96 (± 17.340)			
TGA peak, Change at Day 22	44.46 (± 24.042)			
TGA peak, Change at Day 29	42.72 (± 22.452)			
TGA peak, Change at Day 30	41.70 (± 23.878)			
TGA peak, Change at Day 33	66.42 (± 53.861)			
TGA peak, Change at Day 57	35.53 (± 15.716)			
TGA peak, Change at Day 85	34.16 (± 21.306)			
TGA peak, Change at Day 113	16.32 (± 27.345)			

Notes:

[92] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Endogenous Thrombin Generation (TGA) Potential

End point title	Change From Baseline in Endogenous Thrombin Generation (TGA) Potential

End point description:

An ex vivo pharmacodynamic measure of thrombin generation.The endogenous TGA potential represents the total amount of active thrombin formed during thrombin generation and the peak height the maximal amount of thrombin formed.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[93]	6[94]	6[95]	7[96]
Units: nanomole*minute				
arithmetic mean (standard deviation)				
Endogenous TGA Potential, Change at Day 2	864.0 (± 250.60)	816.8 (± 211.13)	999.8 (± 249.59)	1065.3 (± 161.71)
Endogenous TGA Potential, Change at Day 4	766.7 (± 236.94)	714.8 (± 275.75)	808.7 (± 288.78)	825.1 (± 294.44)
Endogenous TGA Potential, Change at Day 8	691.9 (± 301.43)	659.8 (± 295.11)	796.5 (± 151.00)	918.6 (± 276.26)
Endogenous TGA Potential, Change at Day 15	674.9 (± 244.61)	608.5 (± 242.81)	800.8 (± 334.99)	639.3 (± 145.74)
Endogenous TGA Potential, Change at Day 22	646.9 (± 295.05)	589.0 (± 274.33)	647.0 (± 236.38)	731.4 (± 302.89)

Endogenous TGA Potential, Change at Day 29	588.2 (± 239.00)	623.0 (± 188.84)	618.3 (± 276.51)	660.5 (± 340.36)
Endogenous TGA Potential, Change at Day 30	494.8 (± 247.86)	672.0 (± 226.25)	603.3 (± 332.44)	710.2 (± 272.54)
Endogenous TGA Potential, Change at Day 33	716.5 (± 391.60)	606.0 (± 280.39)	583.7 (± 291.25)	848.8 (± 387.17)
Endogenous TGA Potential, Change at Day 57	586.8 (± 200.04)	445.2 (± 220.86)	564.5 (± 287.43)	579.7 (± 147.04)
Endogenous TGA Potential, Change at Day 85	566.6 (± 202.22)	812.2 (± 198.80)	526.7 (± 297.03)	493.7 (± 368.68)
Endogenous TGA Potential, Change at Day 113	256.4 (± 347.91)	50.5 (± 290.62)	306.5 (± 440.04)	142.3 (± 361.25)

Notes:

[93] - Not all subjects were analyzed for some specific rows of time points.

[94] - Not all subjects were analyzed for some specific rows of time points.

[95] - Not all subjects were analyzed for some specific rows of time points.

[96] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[97]			
Units: nanomole*minute				
arithmetic mean (standard deviation)				
Endogenous TGA Potential, Change at Day 2	964.6 (± 227.95)			
Endogenous TGA Potential, Change at Day 4	795.9 (± 258.54)			
Endogenous TGA Potential, Change at Day 8	805.2 (± 301.66)			
Endogenous TGA Potential, Change at Day 15	657.1 (± 194.32)			
Endogenous TGA Potential, Change at Day 22	689.1 (± 290.60)			
Endogenous TGA Potential, Change at Day 29	624.3 (± 282.93)			
Endogenous TGA Potential, Change at Day 30	592.7 (± 270.33)			
Endogenous TGA Potential, Change at Day 33	776.6 (± 376.05)			
Endogenous TGA Potential, Change at Day 57	583.3 (± 167.42)			
Endogenous TGA Potential, Change at Day 85	532.9 (± 280.20)			
Endogenous TGA Potential, Change at Day 113	203.8 (± 344.10)			

Notes:

[97] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Prothrombin Fragments 1 + 2

End point title	Change From Baseline in Prothrombin Fragments 1 + 2

End point description:

An in vivo pharmacodynamic measure of thrombin generation (prothrombin cleavage). Prothrombin

fragment 1+2 (F 1+2) is the amino terminus fragment of the prothrombin molecule. It is a polypeptide with a half-life of approximately 90 minutes. F 1+2 is released from prothrombin when prothrombin is converted to thrombin by the prothrombinase complex.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[98]	6[99]	6[100]	7[101]
Units: picomole/liter				
arithmetic mean (standard deviation)				
Prothrombin fragments 1 + 2, Change at Day 2	430.0 (± 383.03)	498.3 (± 484.40)	275.7 (± 206.71)	438.9 (± 507.68)
Prothrombin fragments 1 + 2, Change at Day 4	548.1 (± 455.67)	1096.7 (± 1403.57)	574.5 (± 363.37)	730.3 (± 537.21)
Prothrombin fragments 1 + 2, Change at Day 8	450.3 (± 396.09)	562.2 (± 605.07)	413.0 (± 171.50)	580.7 (± 259.63)
Prothrombin fragments 1 + 2, Change at Day 15	481.7 (± 330.26)	349.7 (± 212.59)	389.2 (± 228.56)	571.1 (± 474.23)
Prothrombin fragments 1 + 2, Change at Day 22	608.1 (± 336.97)	322.3 (± 161.76)	420.2 (± 166.66)	524.1 (± 577.08)
Prothrombin fragments 1 + 2, Change at Day 29	650.3 (± 415.58)	288.0 (± 259.19)	577.7 (± 302.76)	429.3 (± 257.91)
Prothrombin fragments 1 + 2, Change at Day 30	655.7 (± 496.35)	486.0 (± 608.26)	521.0 (± 165.25)	580.8 (± 507.83)
Prothrombin fragments 1 + 2, Change at Day 33	761.3 (± 509.02)	642.5 (± 759.02)	1527.7 (± 2499.96)	609.2 (± 380.74)
Prothrombin fragments 1 + 2, Change at Day 57	586.5 (± 473.53)	216.5 (± 173.44)	465.3 (± 300.84)	463.5 (± 397.57)
Prothrombin fragments 1 + 2, Change at Day 85	588.3 (± 483.80)	378.2 (± 207.16)	470.2 (± 244.21)	362.2 (± 378.54)
Prothrombin fragments 1 + 2, Change at Day 113	-6.6 (± 151.87)	16.5 (± 19.09)	-75.5 (± 76.86)	-58.2 (± 121.15)

Notes:

[98] - Not all subjects were analyzed for some specific rows of time points.

[99] - Not all subjects were analyzed for some specific rows of time points.

[100] - Not all subjects were analyzed for some specific rows of time points.

[101] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[102]			
Units: picomole/liter				
arithmetic mean (standard deviation)				
Prothrombin fragments 1 + 2, Change at Day 2	434.4 (± 432.08)			
Prothrombin fragments 1 + 2, Change at Day 4	639.2 (± 487.82)			

Prothrombin fragments 1 + 2, Change at Day 8	515.5 (± 328.78)			
Prothrombin fragments 1 + 2, Change at Day 15	526.4 (± 395.34)			
Prothrombin fragments 1 + 2, Change at Day 22	566.1 (± 456.08)			
Prothrombin fragments 1 + 2, Change at Day 29	531.3 (± 344.06)			
Prothrombin fragments 1 + 2, Change at Day 30	618.3 (± 480.35)			
Prothrombin fragments 1 + 2, Change at Day 33	685.3 (± 435.87)			
Prothrombin fragments 1 + 2, Change at Day 57	525.0 (± 421.78)			
Prothrombin fragments 1 + 2, Change at Day 85	483.9 (± 436.47)			
Prothrombin fragments 1 + 2, Change at Day 113	-30.4 (± 135.52)			

Notes:

[102] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in D-Dimer

End point title	Change From Baseline in D-Dimer

End point description:

An in vivo pharmacodynamic measure of thrombin generation (fibrin degradation). D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. D-dimer is one of the protein fragments produced when a blood clot gets dissolved in the body. It is normally undetectable or detectable at a very low level unless the body is forming and breaking down blood clots. Then, its level in the blood can significantly rise.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[103]	6[104]	6[105]	7[106]
Units: microgram/milliliter				
arithmetic mean (standard deviation)				
D-dimer, Change at Day 2	0.0393 (± 0.16303)	0.0792 (± 0.22238)	0.1900 (± 0.09301)	0.1086 (± 0.30536)
D-dimer, Change at Day 4	0.2050 (± 0.24491)	0.2842 (± 0.36896)	0.3217 (± 0.23248)	0.6729 (± 0.62524)
D-dimer, Change at Day 8	0.0743 (± 0.26111)	0.2017 (± 0.29753)	0.3292 (± 0.40635)	0.5614 (± 0.54901)
D-dimer, Change at Day 15	0.0979 (± 0.25666)	0.1942 (± 0.28748)	0.2500 (± 0.23424)	0.1900 (± 0.82310)

D-dimer, Change at Day 22	0.1364 (± 0.27802)	0.2167 (± 0.33877)	0.2000 (± 0.26109)	0.1829 (± 1.27802)
D-dimer, Change at Day 29	0.0633 (± 0.20029)	0.2308 (± 0.32355)	0.1517 (± 0.42347)	-0.0129 (± 1.17491)
D-dimer, Change at Day 30	0.1350 (± 0.32388)	0.1492 (± 0.26345)	0.2133 (± 0.33914)	-0.0833 (± 1.31549)
D-dimer, Change at Day 33	0.0800 (± 0.28796)	0.1283 (± 0.37519)	0.1233 (± 0.49855)	-0.1700 (± 1.68635)
D-dimer, Change at Day 57	0.1942 (± 0.30049)	0.2175 (± 0.22554)	0.1233 (± 0.36122)	0.4033 (± 0.37120)
D-dimer, Change at Day 85	0.1664 (± 0.30521)	0.5860 (± 1.00003)	0.1833 (± 0.43840)	0.2300 (± 0.60395)
D-dimer, Change at Day 113	-0.1000 (± 0.22127)	0.1875 (± 0.26517)	0.0175 (± 0.41838)	-0.7833 (± 1.60090)

Notes:

[103] - Not all subjects were analyzed for some specific rows of time points.

[104] - Not all subjects were analyzed for some specific rows of time points.

[105] - Not all subjects were analyzed for some specific rows of time points.

[106] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[107]			
Units: microgram/milliliter				
arithmetic mean (standard deviation)				
D-dimer, Change at Day 2	0.0739 (± 0.23790)			
D-dimer, Change at Day 4	0.4389 (± 0.51676)			
D-dimer, Change at Day 8	0.3179 (± 0.48422)			
D-dimer, Change at Day 15	0.1439 (± 0.58769)			
D-dimer, Change at Day 22	0.1596 (± 0.88887)			
D-dimer, Change at Day 29	0.0223 (± 0.84172)			
D-dimer, Change at Day 30	0.0258 (± 0.92048)			
D-dimer, Change at Day 33	-0.0450 (± 1.16076)			
D-dimer, Change at Day 57	0.2988 (± 0.34001)			
D-dimer, Change at Day 85	0.1958 (± 0.44682)			
D-dimer, Change at Day 113	-0.4154 (± 1.10366)			

Notes:

[107] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Dilute Prothrombin Time

End point title	Change From Baseline in Dilute Prothrombin Time

End point description:

An ex vivo pharmacodynamic measure of thrombin generation (via extrinsic pathway). Clotting time is measured using a dilute prothrombin time reagent consisting of a unique formulation of relipidated recombinant tissue factor and calcium.

End point type	Secondary

End point timeframe:

Baseline, Study Day 2, 4, 8, 15, 22, 29, 30, 33, 57, 85 and 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[108]	6[109]	6[110]	7[111]
Units: seconds				
arithmetic mean (standard deviation)				
Dilute prothrombin Time, Change at Day 2	-27.84 (± 21.023)	-13.32 (± 25.780)	-31.25 (± 13.606)	-17.14 (± 26.167)
Dilute prothrombin Time, Change at Day 4	-30.03 (± 24.312)	-17.87 (± 20.042)	-34.50 (± 18.306)	-14.70 (± 30.971)
Dilute prothrombin Time, Change at Day 8	-23.63 (± 19.991)	-15.10 (± 22.129)	-31.23 (± 19.645)	-20.97 (± 33.969)
Dilute prothrombin Time, Change at Day 15	-20.73 (± 23.070)	-19.33 (± 20.853)	-33.53 (± 14.880)	1.11 (± 27.208)
Dilute prothrombin Time, Change at Day 22	-21.40 (± 22.351)	-10.55 (± 16.057)	-26.78 (± 32.501)	-21.61 (± 30.842)
Dilute prothrombin Time, Change at Day 29	-15.32 (± 13.867)	-7.10 (± 20.643)	-40.40 (± 22.458)	-18.03 (± 24.600)
Dilute prothrombin Time, Change at Day 30	-13.27 (± 13.399)	-23.45 (± 19.413)	-45.18 (± 21.372)	-17.47 (± 25.729)
Dilute prothrombin Time, Change at Day 33	-23.35 (± 17.690)	-21.23 (± 20.010)	-29.10 (± 20.783)	-19.97 (± 19.297)
Dilute prothrombin Time, Change at Day 57	-14.75 (± 14.393)	-12.03 (± 30.806)	-26.80 (± 12.911)	-11.72 (± 42.872)
Dilute prothrombin Time, Change at Day 85	-20.99 (± 25.424)	-25.80 (± 24.334)	-23.43 (± 26.166)	-12.42 (± 34.871)
Dilute prothrombin Time, Change at Day 113	-16.44 (± 13.578)	14.30 (± 61.235)	-39.63 (± 20.182)	-12.78 (± 28.226)

Notes:

[108] - Not all subjects were analyzed for some specific rows of time points.

[109] - Not all subjects were analyzed for some specific rows of time points.

[110] - Not all subjects were analyzed for some specific rows of time points.

[111] - Not all subjects were analyzed for some specific rows of time points.

End point values	Overall PF-06741086 300 mg SC			
Subject group type	Subject analysis set			
Number of subjects analysed	14[112]			
Units: seconds				
arithmetic mean (standard deviation)				
Dilute prothrombin Time, Change at Day 2	-22.49 (± 23.470)			
Dilute prothrombin Time, Change at Day 4	-22.36 (± 27.907)			

Dilute prothrombin Time, Change at Day 8	-22.30 (± 26.813)			
Dilute prothrombin Time, Change at Day 15	-9.81 (± 26.753)			
Dilute prothrombin Time, Change at Day 22	-21.51 (± 25.877)			
Dilute prothrombin Time, Change at Day 29	-16.78 (± 19.613)			
Dilute prothrombin Time, Change at Day 30	-15.37 (± 19.680)			
Dilute prothrombin Time, Change at Day 33	-21.66 (± 17.737)			
Dilute prothrombin Time, Change at Day 57	-13.23 (± 30.531)			
Dilute prothrombin Time, Change at Day 85	-17.03 (± 29.148)			
Dilute prothrombin Time, Change at Day 113	-14.75 (± 20.682)			

Notes:

[112] - Not all subjects were analyzed for some specific rows of time points.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Tested Positive for Anti-PF-06741086 Antibody (ADA)

End point title	Number of Subjects Who Tested Positive for Anti-PF-06741086 Antibody (ADA)

End point description:

Human plasma ADA samples were analyzed for the detection of anti PF-06741086 antibodies by using semi-quantitative electrochemiluminescence (ECL) method. The criterion for positive result of ADA samples was ADA titer >=1.53. Treatment induced are negative prior to dosing and become positive during/after dosing. Treatment boosted are positive prior to dosing but titer increases during/after dosing.

End point type	Secondary

End point timeframe:

Baseline up to Study Day 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	6	6	7
Units: Subjects				
ADA incidence	0	1	2	0
Subjects with treatment induced ADA incidence	0	1	2	0
Subjects with treatment boosted ADA incidence	0	0	0	0

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	26		
Units: Subjects				
ADA incidence	0	3		
Subjects with treatment induced ADA incidence	0	3		
Subjects with treatment boosted ADA incidence	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Tested Positive for Neutralizing Antibody (NAb)

End point title	Number of Subjects Who Tested Positive for Neutralizing Antibody (NAb)

End point description:

Human plasma NAb samples were analyzed for the presence or absence of NAb to PF 06741086 using semi-quantitative electrochemiluminescence (ECL) method. Treatment induced are negative prior to dosing and become positive during/after dosing. Treatment boosted are positive prior to dosing but titer increases during/after dosing.

End point type	Secondary

End point timeframe:

Baseline up to Study Day 113

End point values	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC QW Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[113]	1	2	0[114]
Units: Subjects				
NAb incidence|		0	0	
Subjects with treatment induced NAb incidence		0	0	
Subjects with treatment boosted NAb incidence		0	0	

Notes:

[113] - Only subjects who had positive ADA sample were tested in the NAb assay.

[114] - Only subjects who had positive ADA sample were tested in the NAb assay.

End point values	Overall PF-06741086 300 mg SC	Total		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[115]	3		

Units: Subjects				
NAb incidence|		0		
Subjects with treatment induced NAb incidence		0		
Subjects with treatment boosted NAb incidence		0		

Notes:

[115] - Only subjects who had positive ADA sample were tested in the NAb assay.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

113 days

Adverse event reporting additional description:

The same event may appear as both an AE and an SAE. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study. Total number at risk below refers to the number of subjects evaluable for SAEs or AEs.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	PF-06741086 300 mg SC QW Non-Inhibitor

Reporting group description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg subcutaneously (SC) once weekly (QW) from Day 1 to Day 78.

Reporting group title	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor

Reporting group description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg loading dose on Day 1 and 150 mg SC QW from Day 8 to Day 78.

Reporting group title	PF-06741086 450 mg SC QW Non-Inhibitor

Reporting group description:

Subjects without inhibitors to FVIII or FIX in this cohort received PF-06741086 450 mg SC QW from Day 1 to Day 78.

Reporting group title	PF-06741086 300 mg SC QW Inhibitor

Reporting group description:

Subjects with inhibitors to FVIII or FIX in this cohort received PF-06741086 300 mg SC QW from Day 1 to Day 78.

Reporting group title	Overall PF-06741086 300 mg SC

Reporting group description:

The overall PF-06741086 300 mg SC group combined subjects from both the PF-06741086 300 mg SC QW non-inhibitor and inhibitor dose cohorts.

Reporting group title	Total

Reporting group description:

The total group combined subjects from all PF-06741086 cohorts in this study.

Serious adverse events	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	1 / 6 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Social circumstances			

Physical assault			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Gastrointestinal disorders			
Tooth socket haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
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			
Appendicitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (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

Serious adverse events	PF-06741086 300 mg SC QW Inhibitor	Overall PF-06741086 300 mg SC	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	2 / 14 (14.29%)	4 / 26 (15.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Social circumstances			
Physical assault			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Tooth socket haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
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			
Appendicitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
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	PF-06741086 300 mg SC QW Non-Inhibitor	PF-06741086 300 mg SC Loading + 150 mg SC QW Non-Inhibitor	PF-06741086 450 mg SC QW Non-Inhibitor
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	4 / 6 (66.67%)	6 / 6 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	2	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Occupational exposure to product			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Blood fibrinogen decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fibrin D dimer increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)

occurrences (all)	1	0	0
Prothrombin time prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Troponin I increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Troponin increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Cerebrospinal fluid leakage			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Injection site bruising			
subjects affected / exposed	2 / 7 (28.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Injection site erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)

occurrences (all)	0	0	0
Injection site induration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Injection site pain			
subjects affected / exposed	1 / 7 (14.29%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	2	1	6
Injection site pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Injection site warmth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus generalised			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Haemarthrosis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haemophilic arthropathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Periodontitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	PF-06741086 300 mg SC QW Inhibitor	Overall PF-06741086 300 mg SC	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	10 / 14 (71.43%)	20 / 26 (76.92%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	3 / 26 (11.54%)
occurrences (all)	0	0	3
Injury, poisoning and procedural			

complications			
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
Occupational exposure to product			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Road traffic accident			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Investigations			
Blood fibrinogen decreased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Fibrin D dimer increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Prothrombin time prolonged			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Troponin I increased			
subjects affected / exposed	1 / 7 (14.29%)	2 / 14 (14.29%)	2 / 26 (7.69%)
occurrences (all)	1	2	2
Troponin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nervous system disorders			
Cerebrospinal fluid leakage			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1

Headache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	2 / 26 (7.69%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
Injection site bruising			
subjects affected / exposed	0 / 7 (0.00%)	2 / 14 (14.29%)	2 / 26 (7.69%)
occurrences (all)	0	2	2
Injection site erythema			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Injection site haemorrhage			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Injection site induration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	0	1	2
Injection site pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	3 / 26 (11.54%)
occurrences (all)	0	2	9
Injection site pruritus			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Injection site swelling			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	3 / 26 (11.54%)
occurrences (all)	1	1	4
Injection site warmth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	2
Dyspepsia			

subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Pruritus generalised			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Rash erythematous			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	1	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	2 / 14 (14.29%)	2 / 26 (7.69%)
occurrences (all)	1	3	3
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Haemarthrosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Haemophilic arthropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Periodontitis			
subjects affected / exposed	1 / 7 (14.29%)	1 / 14 (7.14%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Respiratory tract infection			

subjects affected / exposed	0 / 7 (0.00%)	0 / 14 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 14 (7.14%)	1 / 26 (3.85%)
occurrences (all)	0	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2016	1. Added EudraCT # on protocol title page 2.Revised inclusion criterion #2 to restrict subjects from>=12 and <18 years of age to cohorts at a dose level and route of administration previously studied which has not met the protocol safety criteria for termination of dose escalation.
02 November 2016	1. Added US IND # to protocol 2. Revised nominal doses planned for Cohorts 2 through 4 added to new section (1.3.3.2 Dose Progression). 3.Removed option for self administration for SC cohorts and specified visits for SC cohorts. 4.Inclusion Criterion #5: criterion was revised to state that only patients currently treated with episodic (on demand) factor replacement therapy are eligible for this study.
12 December 2016	1.Added new criteria and references for dose escalation and stopping rules. 2.Revised Inclusion Criterion #2 to state that only adult subjects (18 to 65 years of age) are eligible for the study, added Exclusion Criterion #4 to state that subjects with pro thrombotic conditions are excluded from the study.
02 October 2017	1.Removed "AND" from "AND/OR" to conform to previous amendment that removed a combination subcutaneous and intravenous dose. 2. Added language anywhere applicable allowing for the inclusion of subjects with inhibitors against FVIII or FIX and specified analyses for inhibitor subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported