Clinical trial results:
An Open Label Extension Study to Investigate the Long Term Safety, Tolerability and Efficacy of PF-02545920 in Subjects With Huntington's Disease Who Previously Completed Study A8241021

Summary

EudraCT number	2014-004900-31
Trial protocol	DE
Global end of trial date	06 February 2017

Results information

Result version number	v1 (current)
This version publication date	10 February 2018
First version publication date	10 February 2018

Trial information

Trial identification

Sponsor protocol code	A8241022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02342548
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 Clinical Trials.gov Call Center Pfizer Clinical Trials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, 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	06 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 February 2017
Global end of trial reached?	Yes
Global end of trial date	06 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess long-term safety and tolerability of 20 mg twice daily (BID) of PF-02545920 in subjects with Huntington's Disease (HD).

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 Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 February 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Germany: 65
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	United Kingdom: 42
Country: Number of subjects enrolled	United States: 44
Worldwide total number of subjects	188
EEA total number of subjects	129

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)	182
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This was an open-label extension study conducted in subjects who had completed study A8241021 (NCT02197130). Treatment assignment was double-blinded from Day 1 to Day 21, and became open-label from Day 22, since all subjects began receiving the same dose level from Day 22.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	20 mg PF-02545920

Arm description:

Subjects who received PF-02545920 20 mg twice daily (BID) in Study A8241021 continued to receive PF-02545920 20 mg BID for 12 months in this study. Four 5-mg tablets were administered orally each time.

Arm type	Experimental
Investigational medicinal product name	PF-02545920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received blinded PF-02545920 20 mg twice daily (BID) from Day 1 to Day 22. Starting from Day 22, the subjects received open-label PF-02545920 20 mg BID to Month 12. Four 5-mg tablets were administered orally each time.

Arm title	5 mg PF-02545920 Titration up to 20 mg

Arm description:

Subjects who received PF-02545920 5 mg twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).

Arm type	Experimental
Investigational medicinal product name	PF-02545920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received PF-02545920 orally according to a double-blind titration schedule: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet) from Day 1 to Day 21. Starting from Day 22, the subjects received open-label PF-02545920 20 mg BID to Month 12 (four 5-mg tablets).

Arm title	Placebo and Titration up to 20 mg PF-02545920

Arm description:

Subjects who received placebo twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).

Arm type	Experimental
Investigational medicinal product name	PF-02545920
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received PF-02545920 orally according to a double-blind titration schedule: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet) from Day 1 to Day 21. Starting from Day 22, the subjects received open-label PF-02545920 20 mg BID to Month 12 (four 5-mg tablets).

Number of subjects in period 1	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920
Started	51	71	66
Completed	17	9	23
Not completed	34	62	43
Consent withdrawn by subject	1	3	4
Adverse event, non-fatal	12	17	13
Study terminated by sponsor	20	39	25
Unspecified	1	1	1
Lost to follow-up	-	1	-
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	20 mg PF-02545920
Reporting group description:	
Subjects who received PF-02545920 20 mg twice daily (BID) in Study A8241021 continued to receive PF-02545920 20 mg BID for 12 months in this study. Four 5-mg tablets were administered orally each time.	
Reporting group title	5 mg PF-02545920 Titration up to 20 mg
Reporting group description:	
Subjects who received PF-02545920 5 mg twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).	
Reporting group title	Placebo and Titration up to 20 mg PF-02545920
Reporting group description:	
Subjects who received placebo twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).	

Reporting group values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920
Number of subjects	51	71	66
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	48	69	65
From 65-84 years	3	2	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	50.2	48.4	51.3
standard deviation	± 9.4	± 8.6	± 9.4
Sex: Female, Male Units: Subjects			
Female	25	33	43
Male	26	38	23

Reporting group values	Total		
Number of subjects	188		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	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)	182		
From 65-84 years	6		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Female	101		
Male	87		

End points

End points reporting groups

Reporting group title	20 mg PF-02545920

Reporting group description:

Subjects who received PF-02545920 20 mg twice daily (BID) in Study A8241021 continued to receive PF-02545920 20 mg BID for 12 months in this study. Four 5-mg tablets were administered orally each time.

Reporting group title	5 mg PF-02545920 Titration up to 20 mg

Reporting group description:

Subjects who received PF-02545920 5 mg twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).

Reporting group title	Placebo and Titration up to 20 mg PF-02545920

Reporting group description:

Subjects who received placebo twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).

Primary: Number of Subjects With Treatment-Emergent Adverse Events and Serious Adverse Events

End point title	Number of Subjects With Treatment-Emergent Adverse Events and Serious Adverse Events[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device, regardless of its causal relationship with study treatment. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; was life-threatening (immediate risk of death); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent AEs are events between first dose of study treatment and up to 28 calendar days after the last administration of study treatment that were absent before treatment or that worsened after treatment. AEs included both serious and non-serious AEs. Safety analysis population was used for analysis, which included all subjects who entered the extension study with at least 1 dose of study medication.

End point type	Primary

End point timeframe:

1 year

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 end point.

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects				
AEs	39	63	62	
SAEs	7	9	5	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Without Regard to Baseline Abnormality)

End point title	Number of Subjects With Laboratory Test Abnormalities (Without Regard to Baseline Abnormality)[2]

End point description:

Lab test included: hematology (hemoglobin, hematocrit, red blood cell, platelet and white blood cell count, absolute total neutrophils, eosinophils, monocytes, basophils, and lymphocytes), chemistry (blood urea nitrogen/urea, creatinine, glucose, glycosylated hemoglobin [diabetics only], calcium, phosphorus, magnesium, creatine kinase, sodium, potassium, chloride, total carbon dioxide, aspartate and alanine aminotransferase, lactate dehydrogenase, total bilirubin, alkaline phosphatase, uric acid, albumin, total protein), urinalysis (color, appearance, specific gravity, pH, qualitative glucose, protein and blood, ketones, nitrites, leukocyte esterase and microscopy), and other tests (follicle stimulating hormone, urine drug screen, urine pregnancy, serum beta human chorionic gonadotropin). Abnormality was determined by the investigator. Safety analysis population was used for analysis, which included all subjects who entered the extension study with at least 1 dose of study drug.

End point type	Primary

End point timeframe:

1 year

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 end point.

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects	19	27	28	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Vital Signs Data Meeting Categorical Summarization Criteria

End point title	Number of Subjects With Vital Signs Data Meeting Categorical Summarization Criteria[3]

End point description:

Number of subjects with data meeting the following criteria is given: supine systolic blood pressure (SBP)<90mmHg; standing SBP<90mmHg; supine diastolic blood pressure (DBP)<50mmHg; standing DBP<50mmHg; supine pulse rate<40 beats per minute (bpm); supine pulse rate>120bpm; standing pulse rate<40 bpm; standing pulse rate>140bpm; max increase from baseline in supine SBP>=30

mmHg; max increase from baseline in standing SBP>= 30mmHg; max increase from baseline in supine DBP>=20 mmHg; max increase from baseline in standing DBP>=20 mmHg; max decrease from baseline in supine SBP>=30mmHg; max decrease from baseline in standing SBP>=30mmHg; max decrease from baseline in supine DBP>=20mmHg; max decrease from baseline in standing DBP>=20mmHg. Analysis population included all subjects who entered the extension study with at least 1 dose of study drug. n in parentheses represents the number of subjects with data contributing to that category for each reporting arm.

End point type	Primary

End point timeframe:

1 year

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 end point.

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects				
Supine SBP <90 mmHg (n=49, 69, 65)	0	0	0	
Standing SBP <90 mmHg (n=49, 69, 65)	0	1	0	
Supine DBP <50 mmHg (n=49, 69, 65)	0	1	0	
Standing DBP <50 mmHg (n=49, 69, 65)	0	1	0	
Supine pulse rate <40 bpm (n=49, 69, 65)	0	0	0	
Supine pulse rate >120 bpm (n=49, 69, 65)	0	0	0	
Standing pulse rate <40 bpm (n=49, 69, 65)	0	0	0	
Standing pulse rate >140 bpm (n=49, 69, 65)	0	0	0	
Supine SBP increase >=30 mmHg (n=49, 69, 65)	3	1	6	
Standing SBP increase >=30 mmHg (n=48, 69, 64)	1	6	4	
Supine DBP increase >=20 mmHg (n=49, 69, 65)	4	2	6	
Standing DBP increase >=20 mmHg (n=48, 69, 65)	3	8	2	
Supine SBP decrease >=30 mmHg (n=49, 69, 65)	2	1	4	
Standing SBP decrease >=30 mmHg (n=48, 69, 64)	0	1	2	
Supine DBP decrease >=20 mmHg (n=49, 69, 65)	0	2	7	
Standing DBP decrease >=20 mmHg (n=48, 69, 64)	1	4	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Electrocardiogram (ECG) Data Meeting Categorical Summarization Criteria

End point title	Number of Subjects With Electrocardiogram (ECG) Data Meeting Categorical Summarization Criteria[4]

End point description:

Maximum absolute values and increases from baseline were summarized for PR interval (interval between start of ECG P wave and start of QRS complex corresponding to the time between onset of atrial depolarization and onset of ventricular depolarization), QRS complex (time from Q wave to end of S wave corresponding to ventricular depolarization), and QTcF interval (time from ECG Q wave to end of T wave corresponding to electrical systole, corrected for heart rate using Fridericia's formula). Number of subjects with data meeting the following criteria is given: PR >=300 msec; QRS >=140 msec; QTcF: 450 to <480 msec; QTcF: 480 to <500 msec; QTcF >=500 msec; PR increase >=25/50 percent; QRS increase >=50 percent; QTcF increase: 30 to <60 msec; QTcF increase >=60 msec. Analysis population included all subjects who entered the extension study with at least 1 dose of study drug. n in parentheses represents the number of subjects with data contributing to that category for each reporting arm.

End point type	Primary

End point timeframe:

1 year

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 end point.

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects				
PR interval >=300 msec (n=50, 69, 66)	0	0	0	
QRS complex >=140 msec (50, 69, 66)	0	0	0	
QTcF interval: 450 to <480 msec (n=50, 69, 66)	2	2	2	
QTcF interval: 480 to <500 msec (n=50, 69, 66)	0	0	1	
QTcF interval >=500 msec (n=50, 69, 66)	0	0	0	
PR increase >=25/50 percent (n=50, 66, 66)	0	0	0	
QRS increase >=50 percent (n=50, 66, 66)	0	0	0	
QTcF increase: 30 to <60 msec (n=50, 66, 66)	3	5	4	
QTcF increase >=60 msec (n=50, 66, 66)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormal White Blood Cell Count and Absolute Neutrophil Count (Without Regard to Baseline Abnormality)

End point title	Number of Subjects With Abnormal White Blood Cell Count and Absolute Neutrophil Count (Without Regard to Baseline

	Abnormality)[5]

End point description:

Number of subjects with white blood cell (WBC) count and absolute neutrophil count (ANC) meeting the following criteria is presented: (1) WBC count <0.6 *the lower limit of normal (LLN); (2) WBC count >1.5 times the upper limit of normal (ULN); (3) ANC <0.8*LLN; and (4) ANC >1.2*ULN. Safety analysis population was used for analysis, which included all subjects who entered the extension study with at least 1 dose of study medication.

End point type	Primary

End point timeframe:

1 year

Notes:

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

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	65	
Units: subjects				
WBC < 0.6*LLN	0	0	0	
WBC > 1.5*ULN	1	0	1	
ANC < 0.8*LLN	1	0	0	
ANC > 1.2*ULN	3	4	7	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Laboratory Test Abnormalities (Normal Baseline)

End point title	Number of Subjects With Laboratory Test Abnormalities (Normal Baseline)[6]

End point description:

Lab test included: hematology (hemoglobin, hematocrit, red blood cell, platelet and white blood cell count, absolute total neutrophils, eosinophils, monocytes, basophils, and lymphocytes), chemistry (blood urea nitrogen/urea, creatinine, glucose, glycosylated hemoglobin [diabetics only], calcium, phosphorus, magnesium, creatine kinase, sodium, potassium, chloride, total carbon dioxide, aspartate and alanine aminotransferase, lactate dehydrogenase, total bilirubin, alkaline phosphatase, uric acid, albumin, total protein), urinalysis (color, appearance, specific gravity, pH, qualitative glucose, protein and blood, ketones, nitrites, leukocyte esterase and microscopy), and other tests (follicle stimulating hormone, urine drug screen, urine pregnancy, serum beta human chorionic gonadotropin). Abnormality was determined by the investigator. Safety analysis population was used for analysis, which included all subjects who entered the extension study with at least 1 dose of study drug.

End point type	Primary

End point timeframe:

1 year

Notes:

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

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects	13	22	23	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events Related to Extrapyramidal Symptoms by Severity

End point title	Number of Subjects With Adverse Events Related to Extrapyramidal Symptoms by Severity[7]

End point description:

Adverse events related to extrapyramidal symptoms included dystonia, akathisia, tardive dyskinesia). Severity was assessed by the investigator. Mild means the AE didn't interfere with the subject's usual function. Moderate means the AE interfered to some extent the subject's usual function. Severe means the AE interfered significantly with the subject's usual function.

End point type	Primary

End point timeframe:

1 year

Notes:

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

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects				
Mild dystonia	0	1	0	
Moderate dystonia	0	1	1	
Severe dystonia	0	0	0	
Mild akathisia	1	1	0	
Moderate akathisia	0	1	3	
Severe akathisia	0	0	1	
Mild dyskinesia	0	2	4	
Moderate dyskinesia	1	1	2	
Severe dyskinesia	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects in Each Columbia Classification Algorithm of Suicide Assessment (C-CASA) Category

End point title	Number of Subjects in Each Columbia Classification Algorithm of Suicide Assessment (C-CASA) Category[8]

End point description:

Columbia Suicide Severity Rating Scale (C-SSRS) was an interview-based rating scale to systematically assess suicidal ideation and suicidal behavior, and was used in this study. C-SSRS responses were mapped onto the Columbia Classification Algorithm of Suicide Assessment (C-CASA). Number of subjects with any of the following behaviors occurring since last visit was summarized: completed suicide; suicide attempt; preparatory acts towards imminent suicidal behavior; suicidal ideation; self-injurious behavior, no suicidal intent. Safety analysis population was used for analysis, which included all subjects who entered the extension study with at least 1 dose of study medication. n in parentheses represents the number of subjects with data contributing to that category for each reporting arm.

End point type	Primary

End point timeframe:

Baseline (Day 1), Weeks 2 and 4, Months 3, 6, 9 and 12, follow-up visit (7-14 days after the last dose of Month 12)

Notes:

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

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	71	66	
Units: subjects				
Day 1 (n=51, 71, 66)	0	1	1	
Week 2 (n=51, 69, 64)	0	0	1	
Week 4 (n=50, 66, 63)	0	1	1	
Month 3 (n=42, 61, 57)	1	0	1	
Month 6 (n=35, 37, 42)	1	0	1	
Month 9 (n=26, 20, 29)	0	1	0	
Month 12 (n=48, 69, 65)	6	0	3	
Follow-up visit (n=23, 13, 26)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington’s Disease Rating Scale (UHDRS) Total Motor Score

End point title	Change From Baseline in Unified Huntington’s Disease Rating Scale (UHDRS) Total Motor Score

End point description:

The UHDRS is a clinical rating scale developed to provide a uniform assessment of the clinical features and course of Huntington’s disease (HD). The components of the full UHDRS assess motor function, cognition, behavior and functional abilities. Total Motor Score (TMS) assesses motor features of HD with standardized ratings of oculomotor function, dysarthria, chorea, dystonia, gait, and postural ability. The total motor impairment scores was the sum of all the individual 31 motor sub-items (each rated from 0 to 4), with higher scores indicating more severe motor impairment than lower scores. The range of TMS is 0-124. Full analysis set (FAS) was used for analysis, which included all subjects who had a baseline efficacy evaluation and completed at least Week 2 visit with a valid UHDRS TMS score, and took >=1

dose of study medication. n in parentheses represents the number of subjects with data contributing to that category for each reporting arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Month 6, and Month 12

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	70	62	
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 6 (n=33, 39, 40)	2.4 (± 7.21)	3.5 (± 7.61)	0.7 (± 7.43)	
Month 12 (n=15, 9, 22)	4.9 (± 10.17)	3.3 (± 6.71)	0.6 (± 8.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Unified Huntington’s Disease Rating Scale (UHDRS) Total Maximum Chorea (TMC) Score

End point title	Change From Baseline in Unified Huntington’s Disease Rating Scale (UHDRS) Total Maximum Chorea (TMC) Score

End point description:

The UHDRS is a clinical rating scale developed to provide a uniform assessment of the clinical features and course of Huntington’s disease (HD). The components of the full UHDRS assess motor function, cognition, behavior and functional abilities. Total Maximum Chorea (TMC) is a subset of the TMS assessment, and composed of the scoring of 7 chorea assessments (face, orobuccolingual, trunk, right and left upper extremities, right and left lower extremities). Each assessment is rated from 0 to 4 (absent to prolonged). TMC is obtained by adding up each of the separate scores, leading to max score of 28. The minimum score is 0. The higher the score, the worse the symptoms. Full analysis set was used for analysis, which included all subjects who had a baseline efficacy evaluation and completed at least Week 2 visit with a valid UHDRS TMS score, and took >=1 dose of study drug. n in parentheses represents the number of subjects with data contributing to that category for each reporting arm.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Month 6, and Month 12

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	70	62	
Units: Units on a scale				
arithmetic mean (standard deviation)				

Month 6 (n=33, 39, 40)	0.1 (± 3.12)	1.3 (± 3.97)	1.4 (± 4.14)	
Month 12 (n=15, 9, 22)	0.1 (± 4.92)	0.8 (± 1.64)	0.7 (± 3.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Value in Clinical Global Impression of Improvement (CGI-I) Score

End point title	Absolute Value in Clinical Global Impression of Improvement (CGI-I) Score

End point description:

Clinical Global Impression of Improvement (CGI-I) is a global measure of improvement or change based on the clinician's assessment of all available clinical data obtained by interviewing the subject. CGI-I consists of a single 7-point rating of total improvement or change from baseline severity, regardless of whether or not the change is due entirely to drug treatment. Raters select 1 response based on the following question, "Compared to your subject's condition at the beginning of treatment, how much has he/she changed?" Scores are: 1: Very much improved; 2: Much improved; 3: Minimally improved; 4: No change; 5: Minimally worse; 6: Much worse; or 7: Very much worse. Full analysis set was used for analysis, which included all subjects who had a baseline efficacy evaluation and completed at least Week 2 visit with a valid UHDRS TMS score, and took >=1 dose of study drug. n in parentheses represents the number of subjects with data contributing to that category for each reporting arm.

End point type	Secondary

End point timeframe:

Month 6 and Month 12

End point values	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	70	62	
Units: units on a scale				
arithmetic mean (standard deviation)				
Month 6 (n=33, 39, 41)	3.9 (± 1.04)	4.2 (± 1.03)	3.7 (± 1.19)	
Month 12 (n=15, 9, 22)	3.5 (± 1.30)	4.6 (± 1.13)	4.0 (± 1.21)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
1 year	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	20 mg PF-02545920
Reporting group description:	
Participants who received PF-02545920 20 mg twice daily (BID) in Study A8241021 continued to receive PF-02545920 20 mg BID for 12 months in this study. Four 5-mg tablets were administered orally each time.	
Reporting group title	5 mg PF-02545920 Titration up to 20 mg
Reporting group description:	
Participants who received PF-02545920 5 mg twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).	
Reporting group title	Placebo and Titration up to 20 mg PF-02545920
Reporting group description:	
Participants who received placebo twice daily (BID) in Study A8241021 were administered PF-02545920 orally according to a double-blind titration schedule in this study: 5 mg BID for 7 days (one 5-mg tablet and 3 placebo tablets); 10 mg BID for 7 days (two 5-mg tablets and 2 placebo tablets); 15 mg BID for 7 days (three 5-mg tablets and 1 placebo tablet); 20 mg BID to Month 12 (four 5-mg tablets).	

Serious adverse events	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 51 (13.73%)	9 / 71 (12.68%)	5 / 66 (7.58%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (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
Reproductive system and breast disorders			
Prostatomegaly			

subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (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
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (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
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 71 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (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
Panic attack			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (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
Suicide attempt			
subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			

subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (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
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Huntington's disease			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (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
Nervous system disorders			
Chorea			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (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
Hyperkinesia			
subjects affected / exposed	2 / 51 (3.92%)	0 / 71 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (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			
Dysphagia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 71 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 71 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 71 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract disorder			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (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
Osteoarthritis			

subjects affected / exposed	1 / 51 (1.96%)	0 / 71 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 51 (0.00%)	1 / 71 (1.41%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	20 mg PF-02545920	5 mg PF-02545920 Titration up to 20 mg	Placebo and Titration up to 20 mg PF-02545920
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 51 (62.75%)	53 / 71 (74.65%)	54 / 66 (81.82%)
Investigations			
Weight decreased			
subjects affected / exposed	3 / 51 (5.88%)	7 / 71 (9.86%)	11 / 66 (16.67%)
occurrences (all)	3	7	11
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 51 (11.76%)	15 / 71 (21.13%)	8 / 66 (12.12%)
occurrences (all)	10	20	11
Nervous system disorders			
Akathisia			
subjects affected / exposed	1 / 51 (1.96%)	2 / 71 (2.82%)	4 / 66 (6.06%)
occurrences (all)	1	4	6
Chorea			
subjects affected / exposed	11 / 51 (21.57%)	11 / 71 (15.49%)	14 / 66 (21.21%)
occurrences (all)	12	15	14
Dizziness			
subjects affected / exposed	0 / 51 (0.00%)	9 / 71 (12.68%)	5 / 66 (7.58%)
occurrences (all)	0	15	5
Dyskinesia			
subjects affected / exposed	1 / 51 (1.96%)	3 / 71 (4.23%)	6 / 66 (9.09%)
occurrences (all)	2	4	6

Headache			
subjects affected / exposed	1 / 51 (1.96%)	5 / 71 (7.04%)	3 / 66 (4.55%)
occurrences (all)	1	5	4
Hyperkinesia			
subjects affected / exposed	7 / 51 (13.73%)	0 / 71 (0.00%)	2 / 66 (3.03%)
occurrences (all)	11	0	3
Sedation			
subjects affected / exposed	1 / 51 (1.96%)	2 / 71 (2.82%)	5 / 66 (7.58%)
occurrences (all)	1	2	9
Somnolence			
subjects affected / exposed	1 / 51 (1.96%)	4 / 71 (5.63%)	9 / 66 (13.64%)
occurrences (all)	1	6	10
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 51 (3.92%)	9 / 71 (12.68%)	9 / 66 (13.64%)
occurrences (all)	2	13	9
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 51 (3.92%)	6 / 71 (8.45%)	4 / 66 (6.06%)
occurrences (all)	2	10	7
Dysphagia			
subjects affected / exposed	2 / 51 (3.92%)	3 / 71 (4.23%)	4 / 66 (6.06%)
occurrences (all)	2	4	4
Nausea			
subjects affected / exposed	2 / 51 (3.92%)	9 / 71 (12.68%)	8 / 66 (12.12%)
occurrences (all)	2	14	9
Vomiting			
subjects affected / exposed	1 / 51 (1.96%)	5 / 71 (7.04%)	3 / 66 (4.55%)
occurrences (all)	2	5	9
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 51 (3.92%)	5 / 71 (7.04%)	7 / 66 (10.61%)
occurrences (all)	2	6	8
Depression			
subjects affected / exposed	3 / 51 (5.88%)	3 / 71 (4.23%)	5 / 66 (7.58%)
occurrences (all)	3	3	5

Insomnia			
subjects affected / exposed	2 / 51 (3.92%)	4 / 71 (5.63%)	9 / 66 (13.64%)
occurrences (all)	2	5	11
Restlessness			
subjects affected / exposed	1 / 51 (1.96%)	2 / 71 (2.82%)	5 / 66 (7.58%)
occurrences (all)	1	4	6
Sleep disorder			
subjects affected / exposed	3 / 51 (5.88%)	3 / 71 (4.23%)	2 / 66 (3.03%)
occurrences (all)	3	3	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 51 (5.88%)	6 / 71 (8.45%)	4 / 66 (6.06%)
occurrences (all)	3	6	4
Muscle spasms			
subjects affected / exposed	3 / 51 (5.88%)	0 / 71 (0.00%)	0 / 66 (0.00%)
occurrences (all)	4	0	0
Infections and infestations			
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 51 (7.84%)	3 / 71 (4.23%)	7 / 66 (10.61%)
occurrences (all)	5	3	9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated on 15 December 2016 due to study A8241021 showing no significant difference on primary endpoint between PF-02545920 and placebo. No safety concerns were associated with this termination.

Notes: