

**Clinical trial results:****A Randomized, 18-Week, Placebo-Controlled, Double Blind, Parallel Group Study of the Safety and Efficacy of PF-05212377 (SAM-760) in Subjects With Mild to-Moderate Alzheimer's Disease With Existing Neuropsychiatric Symptoms on a Stable Daily Dose of Donepezil  
Summary**

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2014-000830-42    |
| Trial protocol           | ES GB             |
| Global end of trial date | 15 September 2015 |

**Results information**

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1                |
| This version publication date  | 11 September 2016 |
| First version publication date | 11 September 2016 |

**Trial information****Trial identification**

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | B2081011 |
|-----------------------|----------|

**Additional study identifiers**

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

Notes:

**Sponsors**

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Pfizer, Inc.  |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, 10017                                     |
| Public contact               | Pfizer, Inc., Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer, Inc., Pfizer, Inc., 001 800-718-1021, 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                       | 17 May 2016       |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 15 September 2015 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 15 September 2015 |
| Was the trial ended prematurely?                     | Yes               |

Notes:

## General information about the trial

Main objective of the trial:

Primary Objective:

To evaluate the efficacy of PF-05212377 (SAM 760) 30 milligram (mg) once daily (QD) as compared to placebo on the primary measure of cognition and memory, the Alzheimer's Disease Assessment Scale cognitive subscale 13 item version (ADAS-cog13) 12 weeks after start of double blind study medication.

Secondary Objective:

To evaluate the efficacy of PF-05212377 30 mg QD as compared to placebo on a broad measure of behavior, the Neuropsychiatric Inventory (NPI) (12 item) at 12 weeks after start of double blind study medication.

Protection of trial subjects:

This study was conducted in compliance with good clinical practice (GCP) guidelines and, where applicable, local country regulations relevant to the use of new therapeutic agents in the country/countries of conduct, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 14 November 2012 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Germany: 12        |
| Country: Number of subjects enrolled | Spain: 1           |
| Country: Number of subjects enrolled | Chile: 39          |
| Country: Number of subjects enrolled | United Kingdom: 2  |
| Country: Number of subjects enrolled | United States: 125 |
| Country: Number of subjects enrolled | Canada: 16         |
| Worldwide total number of subjects   | 195                |
| EEA total number of subjects         | 15                 |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| 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)                     | 15  |
| From 65 to 84 years                      | 151 |
| 85 years and over                        | 29  |

## Subject disposition

### Recruitment

Recruitment details:

This study was a multicenter Phase 2a, randomized, placebo controlled, safety and efficacy study of 18 weeks in duration in subjects with mild-to-moderate Alzheimer's disease (AD) who were stable on treatment with 5 or 10 mg of donepezil and who had existing neuropsychiatric symptoms.

### Pre-assignment

Screening details:

Before entering in the 12-week treatment period, participants were required to enter a 4-week placebo run-in period. 195 participants started the run-in period, of which 185 were eligible for the treatment period. One subject who discontinued during the placebo run-in was incorrectly enrolled into the double-blind period but was never treated.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Placebo Run-in Period       |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Single blind                |
| Roles blinded                | Subject                     |

### Arms

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Placebo Run-in Period |
|------------------|-----------------------|

Arm description:

All subjects receiving placebo during the single-blind placebo run-in period

|  |          |
|--|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Capsule  |
| Routes of administration               | Oral use |

Dosage and administration details:

Placebo was administered as capsule once daily in the morning.

| <b>Number of subjects in period 1</b>     | Placebo Run-in Period |
|---|-----------------------|
| Started                                   | 195                   |
| Completed                                 | 185                   |
| Not completed                             | 10                    |
| Adverse event, non-fatal                  | 2                     |
| No longer willing to participate in study | 1                     |
| No longer met eligibility criteria        | 5                     |
| Unspecified                               | 1                     |
| Lost to follow-up                         | 1                     |

**Period 2**

|                              |                               |
|------------------------------|-------------------------------|
| Period 2 title               | Double-blind treatment period |
| Is this the baseline period? | Yes <sup>[1]</sup>            |
| Allocation method            | Randomised - controlled       |
| Blinding used                | Double blind                  |
| Roles blinded                | Subject, Investigator         |

**Arms**

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | PF-05212377 30 mg |

Arm description:

All subjects receiving PF-05212377 30 mg during double blind period.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | PF-05212377  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

PF-05212377 was provided as 15 mg capsules once daily in the morning

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

All subjects receiving placebo during the double blind period

|  |          |
|--|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Capsule  |
| Routes of administration               | Oral use |

Dosage and administration details:

Placebo was administered as capsule once daily in the morning.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 for this study is considered the placebo run-in period

| <b>Number of subjects in period 2<sup>[2]</sup></b> | PF-05212377 30 mg | Placebo |
|---|-------------------|---------|
| Started   | 91                | 94      |
| Completed   | 77                | 86      |
| Not completed                                       | 15                | 8       |
| Adverse event, serious fatal                        | 1                 | -       |
| Adverse event, non-fatal                            | 2                 | 1       |
| No longer meets eligibility criteria                | 3                 | -       |
| Randomized but not treated                          | 1                 | -       |
| No longer willing to participate in study           | 2                 | 4       |

|                            |   |   |
|----------------------------|---|---|
| Unspecified                | 4 | 1 |
| Lost to follow-up          | 2 | 1 |
| Protocol deviation         | - | 1 |
| Joined                     | 1 | 0 |
| Randomized but not treated | 1 | - |

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Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The worldwide number enrolled in the trial includes all subjects included for safety reporting and enrolled in the placebo run-in period

## Baseline characteristics

### Reporting groups

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Double-blind treatment period |
|-----------------------|-------------------------------|

Reporting group description: -

| Reporting group values                             | Double-blind treatment period | Total |  |
|--|-------------------------------|-------|--|
| Number of subjects                                 | 186                           | 186   |  |
| Age Categorical<br>Units: Subjects                 |                               |       |  |
| In utero   | 0                             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                             | 0     |  |
| Newborns (0-27 days)                               | 0                             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                             | 0     |  |
| Children (2-11 years)                              | 0                             | 0     |  |
| Adolescents (12-17 years)                          | 0                             | 0     |  |
| Adults (18-64 years)                               | 14                            | 14    |  |
| From 65-84 years                                   | 144                           | 144   |  |
| 85 years and over                                  | 28                            | 28    |  |
| Age Continuous<br>Units: years                     |                               |       |  |
| arithmetic mean                                    | 76                            |       |  |
| standard deviation                                 | ± 7.7                         | -     |  |
| Gender Categorical<br>Units: Subjects              |                               |       |  |
| Female   | 101                           | 101   |  |
| Male   | 85                            | 85    |  |

## End points

### End points reporting groups

|  |                       |
|--|-----------------------|
| Reporting group title  | Placebo Run-in Period |
| Reporting group description:<br>All subjects receiving placebo during the single-blind placebo run-in period |                       |
| Reporting group title  | PF-05212377 30 mg     |
| Reporting group description:<br>All subjects receiving PF-05212377 30 mg during double blind period.         |                       |
| Reporting group title  | Placebo               |
| Reporting group description:<br>All subjects receiving placebo during the double blind period                |                       |

### Primary: Change From Baseline in ADAS-cog13 Total Score at Week 16

|   |   |
|---|---|
| End point title   | Change From Baseline in ADAS-cog13 Total Score at Week 16 |
| End point description:<br>ADAS-cog13 (13-item ADAS cog) is a psychometric instrument that evaluates word recall, ability to follow commands, constructional praxis, naming, ideational praxis, orientation, word recognition, memory, comprehension of spoken language, word-finding, and language ability, with a measure of delayed word recall and concentration/ distractibility. The total score of the 13-item scale ranges from 0 to 85, with an increase in score indicating cognitive worsening. The Full Analysis Set (FAS) is defined as all subjects who were randomized. The FAS was the primary analysis set for efficacy data. |   |
| End point type  | Primary   |
| End point timeframe:<br>Baseline (Visit 2, Week 4) and Week 16 (Visit 5)  |   |

| End point values                    | PF-05212377<br>30 mg    | Placebo                   |  |  |
|-------------------------------------|-------------------------|---------------------------|--|--|
| Subject group type                  | Reporting group         | Reporting group           |  |  |
| Number of subjects analysed         | 78                      | 86                        |  |  |
| Units: scores on a scale            |                         |                           |  |  |
| least squares mean (standard error) | 0.111 ( $\pm$<br>0.629) | -0.584 ( $\pm$<br>0.5995) |  |  |

### Statistical analyses

|  |  |
|--|--|
| Statistical analysis title                                 | Difference between PF-05212377 30 mg and placebo |
| Statistical analysis description:<br>Mixed Models Analysis |  |
| Comparison groups  | PF-05212377 30 mg v Placebo                      |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 164                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | other                      |
| Parameter estimate                      | Mean difference (net)      |
| Point estimate                          | 0.695                      |
| Confidence interval                     |                            |
| level                                   | Other: 80 %                |
| sides                                   | 2-sided                    |
| lower limit                             | -0.424                     |
| upper limit                             | 1.814                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.8697                     |

### Secondary: Change From Baseline in the Neuropsychiatric Inventory (NPI) Total Score at Week 16

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in the Neuropsychiatric Inventory (NPI) Total Score at Week 16 |
|-----------------|---|

End point description:

The NPI evaluates both frequency and severity of 12 neuropsychiatric disturbances including delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, motor disturbance, nighttime behaviors, as well as appetite/eating. The NPI total score (for 12 behavioral domains) is calculated as the product of frequency and severity for each domain, and ranges from 0 to 144. An increase in score indicates a worsening of symptoms. The FAS is defined as all subjects who are randomized. The FAS was the primary analysis set for efficacy data.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Visit 2, Week 4) and Week 16 (Visit 5)

|                                     |                      |                      |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| <b>End point values</b>             | PF-05212377<br>30 mg | Placebo              |  |  |
| Subject group type                  | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed         | 78                   | 87                   |  |  |
| Units: scores on scale              |                      |                      |  |  |
| least squares mean (standard error) | -3.99 (±<br>1.2441)  | -6.184 (±<br>1.1801) |  |  |

### Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Difference between PF-05212377 30 mg and placebo |
|-----------------------------------|--|

Statistical analysis description:

Mixed Models Analysis

|                   |                             |
|-------------------|-----------------------------|
| Comparison groups | PF-05212377 30 mg v Placebo |
|-------------------|-----------------------------|

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 165                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | non-inferiority            |
| Parameter estimate                      | Median difference (net)    |
| Point estimate                          | 2.194                      |
| Confidence interval                     |                            |
| level                                   | Other: 80 %                |
| sides                                   | 2-sided                    |
| lower limit                             | -0.013                     |
| upper limit                             | 4.401                      |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 1.7149                     |

### Other pre-specified: Percentage of Subjects with Treatment Emergent Adverse Events (TEAEs) Leading to Discontinuation

|   |  |
|---|--|
| End point title   | Percentage of Subjects with Treatment Emergent Adverse Events (TEAEs) Leading to Discontinuation |
| End point description:  |  |
| Proportion (%) of subjects with TEAEs leading to discontinuation over the 12 week double blind treatment period and washout. Adverse events (AEs) occurring following start of treatment or increasing in severity were counted as treatment emergent. Population analysis was defined as all subjects who received any treatment during double blind period. |  |
| End point type  | Other pre-specified  |
| End point timeframe:  |  |
| Week 4 (Visit 2) to Week 18 (Visit 6)   |  |

| End point values              | PF-05212377<br>30 mg | Placebo         |  |  |
|-------------------------------|----------------------|-----------------|--|--|
| Subject group type            | Reporting group      | Reporting group |  |  |
| Number of subjects analysed   | 91                   | 94              |  |  |
| Units: Percentage of Subjects |                      |                 |  |  |
| number (not applicable)       | 46.2                 | 44.7            |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Proportion of Laboratory Abnormalities of Potential Clinical Concern During Double Blind Period

|   |   |
|---|---|
| End point title   | Proportion of Laboratory Abnormalities of Potential Clinical Concern During Double Blind Period |
| End point description:  |   |
| Proportion of subjects with lab abnormalities of potential clinical concern over the double blind period. The following parameters were analyzed: hematology (hemoglobin, hematocrit, red blood cell count, platelet count, white blood cell count, neutrophils, eosinophils, monocytes, basophils, lymphocytes); blood chemistry (blood urea nitrogen, creatinine, glucose, calcium, sodium, potassium, chloride, total bicarbonate, aspartate aminotransferase, alanine aminotransferase, bilirubin, alkaline phosphatase, uric |   |

acid, albumin, and total protein; urinalysis (pH, glucose, protein/albumin, hemoglobin/blood, ketones/acetone, nitrites, leukocyte esterase, microscopy [if urine dipstick was positive for blood, protein, nitrites or leukocyte esterase]); others (only at screening or needed: urine drug screen, thyroid panel, VB12, methylmalonic acid, folate and HbA1). Analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                                       |                     |
|---------------------------------------|---------------------|
| End point type                        | Other pre-specified |
| End point timeframe:                  |                     |
| Week 4 (Visit 2) to Week 16 (Visit 5) |                     |

|                               |                      |                 |  |  |
|-------------------------------|----------------------|-----------------|--|--|
| <b>End point values</b>       | PF-05212377<br>30 mg | Placebo         |  |  |
| Subject group type            | Reporting group      | Reporting group |  |  |
| Number of subjects analysed   | 91                   | 94              |  |  |
| Units: Percentage of Subjects |                      |                 |  |  |
| number (not applicable)       | 36                   | 52              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected Electrocardiogram (ECG) Change from Baseline - PR Interval at Week 6 (Visit 3)

|                 |   |
|-----------------|---|
| End point title | Selected Electrocardiogram (ECG) Change from Baseline - PR Interval at Week 6 (Visit 3) |
|-----------------|---|

End point description:

The PR interval is the time from the onset of the P wave to the start of the QRS complex (the combination of the Q wave, R wave and S wave, representing ventricular depolarization). The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                               |                     |
|-------------------------------|---------------------|
| End point type                | Other pre-specified |
| End point timeframe:          |                     |
| Baseline and Week 6 (Visit 3) |                     |

|  |                      |                     |  |  |
|--|----------------------|---------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo             |  |  |
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 85                   | 89                  |  |  |
| Units: milliseconds (msec)             |                      |                     |  |  |
| arithmetic mean (full range (min-max)) | -2.8 (-52 to<br>24)  | -3.6 (-82 to<br>35) |  |  |

### Statistical analyses

No statistical analyses for this end point

**Other pre-specified: Selected ECG Change from Baseline - PR Interval at Week 10 (Visit 4)**

|                 |  |
|-----------------|--|
| End point title | Selected ECG Change from Baseline - PR Interval at Week 10 (Visit 4) |
|-----------------|--|

End point description:

The PR interval is the time from the onset of the P wave to the start of the QRS complex (the combination of the Q wave, R wave and S wave, representing ventricular depolarization). The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 10 (Visit 4)

|  |                      |                  |  |  |
|--|----------------------|------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo          |  |  |
| Subject group type                     | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed            | 79                   | 87               |  |  |
| Units: msec                            |                      |                  |  |  |
| arithmetic mean (full range (min-max)) | -0.1 (-42 to 23)     | -1.3 (-61 to 61) |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Other pre-specified: Selected ECG Change from Baseline - PR Interval at Week 16/Early Termination (Visit 5)**

|                 |  |
|-----------------|--|
| End point title | Selected ECG Change from Baseline - PR Interval at Week 16/Early Termination (Visit 5) |
|-----------------|--|

End point description:

The PR interval is the time from the onset of the P wave to the start of the QRS complex (the combination of the Q wave, R wave and S wave, representing ventricular depolarization). The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 16/Early Termination (Visit 5)

|  |                      |                  |  |  |
|--|----------------------|------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo          |  |  |
| Subject group type                     | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed            | 82                   | 85               |  |  |
| Units: msec                            |                      |                  |  |  |
| arithmetic mean (full range (min-max)) | -2.5 (-69 to 24)     | -1.6 (-49 to 33) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Proportion of PR Interval Abnormalities of Potential Clinical Concern

|                 |   |
|-----------------|---|
| End point title | Proportion of PR Interval Abnormalities of Potential Clinical Concern |
|-----------------|---|

End point description:

Proportion (%) of subjects with PR Interval abnormalities meeting categorical criteria over the 12 week double blind treatment period. The PR interval is the time from the onset of the P wave to the start of the QRS complex (the combination of the Q wave, R wave and S wave, representing ventricular depolarization). Subjects with post-baseline PR absolute value  $\geq 300$  msec, a PR increase of  $\geq 25\%$  (for subjects with a baseline value  $\geq 200$  msec), or with an increase  $\geq 50\%$  (for subjects with a baseline value  $< 200$  msec) were counted. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Week 4 (Visit 2) to Week 16 (Visit 5)

| End point values  | PF-05212377<br>30 mg | Placebo         |  |  |
|---|----------------------|-----------------|--|--|
| Subject group type                                      | Reporting group      | Reporting group |  |  |
| Number of subjects analysed                             | 86                   | 90              |  |  |
| Units: Percentage of Subjects                           |                      |                 |  |  |
| number (not applicable)                                 |                      |                 |  |  |
| Post-Baseline Maximum Absolute Value<br>$\geq 300$ msec | 0                    | 4.4             |  |  |
| Post-Baseline Maximum Increase<br>$\geq 25/50\%$        | 0                    | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected ECG Change from Baseline - QRS complex at Week 6 (Visit 3)

|                 |   |
|-----------------|---|
| End point title | Selected ECG Change from Baseline - QRS complex at Week 6 (Visit 3) |
|-----------------|---|

End point description:

The QRS complex is the combination of the Q wave, R wave and S wave, representing ventricular depolarization. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:  
Baseline and Week 6 (Visit 3)

|  |                      |                     |  |  |
|--|----------------------|---------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo             |  |  |
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 88                   | 92                  |  |  |
| Units: msec                            |                      |                     |  |  |
| arithmetic mean (full range (min-max)) | -0.3 (-22 to<br>43)  | -0.8 (-14 to<br>10) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected ECG Change from Baseline - QRS complex at Week 10 (Visit 4)

|                 |  |
|-----------------|--|
| End point title | Selected ECG Change from Baseline - QRS complex at Week 10 (Visit 4) |
|-----------------|--|

End point description:

The QRS complex is the combination of the Q wave, R wave and S wave, representing ventricular depolarization). The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 10 (Visit 4)

|  |                      |                 |  |  |
|--|----------------------|-----------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo         |  |  |
| Subject group type                     | Reporting group      | Reporting group |  |  |
| Number of subjects analysed            | 81                   | 90              |  |  |
| Units: msec                            |                      |                 |  |  |
| arithmetic mean (full range (min-max)) | -0.1 (-13 to<br>45)  | 0.1 (-15 to 22) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected ECG Change from Baseline - QRS complex at Week 16/Early Termination (Visit 5)

|                 |  |
|-----------------|--|
| End point title | Selected ECG Change from Baseline - QRS complex at Week 16/Early Termination (Visit 5) |
|-----------------|--|

End point description:

The QRS complex is the combination of the Q wave, R wave and S wave, representing ventricular depolarization. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

End point type | Other pre-specified

End point timeframe:

Baseline and Week 16/Early Termination (Visit 5)

|  |                      |                  |  |  |
|--|----------------------|------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo          |  |  |
| Subject group type                     | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed            | 85                   | 89               |  |  |
| Units: msec                            |                      |                  |  |  |
| arithmetic mean (full range (min-max)) | 0.1 (-14 to 18)      | -0.3 (-21 to 14) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Proportion of Subjects with QRS Complex Abnormalities of Potential Clinical Concern

End point title | Proportion of Subjects with QRS Complex Abnormalities of Potential Clinical Concern

End point description:

Proportion (%) of subjects with QRS complex abnormalities meeting categorical criteria over the 12 week double blind treatment period. The QRS complex is the combination of the Q wave, R wave and S wave, representing ventricular depolarization). Subjects with post-baseline QRS complex absolute value  $\geq 100$  msec, a QRS complex increase of  $\geq 25\%$  (for subjects with a baseline value  $\geq 100$  msec), or with an increase  $\geq 50\%$  (for subjects with a baseline value  $< 100$  msec) were counted. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

End point type | Other pre-specified

End point timeframe:

Week 4 (Visit 2) to Week 16 (Visit 5)

|  |                      |                 |  |  |
|--|----------------------|-----------------|--|--|
| <b>End point values</b>                              | PF-05212377<br>30 mg | Placebo         |  |  |
| Subject group type                                   | Reporting group      | Reporting group |  |  |
| Number of subjects analysed                          | 91                   | 93              |  |  |
| Units: Percentage of Subjects                        |                      |                 |  |  |
| number (not applicable)                              |                      |                 |  |  |
| Post-Baseline Maximum Absolute Value $\geq 200$ msec | 0                    | 0               |  |  |
| Post-Baseline Maximum Increase $\geq 25/50\%$        | 0                    | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected ECG Change from Baseline - QTcF interval at Week 6 (Visit 3)

|                 |   |
|-----------------|---|
| End point title | Selected ECG Change from Baseline - QTcF interval at Week 6 (Visit 3) |
|-----------------|---|

End point description:

The QTcF interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle, which is corrected for heart rate using Fridericia's formula. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 6 (Visit 3)

| End point values                       | PF-05212377<br>30 mg | Placebo          |  |  |
|--|----------------------|------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed            | 88                   | 92               |  |  |
| Units: msec                            |                      |                  |  |  |
| arithmetic mean (full range (min-max)) | -3 (-31 to 37)       | -4.9 (-35 to 35) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected ECG Change from Baseline - QTcF interval at Week 10 (Visit 4)

|                 |  |
|-----------------|--|
| End point title | Selected ECG Change from Baseline - QTcF interval at Week 10 (Visit 4) |
|-----------------|--|

End point description:

The QTcF interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle, which is corrected for heart rate using Fridericia's formula. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 10 (Visit 4)

|  |                      |                     |  |  |
|--|----------------------|---------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo             |  |  |
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 81                   | 90                  |  |  |
| Units: msec                            |                      |                     |  |  |
| arithmetic mean (full range (min-max)) | -0.2 (-38 to<br>47)  | -5.5 (-40 to<br>48) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Selected ECG Change from Baseline - QTcF interval at Week 16/Early Termination (Visit 5)

|                 |  |
|-----------------|--|
| End point title | Selected ECG Change from Baseline - QTcF interval at Week 16/Early Termination (Visit 5) |
|-----------------|--|

End point description:

The QTcF interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle, which is corrected for heart rate using Fridericia's formula. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 16/Early Termination (Visit 5)

|  |                      |                     |  |  |
|--|----------------------|---------------------|--|--|
| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo             |  |  |
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 85                   | 89                  |  |  |
| Units: msec                            |                      |                     |  |  |
| arithmetic mean (full range (min-max)) | 0.8 (-31 to 34)      | -2.2 (-62 to<br>30) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Proportion of Subjects with QTcF Interval Abnormalities of Potential Clinical Concern

|                 |   |
|-----------------|---|
| End point title | Proportion of Subjects with QTcF Interval Abnormalities of Potential Clinical Concern |
|-----------------|---|

End point description:

Proportion (%) of subjects with QTcF Interval abnormalities meeting categorical criteria over the 12-

week double blind treatment period. The QTcF interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle, which is corrected for heart rate using Fridericia's formula. Subjects with a post-baseline QTcF absolute value of 450 - <480, 480 - <500, or >=500 msec, or with a post-baseline QTcF increase of 30 - <60 or >=60 msec were counted. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Week 4 (Visit 2) to Week 16 (Visit 5)

| End point values                                  | PF-05212377<br>30 mg | Placebo         |  |  |
|---|----------------------|-----------------|--|--|
| Subject group type                                | Reporting group      | Reporting group |  |  |
| Number of subjects analysed                       | 91                   | 93              |  |  |
| Units: Percentage of Subjects                     |                      |                 |  |  |
| number (not applicable)                           |                      |                 |  |  |
| Post-Baseline Absolute Value of 450-<br><480 msec | 15.4                 | 14              |  |  |
| Post-Baseline Absolute Value of 480-<br><500 msec | 4.4                  | 1.1             |  |  |
| Change from Baseline of 30 -<60 msec              | 6.6                  | 3.2             |  |  |
| Change from Baseline >=60 msec                    | 0                    | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Blood Pressure (BP) Changes from Baseline - Week 6 (Visit 3)

|                 |  |
|-----------------|--|
| End point title | Blood Pressure (BP) Changes from Baseline - Week 6 (Visit 3) |
|-----------------|--|

End point description:

The BP changes from baseline at Week 6 (Visit 3) including supine systolic BP, standing systolic BP, standing systolic BP, supine diastolic BP, standing diastolic BP. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Baseline and Week 6 (Visit 3)

| End point values                       | PF-05212377<br>30 mg | Placebo             |  |  |
|--|----------------------|---------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed            | 89                   | 93                  |  |  |
| Units: millimeters of mercury (mm Hg)  |                      |                     |  |  |
| arithmetic mean (full range (min-max)) |                      |                     |  |  |
| Supine Systolic BP                     | -3.6 (-38 to<br>19)  | -3.9 (-52 to<br>30) |  |  |
| Standing Systolic BP                   | -4.1 (-49 to<br>20)  | -3 (-38 to 22)      |  |  |

|                       |                  |                  |  |  |
|-----------------------|------------------|------------------|--|--|
| Supine Diastolic BP   | -2.2 (-37 to 26) | -1.8 (-33 to 20) |  |  |
| Standing Diastolic BP | -1.1 (-23 to 17) | -1 (-23 to 21)   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pulse Rate Changes from Baseline - Week 6 (Visit 3)

|                        |   |
|------------------------|---|
| End point title        | Pulse Rate Changes from Baseline - Week 6 (Visit 3)   |
| End point description: | The pulse rate changes from baseline at Week 6 (Visit 3) including supine pulse rate, and standing pulse rate. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5). |
| End point type         | Other pre-specified   |
| End point timeframe:   | Baseline and Week 6 (Visit 3)   |

| End point values                       | PF-05212377<br>30 mg | Placebo         |  |  |
|--|----------------------|-----------------|--|--|
| Subject group type                     | Reporting group      | Reporting group |  |  |
| Number of subjects analysed            | 89                   | 93              |  |  |
| Units: beats per minute (bpm)          |                      |                 |  |  |
| arithmetic mean (full range (min-max)) |                      |                 |  |  |
| Supine Pulse Rate                      | -1.4 (-30 to 30)     | 1.4 (-21 to 20) |  |  |
| Standing Pulse Rate                    | -0.3 (-20 to 30)     | 1.3 (-12 to 27) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: BP Changes from Baseline - Week 10 (Visit 4)

|                        |  |
|------------------------|--|
| End point title        | BP Changes from Baseline - Week 10 (Visit 4)   |
| End point description: | The BP changes from baseline at Week 10 (Visit 4) including supine systolic BP, standing systolic BP, standing systolic BP, supine diastolic BP, standing diastolic BP. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5). |
| End point type         | Other pre-specified  |
| End point timeframe:   | Baseline and Week 10 (Visit 4)   |

| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo          |  |  |
|--|----------------------|------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed            | 81                   | 91               |  |  |
| Units: mm Hg                           |                      |                  |  |  |
| arithmetic mean (full range (min-max)) |                      |                  |  |  |
| Supine Systolic BP                     | -3.4 (-36 to 20)     | -0.3 (-68 to 34) |  |  |
| Standing Systolic BP                   | -3.8 (-33 to 32)     | 0.8 (-49 to 49)  |  |  |
| Supine Diastolic BP                    | -2.4 (-32 to 20)     | -0.7 (-39 to 25) |  |  |
| Standing Diastolic BP                  | -1.2 (-20 to 20)     | 0.3 (-26 to 39)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pulse Rate Changes from Baseline - Week 10 (Visit 4)

|                        |  |
|------------------------|--|
| End point title        | Pulse Rate Changes from Baseline - Week 10 (Visit 4)   |
| End point description: | The pulse rate changes from baseline at Week 10 (Visit 4) including supine pulse rate, and standing pulse rate. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5). |
| End point type         | Other pre-specified  |
| End point timeframe:   | Baseline and Week 10 (Visit 4)   |

| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo         |  |  |
|--|----------------------|-----------------|--|--|
| Subject group type                     | Reporting group      | Reporting group |  |  |
| Number of subjects analysed            | 81                   | 91              |  |  |
| Units: bpm                             |                      |                 |  |  |
| arithmetic mean (full range (min-max)) |                      |                 |  |  |
| Supine Pulse Rate                      | -0.4 (-26 to 22)     | 0.5 (-24 to 17) |  |  |
| Standing Pulse Rate                    | -0.7 (-20 to 24)     | 1.8 (-19 to 21) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: BP Changes from Baseline - Week 16/Early Termination (Visit 5)

|                 |  |
|-----------------|--|
| End point title | BP Changes from Baseline - Week 16/Early Termination (Visit 5) |
|-----------------|--|

5)

End point description:

The BP changes from baseline at Week 16/Early Termination (Visit 5) including supine systolic BP, standing systolic BP, standing systolic BP, supine diastolic BP, standing diastolic BP. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

End point type

Other pre-specified

End point timeframe:

Baseline and Week 16/Early Termination (Visit 5)

| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo          |  |  |
|--|----------------------|------------------|--|--|
| Subject group type                     | Reporting group      | Reporting group  |  |  |
| Number of subjects analysed            | 85                   | 90               |  |  |
| Units: mmHg                            |                      |                  |  |  |
| arithmetic mean (full range (min-max)) |                      |                  |  |  |
| Supine Systolic BP                     | -1.4 (-30 to 27)     | -1.1 (-30 to 72) |  |  |
| Standing Systolic BP                   | -1 (-30 to 32)       | -1.1 (-26 to 66) |  |  |
| Supine Diastolic BP                    | -2.1 (-39 to 22)     | -0.3 (-18 to 35) |  |  |
| Standing Diastolic BP                  | -0.8 (-23 to 23)     | 0 (-20 to 36)    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Pulse Rate Changes from Baseline - Week 16/Early Termination (Visit 5)

End point title

Pulse Rate Changes from Baseline - Week 16/Early Termination (Visit 5)

End point description:

The pulse rate changes from baseline at Week 16/Early Termination (Visit 5) including supine pulse rate, and standing pulse rate. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

End point type

Other pre-specified

End point timeframe:

Baseline and Week 16/Early Termination (Visit 5)

| <b>End point values</b>                | PF-05212377<br>30 mg | Placebo         |  |  |
|--|----------------------|-----------------|--|--|
| Subject group type                     | Reporting group      | Reporting group |  |  |
| Number of subjects analysed            | 85                   | 90              |  |  |
| Units: bpm                             |                      |                 |  |  |
| arithmetic mean (full range (min-max)) |                      |                 |  |  |
| Supine Pulse Rate                      | -0.8 (-29 to 31)     | 0.6 (-22 to 20) |  |  |
| Standing Pulse Rate                    | -1.9 (-24 to 39)     | 0.8 (-17 to 17) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Proportion of Subjects with Post-Baseline Vital Signs Abnormalities of Potential Clinical Concern

|                 |   |
|-----------------|---|
| End point title | Proportion of Subjects with Post-Baseline Vital Signs Abnormalities of Potential Clinical Concern |
|-----------------|---|

End point description:

Proportion (%) of subjects with vital signs abnormalities (absolute and change from baseline) meeting categorical criteria over the 12-week double blind treatment period were counted. Vital signs data included BP and pulse rate. The analysis population was defined as all subjects who received any treatment during Week 4 (Visit 2) to Week 16 (Visit 5).

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Week 4 (Visit 2) to Week 16 (Visit 5)

| <b>End point values</b>                    | PF-05212377<br>30 mg | Placebo         |  |  |
|--|----------------------|-----------------|--|--|
| Subject group type                         | Reporting group      | Reporting group |  |  |
| Number of subjects analysed                | 91                   | 94              |  |  |
| Units: Percentage of Subjects              |                      |                 |  |  |
| number (not applicable)                    |                      |                 |  |  |
| Absolute Supine Systolic BP < 90 mmHg      | 0                    | 1.1             |  |  |
| Absolute Standing Systolic BP < 90 mmHg    | 0                    | 1.1             |  |  |
| Absolute Supine Diastolic BP < 50 mmHg     | 0                    | 2.1             |  |  |
| Absolute Standing Diastolic BP < 50 mmHg   | 0                    | 0               |  |  |
| Absolute Supine Pulse Rate < 40 bpm        | 0                    | 0               |  |  |
| Absolute Supine Pulse Rate > 120 bpm       | 0                    | 0               |  |  |
| Absolute Standing Pulse Rate < 40 bpm      | 0                    | 0               |  |  |
| Absolute Standing Pulse Rate > 140 bpm     | 0                    | 0               |  |  |
| Increase in Supine Systolic BP ≥ 30 mmHg   | 0                    | 5.3             |  |  |
| Increase in Standing Systolic BP ≥ 30 mmHg | 2.2                  | 3.2             |  |  |
| Increase in Supine Diastolic BP ≥ 20 mmHg  | 4.4                  | 4.3             |  |  |

|  |     |     |  |  |
|--|-----|-----|--|--|
| Increase in Standing Diastolic BP $\geq$ 20 mmHg | 3.3 | 5.3 |  |  |
| Decrease in Supine Systolic BP $\geq$ 30 mmHg    | 5.5 | 5.3 |  |  |
| Decrease in Standing Systolic BP $\geq$ 30 mmHg  | 5.5 | 5.3 |  |  |
| Decrease in Supine Diastolic BP $\geq$ 20 mmHg   | 8.8 | 5.3 |  |  |
| Decrease in Standing Diastolic BP $\geq$ 20 mmHg | 4.4 | 6.4 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Subjects in Each Category of C-CASA Mapped from the C-SSRS Responses

|                 |  |
|-----------------|--|
| End point title | Subjects in Each Category of C-CASA Mapped from the C-SSRS Responses |
|-----------------|--|

End point description:

Subjects in each category of the Columbia Classification Algorithm of Suicide Assessment (C-CASA) mapped from the Columbia-Suicide Severity Rating Scale (C-SSRS) responses were reported. C-CASA Event Code: <1> Completed suicide; <2> Suicide attempt; <3> Preparatory acts towards imminent suicidal behavior; <4> Suicidal Ideation; <7> Self-injurious behavior, no suicidal intent. The suicidality assessments were performed at Screening, Week 0 (Visit 1), Week 4 (Visit 2), Week 6, (Visit 3), Week 10 (Visit 4), Week 16 (Visit 5), and Week 18 (Visit 6). Only subjects falling any category of C-CASA events were listed below. Analysis population was defined as all subjects screened and assigned.

|                |                     |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

From Screening to Week 18/Early Termination (Visit 6)

| End point values                            | PF-05212377<br>30 mg | Placebo         |  |  |
|---|----------------------|-----------------|--|--|
| Subject group type                          | Reporting group      | Reporting group |  |  |
| Number of subjects analysed                 | 91                   | 94              |  |  |
| Units: subjects                             |                      |                 |  |  |
| number (not applicable)                     |                      |                 |  |  |
| Week 4 (Visit 2): <4>                       | 2                    | 1               |  |  |
| Week 6 (Visit 3): <4>                       | 0                    | 1               |  |  |
| Week 10 (Visit 4): <4>                      | 2                    | 0               |  |  |
| Week 16/Early Termination (Visit 5):<br><4> | 1                    | 0               |  |  |
| Week 6 (Visit 3): <7>                       | 1                    | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 18

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |                |
|-----------------------|----------------|
| Reporting group title | Placebo Run-in |
|-----------------------|----------------|

Reporting group description:

Subjects who received placebo during the single blind placebo-run in period

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects who received placebo once daily in the morning during the double blind period.

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | PF-05212377 30 mg |
|-----------------------|-------------------|

Reporting group description:

Subjects who received PF-05212377 30 mg once daily in the morning during the double blind period.

| <b>Serious adverse events</b>                            | Placebo Run-in  | Placebo        | PF-05212377 30 mg |
|--|-----------------|----------------|-------------------|
| <b>Total subjects affected by serious adverse events</b> |                 |                |                   |
| subjects affected / exposed                              | 1 / 195 (0.51%) | 3 / 94 (3.19%) | 5 / 91 (5.49%)    |
| number of deaths (all causes)                            | 0               | 0              | 1                 |
| number of deaths resulting from adverse events           | 0               | 0              | 0                 |
| <b>Injury, poisoning and procedural complications</b>    |                 |                |                   |
| <b>Femoral neck fracture</b>                             |                 |                |                   |
| subjects affected / exposed                              | 1 / 195 (0.51%) | 0 / 94 (0.00%) | 0 / 91 (0.00%)    |
| occurrences causally related to treatment / all          | 0 / 1           | 0 / 0          | 0 / 0             |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0             |
| <b>Foreign body</b>                                      |                 |                |                   |
| subjects affected / exposed                              | 0 / 195 (0.00%) | 1 / 94 (1.06%) | 0 / 91 (0.00%)    |
| occurrences causally related to treatment / all          | 0 / 0           | 0 / 1          | 0 / 0             |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0             |
| <b>Vascular disorders</b>                                |                 |                |                   |
| <b>Orthostatic hypotension</b>                           |                 |                |                   |
| subjects affected / exposed                              | 0 / 195 (0.00%) | 0 / 94 (0.00%) | 1 / 91 (1.10%)    |
| occurrences causally related to treatment / all          | 0 / 0           | 0 / 0          | 0 / 1             |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0             |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| Cardiac disorders                                    |                 |                |                |
| Bradycardia  |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 0 / 94 (0.00%) | 2 / 91 (2.20%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                 |                |                |
| Accidental death                                     |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 0 / 94 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 1          |
| Asthenia   |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 0 / 94 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                              |                 |                |                |
| Cholecystitis acute                                  |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 0 / 94 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Psychiatric disorders                                |                 |                |                |
| Delirium   |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 1 / 94 (1.06%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Infections and infestations                          |                 |                |                |
| Pneumonia  |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 1 / 94 (1.06%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Urinary tract infection                              |                 |                |                |
| subjects affected / exposed                          | 0 / 195 (0.00%) | 0 / 94 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>  | Placebo Run-in                                   | Placebo  | PF-05212377 30 mg                              |
|--|--|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 13 / 195 (6.67%)                                 | 20 / 94 (21.28%)                               | 25 / 91 (27.47%)                               |
| Investigations<br>Weight decreased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 195 (0.51%)<br>1                             | 2 / 94 (2.13%)<br>2                            | 0 / 91 (0.00%)<br>0                            |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all)   | 2 / 195 (1.03%)<br>2                             | 3 / 94 (3.19%)<br>3                            | 3 / 91 (3.30%)<br>3                            |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 195 (0.00%)<br>0                             | 1 / 94 (1.06%)<br>1                            | 2 / 91 (2.20%)<br>2                            |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 0 / 195 (0.00%)<br>0                             | 2 / 94 (2.13%)<br>2                            | 2 / 91 (2.20%)<br>2                            |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 6 / 195 (3.08%)<br>6                             | 3 / 94 (3.19%)<br>3                            | 8 / 91 (8.79%)<br>9                            |
| Psychiatric disorders<br>Hallucination<br>subjects affected / exposed<br>occurrences (all)<br><br>Insomnia<br>subjects affected / exposed<br>occurrences (all) | 0 / 195 (0.00%)<br>0<br><br>0 / 195 (0.00%)<br>0 | 2 / 94 (2.13%)<br>2<br><br>2 / 94 (2.13%)<br>3 | 0 / 91 (0.00%)<br>0<br><br>1 / 91 (1.10%)<br>1 |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis   | 0 / 195 (0.00%)<br>0<br><br>0                    | 1 / 94 (1.06%)<br>1<br><br>1                   | 2 / 91 (2.20%)<br>2<br><br>2                   |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 4 / 195 (2.05%)<br>4 | 2 / 94 (2.13%)<br>2 | 2 / 91 (2.20%)<br>2 |
| Pneumonia  |                      |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 195 (0.00%)<br>0 | 2 / 94 (2.13%)<br>2 | 0 / 91 (0.00%)<br>0 |
| Upper respiratory tract infection                |                      |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 195 (0.00%)<br>0 | 1 / 94 (1.06%)<br>1 | 2 / 91 (2.20%)<br>2 |
| Urinary tract infection                          |                      |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 195 (0.00%)<br>0 | 4 / 94 (4.26%)<br>4 | 5 / 91 (5.49%)<br>5 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 24 June 2013    | The inclusion and exclusion criteria were amended and some more efficacy evaluations were added |
| 02 January 2014 | Numbering of Days for Screening Period was revised. Some sections were reworded                 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported