



## Clinical trial results:

### An Open-Label, Long-Term Safety Study of SD-809 (Deutetrabenazine) for the Treatment of Moderate to Severe Tardive Dyskinesia

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2014-001891-73   |
| Trial protocol           | CZ PL SK HU      |
| Global end of trial date | 14 December 2020 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 19 December 2021 |
| First version publication date | 27 March 2021    |
| Version creation reason        |                  |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | SD-809-C-20 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02198794 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Teva Branded Pharmaceutical Products R&D, Inc.  |
| Sponsor organisation address | 145 Brandywine Parkway, West Chester, United States, 19380  |
| Public contact               | Director, Clinical Research, Teva Branded Pharmaceutical Products R&D, Inc., 001 8884838279, info.eraclinical@teva.de |
| Scientific contact           | Director, Clinical Research, Teva Branded Pharmaceutical Products R&D, Inc., 001 8884838279, info.eraclinical@teva.de |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       |    |
| 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                       | 04 February 2020 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 06 December 2019 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 14 December 2020 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the long-term safety, tolerability, and efficacy of SD-809 in reducing the severity of abnormal involuntary movements of moderate to severe tardive dyskinesia. The purpose of part B is to establish the durability of effect of SD-809 following 1-week period of randomized withdrawal (SD-809 and placebo), followed by 12 weeks of maintenance with SD-809.

Protection of trial subjects:

This study was conducted in full accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (for example, Code of Federal Regulations [CFR] Title 21, Parts 50, 54, 56, 312, and 314; EU Directive 2001/20/EC on the approximation of the laws, regulations, and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use).

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 20 October 2014 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Czechia: 26        |
| Country: Number of subjects enrolled | Germany: 4         |
| Country: Number of subjects enrolled | Hungary: 16        |
| Country: Number of subjects enrolled | Poland: 89         |
| Country: Number of subjects enrolled | Slovakia: 7        |
| Country: Number of subjects enrolled | United States: 195 |
| Worldwide total number of subjects   | 337                |
| EEA total number of subjects         | 142                |

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)                     | 258 |
| From 65 to 84 years                      | 79  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

343 participants who completed previous SD-809 studies, including study SD-809-C-18 (NCT02195700) or SD-809-C-23 (NCT02291861) were enrolled and 337 participants were eligible for analysis. 6 participants were not evaluable and were excluded from the analysis due to site data integrity issues as reported to the US FDA.

### Pre-assignment

Screening details:

Study included 3 parts: A, B, and C. Participants in Part A who were on a stable dose for  $\geq 4$  weeks after a 6-week titration, were invited to participate in Part B. Participants who are noted as "Completed" for Part A: completed the study in Part A plus continued in Part B. EU participants who completed Part B were invited to participate in Part C.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Part A: Open-Label (158 Weeks) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |        |
|-----------|--------|
| Arm title | SD-809 |
|-----------|--------|

Arm description:

Participants received SD-809 orally BID starting at 12 mg/day, which was titrated based on dyskinesia control and tolerability up to a maximum total dose of 48 mg/day. Participants who declined to participate in Part B, continued at their stable dose of SD-809 BID up to Week 158.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | SD-809       |
| Investigational medicinal product code | TEV-50717    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

SD-809 was administered per dose and schedule specified in the arm.

| Number of subjects in period 1           | SD-809 |
|--|--------|
| Started                                  | 337    |
| Received at least 1 dose of study drug   | 337    |
| Intent-to-Treat (ITT) Population         | 337    |
| Participants participated in Part A only | 195    |
| Completed                                | 32     |
| Not completed                            | 305    |
| Adverse event, serious fatal             | 8      |
| Study terminated                         | 1      |
| Consent withdrawn by subject             | 79     |
| Agreed to continue in Part B             | 142    |

|                               |    |
|-------------------------------|----|
| Adverse event, non-fatal      | 33 |
| Protocol deviation            | 1  |
| Noncompliance with study drug | 3  |
| Other than specified          | 5  |
| Lost to follow-up             | 24 |
| Lack of efficacy              | 9  |

## Period 2

|                              |  |
|------------------------------|--|
| Period 2 title               | Part B: Randomized (13 Weeks)          |
| Is this the baseline period? | No                                     |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

## Arms

|                              |                 |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes             |
| <b>Arm title</b>             | Part B: Placebo |

### Arm description:

Participants received placebo matched to SD-809 for 1 week in randomized withdrawal period and thereafter received SD-809 (stable dose) for 12 weeks.

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

### Dosage and administration details:

Placebo matched to SD-809 was administered per schedule specified in the arm.

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | Part B: SD-809 |
|------------------|----------------|

### Arm description:

Participants received SD-809 (stable dose) for 1 week in randomized withdrawal period and continued to receive the same dose of SD-809 for an additional 12 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | SD-809       |
| Investigational medicinal product code | TEV-50717    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

### Dosage and administration details:

SD-809 was administered per dose and schedule specified in the arm.

| Number of subjects in period 2               | Part B: Placebo | Part B: SD-809 |
|--|-----------------|----------------|
| Started                                      | 16              | 16             |
| Completed                                    | 66              | 68             |
| Not completed                                | 5               | 3              |
| Consent withdrawn by subject                 | 3               | 1              |
| Lost to follow-up                            | 2               | 2              |
| Joined                                       | 55              | 55             |
| 142 participants from Part A were randomized | 55              | 55             |

### Period 3

|                              |                                      |
|------------------------------|--------------------------------------|
| Period 3 title               | Part C: Safety Assessment (52 weeks) |
| Is this the baseline period? | No                                   |
| Allocation method            | Not applicable                       |
| Blinding used                | Not blinded                          |

### Arms

|           |                |
|-----------|----------------|
| Arm title | Part C: SD-809 |
|-----------|----------------|

Arm description:

EU participants who completed Part B and willing to continue in the study continued treatment with SD-809 for 52 weeks at the current dose administered during the 12-week open-label period of Part B.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | SD-809       |
| Investigational medicinal product code | TEV-50717    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

SD-809 was administered per dose and schedule specified in the arm.

| Number of subjects in period 3 <sup>[1]</sup> | Part C: SD-809 |
|---|----------------|
| Started                                       | 80             |
| Completed                                     | 73             |
| Not completed                                 | 7              |
| Adverse event, serious fatal                  | 2              |
| Consent withdrawn by subject                  | 3              |
| Adverse event, non-fatal                      | 2              |

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Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Of the 134 participants who completed Part B, 80 participants from the EU enrolled in Part C.

## Baseline characteristics

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | SD-809 |
|-----------------------|--------|

Reporting group description:

Participants received SD-809 orally BID starting at 12 mg/day, which was titrated based on dyskinesia control and tolerability up to a maximum total dose of 48 mg/day. Participants who declined to participate in Part B, continued at their stable dose of SD-809 BID up to Week 158.

| Reporting group values | SD-809 | Total |  |
|------------------------|--------|-------|--|
| Number of subjects     | 337    | 337   |  |
| Age categorical        |        |       |  |
| Units: Subjects        |        |       |  |

|   |         |     |  |
|---|---------|-----|--|
| Age Continuous  |         |     |  |
| Units: years  |         |     |  |
| arithmetic mean   | 56.9    |     |  |
| standard deviation  | ± 10.65 | -   |  |
| Sex: Female, Male   |         |     |  |
| Units: participants   |         |     |  |
| Female  | 188     | 188 |  |
| Male  | 149     | 149 |  |
| Race/Ethnicity, Customized  |         |     |  |
| Units: Subjects   |         |     |  |
| American Indian or Alaskan Native   | 1       | 1   |  |
| Asian   | 2       | 2   |  |
| Black   | 69      | 69  |  |
| White   | 264     | 264 |  |
| Other   | 1       | 1   |  |
| Ethnicity (NIH/OMB)   |         |     |  |
| Units: Subjects   |         |     |  |
| Hispanic or Latino  | 28      | 28  |  |
| Not Hispanic or Latino  | 300     | 300 |  |
| Unknown or Not Reported   | 9       | 9   |  |
| Total Motor Abnormal Involuntary Movement Scale (AIMS) Score  |         |     |  |
| AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. |         |     |  |
| Units: units on a scale   |         |     |  |
| arithmetic mean   | 10.7    |     |  |
| standard deviation  | ± 4.68  | -   |  |
| AIMS Individual Items (8-10) Scores: Severity of abnormal movements (Item 8) Score  |         |     |  |
| AIMS is composed of 12 clinician-administered and -scored items. Item 8 (used as an overall severity index indicating severity of abnormal movements) was rated on a 5-point anchored scale ranging from 0 (no dyskinetic movements) to 4 (severe dyskinetic movements). Items 9 and 10 (provide additional information with regard to participant's incapacitation due to abnormal movements and participant's awareness of abnormal movements) were rated on a 5-point anchored scale ranging from 0 (none or no                |         |     |  |



|   |                 |   |  |
|---|-----------------|---|--|
| awareness) to 4 (severe or aware, severe distress). Higher scores indicated more severe disease.  |                 |   |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation  | 2.6<br>± 0.78   | - |  |
| AIMS Individual Items (8-10) Scores:<br>Incapacitation due to abnormal movements (Item 9) Score   |                 |   |  |
| AIMS is composed of 12 clinician-administered and -scored items. Item 8 (used as an overall severity index indicating severity of abnormal movements) was rated on a 5-point anchored scale ranging from 0 (no dyskinesic movements) to 4 (severe dyskinesic movements). Items 9 and 10 (provide additional information with regard to participant's incapacitation due to abnormal movements and participant's awareness of abnormal movements) were rated on a 5-point anchored scale ranging from 0 (none or no awareness) to 4 (severe or aware, severe distress). Higher scores indicated more severe disease. |                 |   |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation  | 2.0<br>± 1.07   | - |  |
| AIMS Individual Items (8-10) Scores:<br>Participant's awareness of abnormal movements (Item 10) Score   |                 |   |  |
| AIMS is composed of 12 clinician-administered and -scored items. Item 8 (used as an overall severity index indicating severity of abnormal movements) was rated on a 5-point anchored scale ranging from 0 (no dyskinesic movements) to 4 (severe dyskinesic movements). Items 9 and 10 (provide additional information with regard to participant's incapacitation due to abnormal movements and participant's awareness of abnormal movements) were rated on a 5-point anchored scale ranging from 0 (none or no awareness) to 4 (severe or aware, severe distress). Higher scores indicated more severe disease. |                 |   |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation  | 2.2<br>± 1.08   | - |  |
| Modified Craniocervical Dystonia Questionnaire 24 (CDQ-24) Score  |                 |   |  |
| CDQ-24 is a disease-specific quality of life questionnaire developed for use in participants with craniocervical dystonia. CDQ-24 was modified such that the questions focus more directly on the impact of TD on quality of life. The following domains were evaluated in mCDQ-24: stigma, emotional well-being, pain, activities of daily living, and social/family life. Each of the 24 questions were rated by participants on a scale of 0 = never or no impairment to 4 = always or very severe impairment. Total score ranged from 0 – 96, with higher score indicative of severe impairment.                |                 |   |  |
| Units: units on a scale<br>arithmetic mean<br>standard deviation  | 29.2<br>± 18.96 | - |  |

## End points

### End points reporting groups

|  |                             |
|--|-----------------------------|
| Reporting group title  | SD-809                      |
| Reporting group description:<br>Participants received SD-809 orally BID starting at 12 mg/day, which was titrated based on dyskinesia control and tolerability up to a maximum total dose of 48 mg/day. Participants who declined to participate in Part B, continued at their stable dose of SD-809 BID up to Week 158. |                             |
| Reporting group title  | Part B: Placebo             |
| Reporting group description:<br>Participants received placebo matched to SD-809 for 1 week in randomized withdrawal period and thereafter received SD-809 (stable dose) for 12 weeks.  |                             |
| Reporting group title  | Part B: SD-809              |
| Reporting group description:<br>Participants received SD-809 (stable dose) for 1 week in randomized withdrawal period and continued to receive the same dose of SD-809 for an additional 12 weeks.   |                             |
| Reporting group title  | Part C: SD-809              |
| Reporting group description:<br>EU participants who completed Part B and willing to continue in the study continued treatment with SD-809 for 52 weeks at the current dose administered during the 12-week open-label period of Part B.  |                             |
| Subject analysis set title   | Part B: Placebo             |
| Subject analysis set type  | Modified intention-to-treat |
| Subject analysis set description:<br>Participants received placebo matched to SD-809 for 1 week in randomized withdrawal period and thereafter received SD-809 (stable dose) for 12 weeks.   |                             |
| Subject analysis set title   | Part B: SD-809              |
| Subject analysis set type  | Modified intention-to-treat |
| Subject analysis set description:<br>Participants received SD-809 (stable dose) for 1 week in randomized withdrawal period and continued to receive the same dose of SD-809 for an additional 12 weeks.  |                             |

### Primary: Part A, B, and C: Number of Participants With Treatment-Emergent AEs (TEAEs), Serious TEAEs, Severe TEAEs, Drug-Related TEAEs, and TEAEs Leading to Withdrawal

|  |   |
|--|---|
| End point title  | Part A, B, and C: Number of Participants With Treatment-Emergent AEs (TEAEs), Serious TEAEs, Severe TEAEs, Drug-Related TEAEs, and TEAEs Leading to Withdrawal <sup>[1]</sup> |
| End point description:<br>AEs were analyzed as 1 group combined for parts A and B per planned analysis. An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Severe AE=prevents normal daily activities. Drug-related TEAEs=TEAEs with possible, probable, or definite relationship to study drug. Serious AEs=death, life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, significant disability or incapacity, congenital anomaly or birth defect, or an important medical event that jeopardized participant and required medical intervention to prevent 1 of the outcomes listed in the definition. TEAE=an AE that began after the first administration of study drug or existing AEs that worsened after first dose of study drug. A summary of other non-serious AEs and all serious AEs, regardless of causality is located in Reported AE section. Safety population included all participants who received any study drug. |   |
| End point type   | Primary   |
| End point timeframe:<br>Baseline up to the end of follow-up (4 weeks after the last dose of study drug; mean exposure: up to approximately 866.1 days)   |   |

#### 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: Of the 134 participants who completed Part B, 80 participants from the EU enrolled in Part C.

| End point values                       | SD-809          | Part C: SD-809  |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                     | Reporting group | Reporting group |  |  |
| Number of subjects analysed            | 337             | 80              |  |  |
| Units: participants                    |                 |                 |  |  |
| Any TEAEs                              | 269             | 23              |  |  |
| Serious TEAEs                          | 68              | 5               |  |  |
| Severe TEAEs                           | 57              | 3               |  |  |
| Drug-Related TEAEs                     | 154             | 3               |  |  |
| TEAEs Leading to Withdrawal From Study | 42              | 3               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Part B: Change From Day 1 Visit in Total Motor AIMS Score at Day 7 Visit, as Assessed by Blinded Central Video Rating

|                 |   |
|-----------------|---|
| End point title | Part B: Change From Day 1 Visit in Total Motor AIMS Score at Day 7 Visit, as Assessed by Blinded Central Video Rating |
|-----------------|---|

End point description:

The AIMS is an assessment tool used to detect and follow the severity of TD over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The randomized withdrawal modified intent-to-treat (mITT) population included all participants enrolled in Part B who received study drug during the randomized withdrawal period and had a total motor AIMS score as assessed by blinded central video rating at both the pre-withdrawal visit and the post-withdrawal visit.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 of Part B, Day 7 of Part B

| End point values                 | Part B: Placebo      | Part B: SD-809       |  |  |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type               | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed      | 63                   | 65                   |  |  |
| Units: units on a scale          |                      |                      |  |  |
| arithmetic mean (standard error) |                      |                      |  |  |
| Pre-withdrawal                   | 5.7 (± 0.55)         | 5.0 (± 0.49)         |  |  |
| Change at Post-withdrawal        | 0.6 (± 0.28)         | 0 (± 0.29)           |  |  |

## Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The statistical model was an analysis of covariance (ANCOVA) with treatment group and dopamine

receptor antagonist status at the pre-withdrawal visit as fixed effects and the pre-withdrawal visit value as a covariate.

|   |                                   |
|---|-----------------------------------|
| Comparison groups                       | Part B: Placebo v Part B: SD-809  |
| Number of subjects included in analysis | 128                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | other                             |
| P-value                                 | = 0.121 <sup>[2]</sup>            |
| Method                                  | ANCOVA                            |
| Parameter estimate                      | Least Square (LS) Mean Difference |
| Point estimate                          | -0.6                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -1.42                             |
| upper limit                             | 0.17                              |

Notes:

[2] - Threshold for significance at 0.05 level.

### Secondary: Part A: Change From Baseline in Total Motor AIMS Score at Week 145, as Assessed by the Site Rating

|                 |  |
|-----------------|--|
| End point title | Part A: Change From Baseline in Total Motor AIMS Score at Week 145, as Assessed by the Site Rating |
|-----------------|--|

End point description:

The AIMS is an assessment tool used to detect and follow the severity of tardive dyskinesia (TD) over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

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

End point timeframe:

Baseline, Week 145

|                                  |                 |  |  |  |
|----------------------------------|-----------------|--|--|--|
| <b>End point values</b>          | SD-809          |  |  |  |
| Subject group type               | Reporting group |  |  |  |
| Number of subjects analysed      | 160             |  |  |  |
| Units: units on a scale          |                 |  |  |  |
| arithmetic mean (standard error) | -6.6 (± 0.37)   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Change From Baseline in Total Motor AIMS Score at Week 158, as Assessed by the Site Rating

|                 |   |
|-----------------|---|
| End point title | Part A: Change From Baseline in Total Motor AIMS Score at |
|-----------------|---|

## End point description:

The AIMS is an assessment tool used to detect and follow the severity of TD over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

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

End point timeframe:

Baseline, Week 158

| End point values                 | SD-809             |  |  |  |
|----------------------------------|--------------------|--|--|--|
| Subject group type               | Reporting group    |  |  |  |
| Number of subjects analysed      | 34                 |  |  |  |
| Units: units on a scale          |                    |  |  |  |
| arithmetic mean (standard error) | -6.3 ( $\pm$ 0.85) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percent Change From Baseline in Total Motor AIMS Score at Week 145, as Assessed by the Site Rating

|                 |  |
|-----------------|--|
| End point title | Part A: Percent Change From Baseline in Total Motor AIMS Score at Week 145, as Assessed by the Site Rating |
|-----------------|--|

## End point description:

The AIMS is an assessment tool used to detect and follow the severity of TD over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

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

End point timeframe:

Baseline, Week 145

| End point values                 | SD-809          |  |  |  |
|----------------------------------|-----------------|--|--|--|
| Subject group type               | Reporting group |  |  |  |
| Number of subjects analysed      | 159             |  |  |  |
| Units: percent change            |                 |  |  |  |
| arithmetic mean (standard error) | -57.0 (± 2.43)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percent Change From Baseline in Total Motor AIMS Score at Week 158, as Assessed by the Site Rating

|                 |  |
|-----------------|--|
| End point title | Part A: Percent Change From Baseline in Total Motor AIMS Score at Week 158, as Assessed by the Site Rating |
|-----------------|--|

End point description:

The AIMS is an assessment tool used to detect and follow the severity of TD over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

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

End point timeframe:

Baseline, Week 158

| End point values                 | SD-809          |  |  |  |
|----------------------------------|-----------------|--|--|--|
| Subject group type               | Reporting group |  |  |  |
| Number of subjects analysed      | 34              |  |  |  |
| Units: percent change            |                 |  |  |  |
| arithmetic mean (standard error) | -54.9 (± 6.76)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants who had a 50% or Greater Reduction From Baseline in Total Motor AIMS Score, as Assessed by the Site Rating

|                 |   |
|-----------------|---|
| End point title | Part A: Percentage of Participants who had a 50% or Greater Reduction From Baseline in Total Motor AIMS Score, as Assessed by the Site Rating |
|-----------------|---|

End point description:

The AIMS is an assessment tool used to detect and follow the severity of TD over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral

movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline to Week 145 |           |

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | SD-809          |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 159             |  |  |  |
| Units: percentage of participants | 67              |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part A: Change From Baseline in AIMS Items 8, 9, and 10 Score at Week 145, as Assessed by the Site Rating

|                 |   |
|-----------------|---|
| End point title | Part A: Change From Baseline in AIMS Items 8, 9, and 10 Score at Week 145, as Assessed by the Site Rating |
|-----------------|---|

End point description:

AIMS is composed of 12 clinician-administered and -scored items. Items 8 to 10 deal with global severity as judged by the examiner, and the participant's awareness of the movements and distress associated with them. Item 8 (used as an overall severity index indicating severity of abnormal movements) was rated on a 5-point anchored scale ranging from 0 (no dyskinetic movements) to 4 (severe dyskinetic movements). Items 9 and 10 (provide additional information with regard to participant's incapacitation due to abnormal movements and participant's awareness of abnormal movements) were rated on a 5-point anchored scale ranging from 0 (none or no awareness) to 4 (severe or aware, severe distress). Higher scores indicated more severe disease. ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this endpoint.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline, Week 145   |           |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| <b>End point values</b>                  | SD-809          |  |  |  |
| Subject group type                       | Reporting group |  |  |  |
| Number of subjects analysed              | 160             |  |  |  |
| Units: units on a scale                  |                 |  |  |  |
| arithmetic mean (standard error)         |                 |  |  |  |
| Severity of abnormal movements           | -1.3 (± 0.07)   |  |  |  |
| Incapacitation due to abnormal movements | -1.3 (± 0.08)   |  |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| Participant's awareness of abnormal movements | -1.3 (± 0.09) |  |  |  |
|---|---------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants who had a 70% or Greater Reduction From Baseline in Total Motor AIMS Score, as Assessed by the Site Rating

|  |   |
|--|---|
| End point title  | Part A: Percentage of Participants who had a 70% or Greater Reduction From Baseline in Total Motor AIMS Score, as Assessed by the Site Rating |
| End point description:   |   |
| The AIMS is an assessment tool used to detect and follow the severity of TD over time. The AIMS is composed of 12 clinician-administered and -scored items. A total motor score from Items 1 to 7 (orofacial, extremity, and truncal movements) was calculated. Items 1 through 7 included facial and oral movements (Items 1-4), extremity movements (Items 5-6), and trunk movements (Item 7). Each item was rated on a 5-point anchored scale ranging from 0 (no dyskinesia) to 4 (severe dyskinesia). Total motor AIMS score for Items 1-7 ranged from 0 to 28, with higher scores indicative of more severe dyskinesia. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this outcome measure. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline to Week 145   |   |

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | SD-809          |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 159             |  |  |  |
| Units: percentage of participants | 42              |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants who Were a Treatment Success, Based on the Clinical Global Impression of Change (CGIC)

|   |   |
|---|---|
| End point title   | Part A: Percentage of Participants who Were a Treatment Success, Based on the Clinical Global Impression of Change (CGIC) |
| End point description:  |   |
| A treatment success was defined as much or very much improved on the CGIC from baseline of this study. The CGIC is a single-item questionnaire that asks the investigator to assess a participant's TD symptoms at specific visits/weeks after initiating therapy. The CGIC uses a 7-point Likert scale, ranging from -3 to +3 (-3 = very much worse, -2 = much worse, -1 = minimally worse, 0 = not changed, 1 = minimally improved, 2 = much improved, 3 = very much improved), to assess overall response to therapy. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants |   |



analyzed' signifies participants evaluable for this endpoint.

|                         |           |
|-------------------------|-----------|
| End point type          | Secondary |
| End point timeframe:    |           |
| Baseline up to Week 145 |           |

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | SD-809          |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 160             |  |  |  |
| Units: percentage of participants | 73              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Percentage of Participants who Were a Treatment Success, Based on the Patient Global Impression of Change (PGIC)

|                 |  |
|-----------------|--|
| End point title | Part A: Percentage of Participants who Were a Treatment Success, Based on the Patient Global Impression of Change (PGIC) |
|-----------------|--|

End point description:

A treatment success was defined as much or very much improved on the PGIC from baseline of this study. The PGIC is single-item questionnaire that asks the participant to assess their TD symptoms at specific visits/weeks after initiating therapy. The PGIC uses a 7-point Likert scale, ranging from -3 to +3 (-3 = very much worse, -2 = much worse, -1 = minimally worse, 0 = not changed, 1 = minimally improved, 2 = much improved, 3 = very much improved), to assess overall response to therapy. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this endpoint.

|                         |           |
|-------------------------|-----------|
| End point type          | Secondary |
| End point timeframe:    |           |
| Baseline up to Week 145 |           |

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | SD-809          |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 161             |  |  |  |
| Units: percentage of participants | 63              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Part A: Change From Baseline in Modified CDQ-24 Score at Week 158

|                 |  |
|-----------------|--|
| End point title | Part A: Change From Baseline in Modified CDQ-24 Score at |
|-----------------|--|

**End point description:**

The CDQ-24 is a disease-specific quality of life questionnaire developed for use in participants with craniocervical dystonia, including both cervical dystonia (CD) and blepharospasm (BPS). The CDQ-24 was modified such that the questions focus more directly on the impact of TD (as opposed to CD/BPS) on quality of life. The following domains were evaluated in the mCDQ-24: stigma, emotional well-being, pain, activities of daily living, and social/family life. Each of the 24 questions were rated by participants on a scale of 0 = never or no impairment to 4 = always or very severe impairment. Total score ranged from 0 – 96, with higher score indicative of severe impairment. The ITT population included all participants who were enrolled in the study, regardless of whether or not a participant received a dose of study drug. Here, 'Overall number of participants analyzed' signifies participants evaluable for this endpoint.

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

**End point timeframe:**

Baseline, Week 158

| End point values                 | SD-809          |  |  |  |
|----------------------------------|-----------------|--|--|--|
| Subject group type               | Reporting group |  |  |  |
| Number of subjects analysed      | 39              |  |  |  |
| Units: units on a scale          |                 |  |  |  |
| arithmetic mean (standard error) | -6.3 (± 2.61)   |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to the end of follow-up (4 weeks after the last dose of study drug; mean exposure: up to approximately 866.1 days)

Adverse event reporting additional description:

Adverse events were analyzed as one group combined for Parts A and B and as a separate group for Part C per planned analysis.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Part A and Part B Participants |
|-----------------------|--------------------------------|

Reporting group description:

Participants received SD-809 orally BID starting at 12 mg/day, which was titrated based on dyskinesia control and tolerability up to a maximum total dose of 48 mg/day. Participants who declined to participate in Part B, continued at their stable dose of SD-809 BID up to Week 158. Participants who agreed to participate in Part B, received SD-809 or placebo matched to SD-809 for 1 week in randomized withdrawal period and thereafter received SD-809 (stable dose) for 12 weeks.

|                       |                |
|-----------------------|----------------|
| Reporting group title | Part C: SD-809 |
|-----------------------|----------------|

Reporting group description:

EU participants who completed Part B and willing to continue in the study continued treatment with SD-809 for 52 weeks at the current dose administered during the 12-week open-label period of Part B.

| Serious adverse events  | Part A and Part B Participants | Part C: SD-809 |  |
|---|--------------------------------|----------------|--|
| Total subjects affected by serious adverse events                   |                                |                |  |
| subjects affected / exposed   | 68 / 337 (20.18%)              | 5 / 80 (6.25%) |  |
| number of deaths (all causes)                                       | 8                              | 2              |  |
| number of deaths resulting from adverse events                      |                                |                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                |                |  |
| Anal squamous cell carcinoma  |                                |                |  |
| subjects affected / exposed   | 1 / 337 (0.30%)                | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 1                          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0                          | 0 / 0          |  |
| Benign breast neoplasm  |                                |                |  |
| subjects affected / exposed   | 1 / 337 (0.30%)                | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 1                          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0                          | 0 / 0          |  |
| Breast cancer   |                                |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Prostate cancer                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Squamous cell carcinoma of skin                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Squamous cell carcinoma of the tongue           |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Transitional cell carcinoma                     |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Vascular disorders                              |                 |                |  |
| Deep vein thrombosis                            |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Iliac artery occlusion                          |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Peripheral ischaemia                            |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Circulatory collapse                            |                 |                |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed                          | 0 / 337 (0.00%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1          |  |
| General disorders and administration site conditions |                 |                |  |
| Non-cardiac chest pain                               |                 |                |  |
| subjects affected / exposed                          | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                |  |
| Acute respiratory failure                            |                 |                |  |
| subjects affected / exposed                          | 1 / 337 (0.30%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1          |  |
| Chronic obstructive pulmonary disease                |                 |                |  |
| subjects affected / exposed                          | 4 / 337 (1.19%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 8           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Interstitial lung disease                            |                 |                |  |
| subjects affected / exposed                          | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Pneumonia aspiration                                 |                 |                |  |
| subjects affected / exposed                          | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Pulmonary embolism                                   |                 |                |  |
| subjects affected / exposed                          | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Respiratory failure                                  |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Psychiatric disorders                           |                 |                |  |
| Anxiety   |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Depression                                      |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Depressive symptom                              |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Homicidal ideation                              |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypomania                                       |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Mania   |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Mental status changes                           |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Psychotic disorder                              |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Schizoaffective disorder                        |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Schizophrenia                                   |                 |                |  |
| subjects affected / exposed                     | 5 / 337 (1.48%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Suicidal ideation                               |                 |                |  |
| subjects affected / exposed                     | 3 / 337 (0.89%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Suicide attempt                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Schizophrenia, paranoid type                    |                 |                |  |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                 |                |  |
| Ankle fracture                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Burns second degree                             |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Carbon monoxide poisoning                       |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Facial bones fracture                           |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Femur fracture                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Humerus fracture                                |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Intentional overdose                            |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Procedural pain                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Spinal fracture                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Tendon rupture                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Thermal burn                                    |                 |                |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Tibia fracture                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Traumatic haemothorax                           |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cardiac disorders                               |                 |                |  |
| Angina pectoris                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cardiac arrest                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Cardiac failure                                 |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1          |  |
| Cardiopulmonary failure                         |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Cardiovascular insufficiency                    |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Myocardial infarction                           |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Ventricular tachycardia                         |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Acute myocardial infarction                     |                 |                |  |
| subjects affected / exposed                     | 0 / 337 (0.00%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Nervous system disorders                        |                 |                |  |
| Cerebrovascular accident                        |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Epilepsy  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Generalised non-convulsive epilepsy             |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Migraine  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Transient ischaemic attack                      |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders            |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Anaemia   |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastrointestinal disorders                      |                 |                |  |
| Diarrhoea                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastric ulcer perforation                       |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pancreatic duct stenosis                        |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hepatobiliary disorders                         |                 |                |  |
| Cholelithiasis                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hepatic cyst                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Liver disorder                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Renal and urinary disorders                     |                 |                |  |
| Renal failure acute                             |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Stress urinary incontinence                     |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Osteoarthritis                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| Appendicitis                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cholecystitis infective                         |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Colonic abscess                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cystitis  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Diverticulitis                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Gangrene  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastroenteritis                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Mycobacterium avium complex infection           |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia                                       |                 |                |  |
| subjects affected / exposed                     | 4 / 337 (1.19%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pulmonary tuberculosis                          |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sepsis  |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Septic shock                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Urinary tract infection                         |                 |                |  |
| subjects affected / exposed                     | 2 / 337 (0.59%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Metabolism and nutrition disorders              |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Dehydration                                     |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 1 / 80 (1.25%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Diabetic ketoacidosis                           |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Failure to thrive                               |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypoglycaemia                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hyponatraemia                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 337 (0.30%) | 0 / 80 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Part A and Part B<br>Participants | Part C: SD-809 |  |
|---|-----------------------------------|----------------|--|
| Total subjects affected by non-serious adverse events |                                   |                |  |
| subjects affected / exposed                           | 172 / 337 (51.04%)                | 5 / 80 (6.25%) |  |
| Investigations  |                                   |                |  |
| Weight decreased                                      |                                   |                |  |
| subjects affected / exposed                           | 32 / 337 (9.50%)                  | 0 / 80 (0.00%) |  |
| occurrences (all)                                     | 34                                | 0              |  |
| Injury, poisoning and procedural complications        |                                   |                |  |
| Fall  |                                   |                |  |
| subjects affected / exposed                           | 18 / 337 (5.34%)                  | 0 / 80 (0.00%) |  |
| occurrences (all)                                     | 23                                | 0              |  |

|  |   |   |  |
|--|---|---|--|
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)   | 23 / 337 (6.82%)<br>25  | 1 / 80 (1.25%)<br>1   |  |
| Nervous system disorders<br>Dyskinesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Somnolence<br>subjects affected / exposed<br>occurrences (all) | 22 / 337 (6.53%)<br>29<br><br>24 / 337 (7.12%)<br>31<br><br>34 / 337 (10.09%)<br>41 | 2 / 80 (2.50%)<br>2<br><br>0 / 80 (0.00%)<br>0<br><br>0 / 80 (0.00%)<br>0 |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 27 / 337 (8.01%)<br>32  | 0 / 80 (0.00%)<br>0   |  |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)<br><br>Depression<br>subjects affected / exposed<br>occurrences (all)   | 41 / 337 (12.17%)<br>51<br><br>35 / 337 (10.39%)<br>45                              | 0 / 80 (0.00%)<br>0<br><br>0 / 80 (0.00%)<br>0                            |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)  | 20 / 337 (5.93%)<br>28<br><br>31 / 337 (9.20%)<br>56                                | 2 / 80 (2.50%)<br>2<br><br>0 / 80 (0.00%)<br>0                            |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 14 October 2015   | <p>The following major procedural changes (not all-inclusive) were made to the protocol:</p> <ul style="list-style-type: none"><li>- Participants who previously participated in another study of TEV-50717 for the treatment of moderate to severe TD, including Study C-23, were allowed to participate in Study C-20.</li><li>- The long-term treatment period was extended from 1 year to 2 years, and clinic visits were added at Weeks 67, 80, 93, and 106/end of treatment (ET). The follow-up clinic visit was changed to Week 107, and telephone contact was changed to Week 110.</li><li>- Hepatic or renal impairment at screening of the parent study was considered exclusionary.</li></ul>  |
| 27 September 2016 | <p>The following major procedural changes (not all-inclusive) were made to the protocol:</p> <ul style="list-style-type: none"><li>- The long-term treatment period was extended from 2 years to 3 years, and clinic visits were added at Weeks 119, 132, 145, and 158/ET. The follow-up clinic visit was changed to Week 159, and telephone contact was changed to Week 162.</li><li>- Treatment modification instructions regarding maximum dosage were expanded with greater detail for weight-based dosing and strong CYP2D6 inhibitor use, allowing doses up to 42 mg for participants <math>\geq 100</math> kg and doses up to 36 for participants <math>&lt; 100</math> mg.</li><li>- It was added that participants who have not achieved adequate control of dyskinesia during the study may have up to 2 blood samples collected for future pharmacokinetic assessment of <math>\alpha</math>- and <math>\beta</math>- dihydrotetrabenazine (HTBZ).</li></ul> |
| 08 February 2017  | <p>The following major procedural changes (not all-inclusive) were made to the protocol:</p> <ul style="list-style-type: none"><li>- As hypokalemia and hypomagnesaemia may contribute to QT prolongation, criteria for suspending treatment were added in case a participant's potassium or magnesium levels fall below the lower limit of normal.</li><li>- If the participant met either of the following criteria, study treatment was discontinued and an ET visit was conducted: a mean QTcF value <math>&gt; 500</math> msec or a mean change in QTcF of <math>&gt; 60</math> msec from baseline.</li><li>- Given the potential for many antipsychotics to prolong the QT interval, additional electrocardiogram (ECG) monitoring was added if participants increased antipsychotic dose, switched to a new antipsychotic, or had a new antipsychotic treatment added to their regimen.</li></ul>  |
| 23 January 2018   | <p>The following major procedural changes (not all-inclusive) were made to the protocol:</p> <ul style="list-style-type: none"><li>- The optional double-blind, placebo-controlled randomization withdrawal period (Part B) was added to the study with the objective to evaluate the persistence of the therapeutic effect of TEV-50717. The previous study design was labeled Part A for differentiation.</li><li>- The time period was updated from 3 to 4 weeks after EOT/ET visit.</li><li>- The requirement for participants to discuss reasons for study withdrawal with medical monitor or sponsor clinician was removed.</li><li>- Dose reduction instructions to include CYP2D were added.</li><li>- The AIMS video recording measure was removed.</li></ul>  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No



## Limitations and caveats

None reported