

**Clinical trial results:****A Double-blind, Randomized, Placebo-controlled Phase 3 Study of Orally Administered PLX3397 in Subjects with Pigmented Villonodular Synovitis or Giant Cell Tumor of the Tendon Sheath****Summary**

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2014-000148-14          |
| Trial protocol           | HU DE DK GB NL ES PL IT |
| Global end of trial date | 30 April 2021           |

**Results information**

|                                |                                                                                                                             |
|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| Result version number          | v2 (current)                                                                                                                |
| This version publication date  | 15 May 2022                                                                                                                 |
| First version publication date | 26 July 2019                                                                                                                |
| Version creation reason        | <ul style="list-style-type: none"><li>• New data added to full data set</li><li>New data to add to full data set.</li></ul> |

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

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | PLX108-10 |
|-----------------------|-----------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02371369 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |                                                                                   |
|------------------------------|-----------------------------------------------------------------------------------|
| Sponsor organisation name    | Daiichi Sankyo, Inc.                                                              |
| Sponsor organisation address | 211 Mount Airy Road, Basking Ridge, NJ, United States, 07920                      |
| Public contact               | Clinical Trial Information, Daiichi Sankyo, Inc., 1 908-992-6400, CTRinfo@dsi.com |
| Scientific contact           | Clinical Trial Information, Daiichi Sankyo, Inc., 1 908-992-6400, CTRinfo@dsi.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                       | 27 March 2017 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 27 March 2017 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 30 April 2021 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the response rate of PLX3397 with that of placebo per Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST 1.1) at Week 25 in subjects with symptomatic, locally advanced pigmented villonodular synovitis (PVNS) or giant cell tumor of tendon sheath (GCT-TS).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the ICH Harmonised Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 31 March 2015    |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 4 Years          |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 12     |
| Country: Number of subjects enrolled | Canada: 5         |
| Country: Number of subjects enrolled | Netherlands: 11   |
| Country: Number of subjects enrolled | Poland: 2         |
| Country: Number of subjects enrolled | Spain: 8          |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Denmark: 3        |
| Country: Number of subjects enrolled | France: 7         |
| Country: Number of subjects enrolled | Germany: 6        |
| Country: Number of subjects enrolled | Hungary: 3        |
| Country: Number of subjects enrolled | Italy: 17         |
| Country: Number of subjects enrolled | United States: 45 |
| Worldwide total number of subjects   | 120               |
| EEA total number of subjects         | 58                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| 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)                      | 113 |
| From 65 to 84 years                       | 7   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Part 1 was a double-blind, randomized, placebo-controlled study in subjects with symptomatic TGCT for whom surgical resection would be associated with potentially worsening functional limitation or severe morbidity. Part 2 is a long-term treatment phase in which subjects receive open-label pexidartinib.

### Pre-assignment

Screening details:

Subjects were screened for inclusion and exclusion criteria. Screening procedures were performed after consent was obtained and within the 42 days before the first dose of study drug, unless otherwise noted.

### Period 1

|                              |                           |
|------------------------------|---------------------------|
| Period 1 title               | Part 1 (randomized phase) |
| Is this the baseline period? | Yes                       |
| Allocation method            | Randomised - controlled   |
| Blinding used                | Double blind              |
| Roles blinded                | Subject, Investigator     |

Blinding implementation details:

The pexidartinib and placebo capsules were identical in appearance to maintain the blind during Part 1.

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | Pexidartinib (Part 1) |

Arm description:

Subjects randomized to pexidartinib for 24 weeks administered twice a day.

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

Dosage and administration details:

1000 mg (5 capsules per day) for 2 weeks, then 800 mg (4 capsules per day) for 22 weeks; each capsule contained 200 mg of pexidartinib; oral administration twice a day.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Placebo (Part 1) |
|------------------|------------------|

Arm description:

Subjects randomized to matching placebo for 24 weeks administered twice a day.

|                                        |          |
|----------------------------------------|----------|
| 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 capsule matching pexidartinib capsule was administered orally (5 capsules per day) for 2 weeks, then matching placebo (4 capsules per day).

| Number of subjects in period 1 | Pexidartinib (Part 1) | Placebo (Part 1) |
|--------------------------------|-----------------------|------------------|
| Started                        | 61                    | 59               |
| Completed                      | 52                    | 48               |
| Not completed                  | 9                     | 11               |
| Subject noncompliance          | -                     | 1                |
| Consent withdrawn by subject   | 1                     | 6                |
| Physician decision             | -                     | 3                |
| Disease progression            | -                     | 1                |
| Adverse event, non-fatal       | 8                     | -                |

## Period 2

|                              |                           |
|------------------------------|---------------------------|
| Period 2 title               | Part 2 (open-label phase) |
| Is this the baseline period? | No                        |
| Allocation method            | Not applicable            |
| Blinding used                | Not blinded               |

## Arms

|                              |                              |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | No                           |
| <b>Arm title</b>             | Pexidartinib (Parts 1 and 2) |

### Arm description:

Subjects received pexidartinib in Part 1 and Part 2 at their prescribed dose.

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

### Dosage and administration details:

Dose in Part 2 was the pexidartinib dose received at the end of Part 1.

|                  |                                                   |
|------------------|---------------------------------------------------|
| <b>Arm title</b> | Placebo (Part 1), Crossover Pexidartinib (Part 2) |
|------------------|---------------------------------------------------|

### Arm description:

Subjects received placebo in Part 1 and pexidartinib in Part 2 at their prescribed dose.

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

### Dosage and administration details:

Dose in Part 2 was the pexidartinib equivalent dose of placebo at the end of Part 1.

|                                        |         |
|----------------------------------------|---------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code |         |
| Other name                             |         |
| Pharmaceutical forms                   | Capsule |

|                          |          |
|--------------------------|----------|
| Routes of administration | Oral use |
|--------------------------|----------|

Dosage and administration details:

Placebo capsule matching pexidartinib capsule was administered orally (5 capsules per day) for 2 weeks, then matching placebo (4 capsules per day).

| Number of subjects in period 2                    | Pexidartinib (Parts 1 and 2) | Placebo (Part 1), Crossover Pexidartinib (Part 2) |
|---------------------------------------------------|------------------------------|---------------------------------------------------|
|                                                   |                              |                                                   |
| Started                                           | 48                           | 30                                                |
| Completed                                         | 0                            | 0                                                 |
| Not completed                                     | 48                           | 30                                                |
| Subject noncompliance                             | 1                            | -                                                 |
| Physician decision                                | 1                            | 2                                                 |
| Disease progression                               | 1                            | -                                                 |
| Adverse Event                                     | 6                            | 5                                                 |
| Lost to Follow-up                                 | 1                            | 1                                                 |
| Subject moved to another DS pexidartinib protocol | 15                           | -                                                 |
| Death                                             | -                            | 1                                                 |
| Not specified                                     | -                            | 1                                                 |
| Subject moved to another DS pexidartinib protocol | -                            | 9                                                 |
| Withdrawal by Subject                             | 16                           | 6                                                 |
| Subject transitioned to commercial supply         | 6                            | 4                                                 |
| Surgical resection of tumor                       | 1                            | 1                                                 |

## Baseline characteristics

### Reporting groups

|                                                                                                                |                       |
|----------------------------------------------------------------------------------------------------------------|-----------------------|
| Reporting group title                                                                                          | Pexidartinib (Part 1) |
| Reporting group description:<br>Subjects randomized to pexidartinib for 24 weeks administered twice a day.     |                       |
| Reporting group title                                                                                          | Placebo (Part 1)      |
| Reporting group description:<br>Subjects randomized to matching placebo for 24 weeks administered twice a day. |                       |

| Reporting group values                                | Pexidartinib (Part 1) | Placebo (Part 1) | Total |
|-------------------------------------------------------|-----------------------|------------------|-------|
| Number of subjects                                    | 61                    | 59               | 120   |
| Age categorical<br>Units: Subjects                    |                       |                  |       |
| In utero                                              | 0                     | 0                | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0                     | 0                | 0     |
| Newborns (0-27 days)                                  | 0                     | 0                | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0                     | 0                | 0     |
| Children (2-11 years)                                 | 0                     | 0                | 0     |
| Adolescents (12-17 years)                             | 0                     | 0                | 0     |
| Adults (18-64 years)                                  | 57                    | 56               | 113   |
| From 65-84 years                                      | 4                     | 3                | 7     |
| 85 years and over                                     | 0                     | 0                | 0     |
| Age continuous<br>Units: years                        |                       |                  |       |
| arithmetic mean                                       | 44.6                  | 44.3             |       |
| standard deviation                                    | ± 13.2                | ± 13.6           | -     |
| Gender categorical<br>Units: Subjects                 |                       |                  |       |
| Female                                                | 35                    | 36               | 71    |
| Male                                                  | 26                    | 23               | 49    |

### Subject analysis sets

|                                                                                                                                                                                                                                                                                                                                      |                                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| Subject analysis set title                                                                                                                                                                                                                                                                                                           | All Pexidartinib Treated            |
| Subject analysis set type                                                                                                                                                                                                                                                                                                            | Intention-to-treat                  |
| Subject analysis set description:<br>Includes all subjects who received pexidartinib in Part 1 and Part 2 (placebo crossed over to pexidartinib).                                                                                                                                                                                    |                                     |
| Subject analysis set title                                                                                                                                                                                                                                                                                                           | Pexidartinib Part 1 and Part 2      |
| Subject analysis set type                                                                                                                                                                                                                                                                                                            | Sub-group analysis                  |
| Subject analysis set description:<br>Participants received treatment of Pexidartinib, 1000 mg (5 capsules per day) for 2 weeks, then 800 mg (4 capsules per day) for 22 weeks and also received Pexidartinib in Part 2 at their prescribed dose. Pexidartinib: Each capsule contains 200 mg of Pexidartinib for oral administration. |                                     |
| Subject analysis set title                                                                                                                                                                                                                                                                                                           | Placebo Part 1, Pexidartinib Part 2 |
| Subject analysis set type                                                                                                                                                                                                                                                                                                            | Sub-group analysis                  |

Subject analysis set description:

Participants received treatment of matching placebo (5 capsules per day) for 2 weeks, then matching placebo (4 capsules per day) for 22 weeks in Part 1 and also received Pexidartinib in Part 2 at their prescribed dose. Placebo: Placebo capsule matching Pexidartinib capsule for oral administration  
Pexidartinib: Each capsule contains 200 mg of Pexidartinib for oral administration.

| Reporting group values                             | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |
|----------------------------------------------------|--------------------------|--------------------------------|-------------------------------------|
| Number of subjects                                 | 91                       | 61                             | 30                                  |
| Age categorical<br>Units: Subjects                 |                          |                                |                                     |
| In utero                                           | 0                        |                                |                                     |
| Preterm newborn infants (gestational age < 37 wks) | 0                        |                                |                                     |
| Newborns (0-27 days)                               | 0                        |                                |                                     |
| Infants and toddlers (28 days-23 months)           | 0                        |                                |                                     |
| Children (2-11 years)                              | 0                        |                                |                                     |
| Adolescents (12-17 years)                          | 0                        |                                |                                     |
| Adults (18-64 years)                               | 85                       |                                |                                     |
| From 65-84 years                                   | 6                        |                                |                                     |
| 85 years and over                                  | 0                        |                                |                                     |
| Age continuous<br>Units: years                     |                          |                                |                                     |
| arithmetic mean                                    | 45.6                     |                                |                                     |
| standard deviation                                 | ± 13.2                   | ±                              | ±                                   |
| Gender categorical<br>Units: Subjects              |                          |                                |                                     |
| Female                                             | 51                       |                                |                                     |
| Male                                               | 40                       |                                |                                     |



## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                               | Pexidartinib (Part 1)                             |
| Reporting group description:<br>Subjects randomized to pexidartinib for 24 weeks administered twice a day.                                                                                                                                                                                                                                                                                                                          |                                                   |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                               | Placebo (Part 1)                                  |
| Reporting group description:<br>Subjects randomized to matching placebo for 24 weeks administered twice a day.                                                                                                                                                                                                                                                                                                                      |                                                   |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                               | Pexidartinib (Parts 1 and 2)                      |
| Reporting group description:<br>Subjects received pexidartinib in Part 1 and Part 2 at their prescribed dose.                                                                                                                                                                                                                                                                                                                       |                                                   |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                               | Placebo (Part 1), Crossover Pexidartinib (Part 2) |
| Reporting group description:<br>Subjects received placebo in Part 1 and pexidartinib in Part 2 at their prescribed dose.                                                                                                                                                                                                                                                                                                            |                                                   |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                          | All Pexidartinib Treated                          |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                           | Intention-to-treat                                |
| Subject analysis set description:<br>Includes all subjects who received pexidartinib in Part 1 and Part 2 (placebo crossed over to pexidartinib).                                                                                                                                                                                                                                                                                   |                                                   |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                          | Pexidartinib Part 1 and Part 2                    |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                           | Sub-group analysis                                |
| Subject analysis set description:<br>Participants received treatment of Pexidartinib, 1000 mg (5 capsules per day) for 2 weeks, then 800 mg (4 capsules per day) for 22 weeks and also received Pexidartinib in Part 2 at their prescribed dose. Pexidartinib: Each capsule contains 200 mg of Pexidartinib for oral administration.                                                                                                |                                                   |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                          | Placebo Part 1, Pexidartinib Part 2               |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                           | Sub-group analysis                                |
| Subject analysis set description:<br>Participants received treatment of matching placebo (5 capsules per day) for 2 weeks, then matching placebo (4 capsules per day) for 22 weeks in Part 1 and also received Pexidartinib in Part 2 at their prescribed dose. Placebo: Placebo capsule matching Pexidartinib capsule for oral administration. Pexidartinib: Each capsule contains 200 mg of Pexidartinib for oral administration. |                                                   |

### **Primary: Percentage of Subjects With Symptomatic, Locally Advanced Tenosynovial Giant Cell Tumor (TGCT) Achieving Complete or Partial Response to Pexidartinib Compared With That of Placebo per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 at Week 25**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Percentage of Subjects With Symptomatic, Locally Advanced Tenosynovial Giant Cell Tumor (TGCT) Achieving Complete or Partial Response to Pexidartinib Compared With That of Placebo per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 at Week 25 |
| End point description:<br>Complete (CR) and partial responses (PR) were assessed based on centrally-read magnetic resonance imaging (MRI) scans and Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST 1.1). A CR was defined as disappearance of all tumors and a PR was defined as at least a 30% decrease in the sum of diameters of target tumors using the baseline sum diameters as the reference. Best overall response was assessed in the ITT population. |                                                                                                                                                                                                                                                              |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Primary                                                                                                                                                                                                                                                      |
| End point timeframe:<br>Week 25                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                              |

| <b>End point values</b>       | Pexidartinib (Part 1) | Placebo (Part 1) |  |  |
|-------------------------------|-----------------------|------------------|--|--|
| Subject group type            | Reporting group       | Reporting group  |  |  |
| Number of subjects analysed   | 61                    | 59               |  |  |
| Units: Percentage of subjects |                       |                  |  |  |
| number (not applicable)       |                       |                  |  |  |
| CR                            | 14.8                  | 0                |  |  |
| PR                            | 24.6                  | 0                |  |  |
| Response (CR or PR)           | 39.3                  | 0                |  |  |

## Statistical analyses

|                                                                             |                                          |
|-----------------------------------------------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>                                           | Pexidartinib vs Placebo                  |
| Statistical analysis description:                                           |                                          |
| Treatment comparison between the pexidartinib and placebo groups at Week 25 |                                          |
| Comparison groups                                                           | Placebo (Part 1) v Pexidartinib (Part 1) |
| Number of subjects included in analysis                                     | 120                                      |
| Analysis specification                                                      | Pre-specified                            |
| Analysis type                                                               | other <sup>[1]</sup>                     |
| P-value                                                                     | < 0.0001                                 |
| Method                                                                      | Fisher's Exact Test                      |

Notes:

[1] - Treatment comparison analysis

## Secondary: Mean Change From Baseline for Range of Motion (ROM) Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 25

|                 |                                                                                                                                           |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline for Range of Motion (ROM) Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 25 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Range of motion (ROM) of the joint was assessed by a qualified, independent, and blinded or third-party assessors at the clinical site. Measurements were recorded in degrees. At baseline, the plane of movement with the smallest relative value (worst) was identified and this plane was used for evaluating the relative change of motion subsequently. Only the plane with the worst impaired ROM at baseline was selected for subsequent analyses. ROM was assessed in the ITT population.

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

End point timeframe:

Baseline, Week 13, Week 25

| End point values                              | Pexidartinib (Part 1) | Placebo (Part 1) |  |  |
|-----------------------------------------------|-----------------------|------------------|--|--|
| Subject group type                            | Reporting group       | Reporting group  |  |  |
| Number of subjects analysed                   | 61                    | 59               |  |  |
| Units: Least square mean change from baseline |                       |                  |  |  |
| least squares mean (standard error)           |                       |                  |  |  |
| Baseline (N=61, 58)                           | 62.5 (± 3.2)          | 62.9 (± 2.9)     |  |  |
| Week 13 (N=52, 53)                            | 13.0 (± 2.3)          | 4.8 (± 2.6)      |  |  |
| Week 25 (N=45, 43)                            | 15.1 (± 2.1)          | 6.2 (± 2.4)      |  |  |

## Statistical analyses

| Statistical analysis title                                                  | Pexidartinib vs Placebo                  |
|-----------------------------------------------------------------------------|------------------------------------------|
| Statistical analysis description:                                           |                                          |
| Treatment comparison between the pexidartinib and placebo groups at Week 25 |                                          |
| Comparison groups                                                           | Pexidartinib (Part 1) v Placebo (Part 1) |
| Number of subjects included in analysis                                     | 120                                      |
| Analysis specification                                                      | Pre-specified                            |
| Analysis type                                                               | other <sup>[2]</sup>                     |
| P-value                                                                     | = 0.0043                                 |
| Method                                                                      | Fisher's Exact Test                      |

Notes:

[2] - Treatment comparison analysis

## Secondary: Percentage of Subjects With Symptomatic, Locally Advanced TGCT Achieving Complete or Partial Response Based on Tumor Volume Score (TVS) After Receiving Pexidartinib Compared With Those on Placebo at Week 25

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Percentage of Subjects With Symptomatic, Locally Advanced TGCT Achieving Complete or Partial Response Based on Tumor Volume Score (TVS) After Receiving Pexidartinib Compared With Those on Placebo at Week 25 |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                |
| Complete (CR) and partial responses (PR) were assessed using tumor volume score (TVS). A CR was defined as disappearance of all tumors and a PR was defined as at least a 30% decrease in the sum of diameters of target tumors using the baseline sum diameters as the reference. TVS is a semi-quantitative MRI scoring system that describes tumor mass and is based on 10% increments of the estimated volume of the maximally distended synovial cavity or tendon sheath involved. A tumor that is equal in volume to that of a maximally distended synovial cavity or tendon sheath was scored 10; a score of 0 indicated no evidence of tumor. Best overall response was assessed in the ITT population. |                                                                                                                                                                                                                |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Secondary                                                                                                                                                                                                      |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                |
| Week 25                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                |

| End point values              | Pexidartinib (Part 1) | Placebo (Part 1) |  |  |
|-------------------------------|-----------------------|------------------|--|--|
| Subject group type            | Reporting group       | Reporting group  |  |  |
| Number of subjects analysed   | 61                    | 59               |  |  |
| Units: Percentage of subjects |                       |                  |  |  |
| number (not applicable)       |                       |                  |  |  |
| CR                            | 4.9                   | 0                |  |  |
| PR                            | 50.8                  | 0                |  |  |
| Response (CR or PR)           | 55.7                  | 0                |  |  |

## Statistical analyses

|                                                                             |                                          |
|-----------------------------------------------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>                                           | Pexidartinib vs Placebo                  |
| Statistical analysis description:                                           |                                          |
| Treatment comparison between the pexidartinib and placebo groups at Week 25 |                                          |
| Comparison groups                                                           | Pexidartinib (Part 1) v Placebo (Part 1) |
| Number of subjects included in analysis                                     | 120                                      |
| Analysis specification                                                      | Pre-specified                            |
| Analysis type                                                               | other <sup>[3]</sup>                     |
| P-value                                                                     | < 0.0001                                 |
| Method                                                                      | Fisher's Exact Test                      |

Notes:

[3] - Treatment comparison analysis

## Secondary: Mean Change From Baseline in the Patient-reported Outcomes Measurement Information System (PROMIS) Physical Function Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 25

|                 |                                                                                                                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline in the Patient-reported Outcomes Measurement Information System (PROMIS) Physical Function Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 25 |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The Patient-reported Outcomes Measurement Information System (PROMIS) physical function scale was used to assess physical function of the upper and lower limbs. Physical function was assessed in the ITT population.

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

End point timeframe:

Baseline, Week 9, Week 17, Week 25

| End point values                              | Pexidartinib (Part 1) | Placebo (Part 1) |  |  |
|-----------------------------------------------|-----------------------|------------------|--|--|
| Subject group type                            | Reporting group       | Reporting group  |  |  |
| Number of subjects analysed                   | 61                    | 59               |  |  |
| Units: Least square mean change from baseline |                       |                  |  |  |
| least squares mean (standard error)           |                       |                  |  |  |
| Baseline (N=60, 57)                           | 37.5 (± 0.6)          | 38.9 (± 0.8)     |  |  |
| Week 9 (N=38, 41)                             | 2.8 (± 1.0)           | -0.4 (± 0.8)     |  |  |
| Week 17 (N=39, 40)                            | 3.2 (± 1.1)           | 0.2 (± 1.0)      |  |  |

|                    |                  |                   |  |  |
|--------------------|------------------|-------------------|--|--|
| Week 25 (N=38, 31) | 4.1 ( $\pm$ 1.1) | -0.9 ( $\pm$ 1.0) |  |  |
|--------------------|------------------|-------------------|--|--|

## Statistical analyses

|                                   |                         |
|-----------------------------------|-------------------------|
| <b>Statistical analysis title</b> | Pexidartinib vs Placebo |
|-----------------------------------|-------------------------|

Statistical analysis description:

Treatment comparison between the pexidartinib and placebo groups at Week 25

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| Comparison groups                       | Pexidartinib (Part 1) v Placebo (Part 1) |
| Number of subjects included in analysis | 120                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other <sup>[4]</sup>                     |
| P-value                                 | = 0.0019                                 |
| Method                                  | Mixed effects model for repeated measure |

Notes:

[4] - Treatment comparison analysis

## Secondary: Mean Change From Baseline for Worst Stiffness Numeric Rating Scale Score (NRS) in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 25

|                 |                                                                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline for Worst Stiffness Numeric Rating Scale Score (NRS) in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 25 |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The Worst Stiffness Numeric Rating Scale (NRS) was a 1-item, self-administered questionnaire assessing the "worst" stiffness in the last 24 hours. The NRS for this item ranged from 0 (no stiffness) to 10 (stiffness as bad as you can imagine). Worst stiffness was assessed in the ITT population.

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

End point timeframe:

Baseline, Week 9, Week 17, Week 25

| <b>End point values</b>                       | Pexidartinib (Part 1) | Placebo (Part 1)  |  |  |
|-----------------------------------------------|-----------------------|-------------------|--|--|
| Subject group type                            | Reporting group       | Reporting group   |  |  |
| Number of subjects analysed                   | 61                    | 59                |  |  |
| Units: Least square mean change from baseline |                       |                   |  |  |
| least squares mean (standard error)           |                       |                   |  |  |
| Baseline (N=59, 58)                           | 5.6 ( $\pm$ 0.2)      | 5.9 ( $\pm$ 0.3)  |  |  |
| Week 9 (N=30, 38)                             | -1.5 ( $\pm$ 0.3)     | -0.5 ( $\pm$ 0.3) |  |  |
| Week 17 (N=37, 30)                            | -2.4 ( $\pm$ 0.3)     | -0.4 ( $\pm$ 0.3) |  |  |
| Week 25 (N=33, 35)                            | -2.5 ( $\pm$ 0.3)     | -0.3 ( $\pm$ 0.3) |  |  |

## Statistical analyses

|                                                                             |                                          |
|-----------------------------------------------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>                                           | Pexidartinib vs Placebo                  |
| Statistical analysis description:                                           |                                          |
| Treatment comparison between the pexidartinib and placebo groups at Week 25 |                                          |
| Comparison groups                                                           | Placebo (Part 1) v Pexidartinib (Part 1) |
| Number of subjects included in analysis                                     | 120                                      |
| Analysis specification                                                      | Pre-specified                            |
| Analysis type                                                               | other <sup>[5]</sup>                     |
| P-value                                                                     | < 0.0001                                 |
| Method                                                                      | Mixed effects model for repeated measure |
| Notes:                                                                      |                                          |
| [5] - Treatment comparison analysis                                         |                                          |

**Secondary: Percentage of Participants Who Responded With a Decrease of at Least 30% in the Mean Brief Pain Inventory Worst Pain Numeric Rating Scale Score Among Participants Receiving Pexidartinib Compared With Those on Placebo at Week 25**

|                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                   | Percentage of Participants Who Responded With a Decrease of at Least 30% in the Mean Brief Pain Inventory Worst Pain Numeric Rating Scale Score Among Participants Receiving Pexidartinib Compared With Those on Placebo at Week 25 |
| End point description:                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                     |
| The Brief Pain Inventory (BPI) Worst Pain NRS was a 1-item, self-administered questionnaire assessing the "worst" pain in the last 24 hours. The NRS for this item ranged from 0 (no pain) to 10 (pain as bad as you can imagine). Worst pain was assessed in the ITT population. |                                                                                                                                                                                                                                     |
| End point type                                                                                                                                                                                                                                                                    | Secondary                                                                                                                                                                                                                           |
| End point timeframe:                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                     |
| Week 25                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                     |

| <b>End point values</b>             | Pexidartinib (Part 1) | Placebo (Part 1) |  |  |
|-------------------------------------|-----------------------|------------------|--|--|
| Subject group type                  | Reporting group       | Reporting group  |  |  |
| Number of subjects analysed         | 61                    | 59               |  |  |
| Units: Proportion of responders     |                       |                  |  |  |
| number (not applicable)             |                       |                  |  |  |
| Proportion of responders (N=35, 33) | 31.1                  | 15.3             |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Responders to Pexidartinib With and Without Disease Progression**

|                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                    | Number of Responders to Pexidartinib With and Without Disease Progression |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                             |                                                                           |
| Duration of response (DOR) is defined as the date of the first recorded response to the first date of documented disease progression. The overall number of responses and the number of subjects with and without disease progression was assessed in the ITT population. The overall number of responses and the number of participants with and without disease progression were assessed in the ITT population, |                                                                           |

specifically among the Pexidartinib Part 1, Pexidartinib Part 2; Pexidartinib Part 2 only; and All Pexidartinib Treated participants. Participants randomized to Placebo Part 1 only were not analyzed.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| By Week 96           |           |

| End point values                               | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|------------------------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type                             | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed                    | 91                       | 61                             | 30                                  |  |
| Units: Number of responders                    |                          |                                |                                     |  |
| number (not applicable)                        |                          |                                |                                     |  |
| Number of responses                            | 35                       | 23                             | 12                                  |  |
| Week 12 (Day 84); Without disease progression  | 35                       | 23                             | 12                                  |  |
| Week 12 (Day 84); With disease progression     | 0                        | 0                              | 0                                   |  |
| Week 24 (Day 168); Without disease progression | 35                       | 23                             | 12                                  |  |
| Week 24 (Day 168); With disease progression    | 0                        | 0                              | 0                                   |  |
| Week 48 (Day 336); Without disease progression | 24                       | 15                             | 9                                   |  |
| Week 48 (Day 336); With disease progression    | 1                        | 1                              | 0                                   |  |
| Week 72 (Day 504); Without disease progression | 12                       | 9                              | 3                                   |  |
| Week 72 (Day 504); With disease progression    | 1                        | 1                              | 0                                   |  |
| Week 96 (Day 672); Without disease progression | 3                        | 2                              | 1                                   |  |
| Week 96 (Day 672); With disease progression    | 1                        | 1                              | 0                                   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Responders to Pexidartinib With and Without Disease Progression Based on Tumor Volume Score

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Number of Responders to Pexidartinib With and Without Disease Progression Based on Tumor Volume Score |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       |
| TVS is a semi-quantitative MRI scoring system that describes tumor mass and is based on 10% increments of the estimated volume of the maximally distended synovial cavity or tendon sheath involved. A tumor that is equal in volume to that of a maximally distended synovial cavity or tendon sheath was scored 10; a score of 0 indicated no evidence of tumor. The overall number of responses and the number of subjects with and without disease progression was assessed. The overall number of responses and the number of participants with and without disease progression was assessed in the ITT population, specifically among the Pexidartinib Part 1, Pexidartinib Part 2; Pexidartinib Part 2 only; and All Pexidartinib Treated participants. Participants who received Placebo Part 1 only were not analyzed. |                                                                                                       |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Secondary                                                                                             |

End point timeframe:

By Week 120

| End point values                                | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|-------------------------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type                              | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed                     | 91                       | 61                             | 30                                  |  |
| Units: Number of responders                     |                          |                                |                                     |  |
| number (not applicable)                         |                          |                                |                                     |  |
| Number of responses                             | 52                       | 34                             | 18                                  |  |
| Week 12 (Day 84); Without disease progression   | 51                       | 33                             | 18                                  |  |
| Week 12 (Day 84); With disease progression      | 0                        | 0                              | 0                                   |  |
| Week 24 (Day 168); Without disease progression  | 50                       | 32                             | 18                                  |  |
| Week 24 (Day 168); With disease progression     | 0                        | 0                              | 0                                   |  |
| Week 48 (Day 336); Without disease progression  | 35                       | 23                             | 13                                  |  |
| Week 48 (Day 336); With disease progression     | 4                        | 3                              | 1                                   |  |
| Week 72 (Day 504); Without disease progression  | 16                       | 13                             | 3                                   |  |
| Week 72 (Day 504); With disease progression     | 4                        | 3                              | 1                                   |  |
| Week 96 (Day 672); Without disease progression  | 4                        | 3                              | 1                                   |  |
| Week 96 (Day 672); With disease progression     | 4                        | 3                              | 1                                   |  |
| Week 120 (Day 840); Without disease progression | 1                        | 1                              | 0                                   |  |
| Week 120 (Day 840); With disease progression    | 4                        | 3                              | 1                                   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects Reporting Frequent ( $\geq 10\%$ ) Treatment-Emergent Adverse Events by Preferred Term

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Percentage of Subjects Reporting Frequent ( $\geq 10\%$ ) Treatment-Emergent Adverse Events by Preferred Term |
| End point description:<br>Treatment-emergent adverse events (TEAEs) were defined as adverse events that started or worsened after the first dose of treatment and within 28 days after the last dose. The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.0 was used to grade adverse events. Any Grade and Grade $\geq 3$ (severe) TEAEs are reported. TEAEs were coded using MedDRA version 17.1. All safety events were assessed in the Safety Analysis Set. |                                                                                                               |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Secondary                                                                                                     |

End point timeframe:

After the first dose of treatment up to 28 days after the last dose



| <b>End point values</b>            | Pexidartinib<br>(Part 1) | Pexidartinib<br>(Parts 1 and 2) | Placebo (Part<br>1) | Placebo (Part<br>1), Crossover<br>Pexidartinib<br>(Part 2) |
|------------------------------------|--------------------------|---------------------------------|---------------------|------------------------------------------------------------|
| Subject group type                 | Reporting group          | Reporting group                 | Reporting group     | Reporting group                                            |
| Number of subjects analysed        | 61                       | 48                              | 59                  | 30                                                         |
| Units: Percentage of subjects      |                          |                                 |                     |                                                            |
| number (not applicable)            |                          |                                 |                     |                                                            |
| Any Hair color changes             | 67.2                     | 73.8                            | 3.4                 | 83.3                                                       |
| Grade ≥3 Hair color changes        | 0                        | 0                               | 0                   | 0                                                          |
| Any Pruritis                       | 9.8                      | 16.4                            | 3.4                 | 20.0                                                       |
| Grade ≥3 Pruritis                  | 0                        | 1.6                             | 0                   | 0                                                          |
| Any Rash maculopapular             | 9.8                      | 14.8                            | 1.7                 | 10.0                                                       |
| Grade ≥3 Rash maculopapular        | 0                        | 1.6                             | 0                   | 0                                                          |
| Any Pruritis generalized           | 8.2                      | 8.2                             | 0                   | 10.0                                                       |
| Grade ≥3 Pruritis generalized      | 0                        | 0                               | 0                   | 0                                                          |
| Any Erythema                       | 1.6                      | 3.3                             | 0                   | 20.0                                                       |
| Grade ≥3 Erythema                  | 0                        | 0                               | 0                   | 0                                                          |
| Any Dry skin                       | 3.3                      | 6.6                             | 3.4                 | 10.0                                                       |
| Grade ≥3 Dry skin                  | 0                        | 0                               | 0                   | 3.3                                                        |
| Any Photosensitivity reaction      | 0                        | 1.6                             | 0                   | 10.0                                                       |
| Grade ≥3 Photosensitivity reaction | 0                        | 0                               | 0                   | 0                                                          |
| Any Nausea                         | 37.7                     | 44.3                            | 40.7                | 20.0                                                       |
| Grade ≥3 Nausea                    | 0                        | 0                               | 0                   | 0                                                          |
| Any Diarrhea                       | 19.7                     | 26.2                            | 25.4                | 30.0                                                       |
| Grade ≥3 Diarrhea                  | 0                        | 0                               | 0                   | 0                                                          |
| Any Vomiting                       | 19.7                     | 23.0                            | 5.1                 | 6.7                                                        |
| Grade ≥3 Vomiting                  | 1.6                      | 1.6                             | 0                   | 0                                                          |
| Any Abdominal Pain                 | 16.4                     | 21.3                            | 10.2                | 6.7                                                        |
| Grade ≥3 Abdominal Pain            | 0                        | 0                               | 0                   | 0                                                          |
| Any Dry mouth                      | 9.8                      | 13.1                            | 3.4                 | 13.3                                                       |
| Grade ≥3 Dry mouth                 | 0                        | 0                               | 0                   | 0                                                          |
| Any Constipation                   | 11.5                     | 14.8                            | 5.1                 | 10.0                                                       |
| Grade ≥3 Constipation              | 0                        | 0                               | 0                   | 0                                                          |
| Any Stomatitis                     | 6.6                      | 8.2                             | 1.7                 | 10.0                                                       |
| Grade ≥3 Stomatitis                | 0                        | 0                               | 0                   | 0                                                          |
| Any Fatigue                        | 54.1                     | 55.7                            | 35.6                | 26.7                                                       |
| Grade ≥3 Fatigue                   | 0                        | 0                               | 0                   | 0                                                          |
| Any Edema peripheral               | 13.1                     | 16.4                            | 3.4                 | 20.0                                                       |
| Grade ≥3 Edema peripheral          | 0                        | 0                               | 0                   | 0                                                          |
| Any Face edema                     | 13.1                     | 14.8                            | 1.7                 | 20.0                                                       |
| Grade ≥3 Face edema                | 0                        | 1.6                             | 0                   | 3.3                                                        |
| Any Asthenia                       | 9.8                      | 11.5                            | 5.1                 | 20.0                                                       |
| Grade ≥3 Asthenia                  | 0                        | 0                               | 0                   | 0                                                          |
| Any Pyrexia                        | 6.6                      | 8.2                             | 1.7                 | 13.3                                                       |
| Grade ≥3 Pyrexia                   | 0                        | 0                               | 0                   | 0                                                          |
| Any AST increased                  | 39.3                     | 44.3                            | 0                   | 16.7                                                       |
| Grade ≥3 AST increased             | 9.8                      | 9.8                             | 0                   | 6.7                                                        |
| Any ALT increased                  | 27.9                     | 31.1                            | 1.7                 | 23.3                                                       |

|                                            |      |      |      |      |
|--------------------------------------------|------|------|------|------|
| Grade ≥3 ALT increased                     | 9.8  | 9.8  | 0    | 10.0 |
| Any ALP increased                          | 14.8 | 14.8 | 0    | 3.3  |
| Grade ≥3 ALP increased                     | 6.6  | 6.6  | 0    | 3.3  |
| Any LDH increased                          | 11.5 | 11.5 | 0    | 10.0 |
| Grade ≥3 LDH increased                     | 1.6  | 1.6  | 0    | 0    |
| Any Weight increased                       | 3.3  | 4.9  | 0    | 10.0 |
| Grade ≥3 Weight increased                  | 0    | 0    | 0    | 0    |
| Any Dysgeusia                              | 24.6 | 27.9 | 1.7  | 23.3 |
| Grade ≥3 Dysgeusia                         | 0    | 0    | 0    | 0    |
| Any Headache                               | 19.7 | 23.0 | 18.6 | 20.0 |
| Grade ≥3 Headache                          | 0    | 1.6  | 0    | 0    |
| Any Dizziness                              | 9.8  | 13.1 | 15.3 | 13.3 |
| Grade ≥3 Dizziness                         | 1.6  | 1.6  | 0    | 0    |
| Any Paresthesia                            | 1.6  | 8.2  | 1.7  | 10.0 |
| Grade ≥3 Paresthesia                       | 0    | 0    | 0    | 0    |
| Any Memory impairment                      | 0    | 1.6  | 1.7  | 10.0 |
| Grade ≥3 Memory impairment                 | 0    | 0    | 0    | 0    |
| Any Arthralgia                             | 23.0 | 27.9 | 25.4 | 30.0 |
| Grade ≥3 Arthralgia                        | 3.3  | 3.3  | 1.7  | 0    |
| Any Pain in extremity                      | 6.6  | 9.8  | 6.8  | 13.3 |
| Grade ≥3 Pain in extremity                 | 0    | 0    | 1.7  | 0    |
| Any Periorbital edema                      | 18.0 | 24.6 | 1.7  | 13.3 |
| Grade ≥3 Periorbital edema                 | 1.6  | 1.6  | 0    | 0    |
| Any Eyelid edema                           | 3.3  | 4.9  | 0    | 10.0 |
| Grade ≥3 Eyelid edema                      | 0    | 0    | 0    | 0    |
| Any Decreased appetite                     | 16.4 | 18.0 | 10.2 | 10.0 |
| Grade ≥3 Decreased appetite                | 0    | 0    | 0    | 0    |
| Any Hypertension                           | 14.8 | 19.7 | 10.2 | 30.0 |
| Grade ≥3 Hypertension                      | 4.9  | 4.9  | 0    | 6.7  |
| Any Upper respiratory tract infection      | 1.6  | 11.5 | 0    | 3.3  |
| Grade ≥3 Upper respiratory tract infection | 0    | 0    | 0    | 0    |
| Any Cough                                  | 4.9  | 6.6  | 5.1  | 10.0 |
| Grade ≥3 Cough                             | 0    | 0    | 0    | 0    |
| Any Dyspnea                                | 1.6  | 4.9  | 0    | 10.0 |
| Grade ≥3 Dyspnea                           | 0    | 0    | 0    | 0    |
| Any Insomnia                               | 4.9  | 4.9  | 3.4  | 10.0 |
| Grade ≥3 Insomnia                          | 0    | 0    | 0    | 0    |
| Any Rash                                   | 14.8 | 27.9 | 5.1  | 23.3 |
| Grade ≥3 Rash                              | 1.6  | 1.6  | 0    | 0    |

| End point values              | All Pexidartinib Treated |  |  |  |
|-------------------------------|--------------------------|--|--|--|
| Subject group type            | Subject analysis set     |  |  |  |
| Number of subjects analysed   | 91                       |  |  |  |
| Units: Percentage of subjects |                          |  |  |  |
| number (not applicable)       |                          |  |  |  |
| Any Hair color changes        | 76.9                     |  |  |  |
| Grade ≥3 Hair color changes   | 0                        |  |  |  |
| Any Pruritis                  | 17.6                     |  |  |  |

|                                    |      |  |  |  |
|------------------------------------|------|--|--|--|
| Grade ≥3 Pruritis                  | 1.1  |  |  |  |
| Any Rash maculopapular             | 13.2 |  |  |  |
| Grade ≥3 Rash maculopapular        | 1.1  |  |  |  |
| Any Pruritis generalized           | 8.8  |  |  |  |
| Grade ≥3 Pruritis generalized      | 0    |  |  |  |
| Any Erythema                       | 8.8  |  |  |  |
| Grade ≥3 Erythema                  | 0    |  |  |  |
| Any Dry skin                       | 7.7  |  |  |  |
| Grade ≥3 Dry skin                  | 1.1  |  |  |  |
| Any Photosensitivity reaction      | 4.4  |  |  |  |
| Grade ≥3 Photosensitivity reaction | 0    |  |  |  |
| Any Nausea                         | 36.3 |  |  |  |
| Grade ≥3 Nausea                    | 0    |  |  |  |
| Any Diarrhea                       | 27.5 |  |  |  |
| Grade ≥3 Diarrhea                  | 0    |  |  |  |
| Any Vomiting                       | 17.6 |  |  |  |
| Grade ≥3 Vomiting                  | 1.1  |  |  |  |
| Any Abdominal Pain                 | 16.5 |  |  |  |
| Grade ≥3 Abdominal Pain            | 0    |  |  |  |
| Any Dry mouth                      | 13.2 |  |  |  |
| Grade ≥3 Dry mouth                 | 0    |  |  |  |
| Any Constipation                   | 13.2 |  |  |  |
| Grade ≥3 Constipation              | 0    |  |  |  |
| Any Stomatitis                     | 8.8  |  |  |  |
| Grade ≥3 Stomatitis                | 0    |  |  |  |
| Any Fatigue                        | 46.2 |  |  |  |
| Grade ≥3 Fatigue                   | 0    |  |  |  |
| Any Edema peripheral               | 17.6 |  |  |  |
| Grade ≥3 Edema peripheral          | 0    |  |  |  |
| Any Face edema                     | 16.5 |  |  |  |
| Grade ≥3 Face edema                | 2.2  |  |  |  |
| Any Asthenia                       | 14.3 |  |  |  |
| Grade ≥3 Asthenia                  | 0    |  |  |  |
| Any Pyrexia                        | 9.9  |  |  |  |
| Grade ≥3 Pyrexia                   | 0    |  |  |  |
| Any AST increased                  | 35.2 |  |  |  |
| Grade ≥3 AST increased             | 8.8  |  |  |  |
| Any ALT increased                  | 28.6 |  |  |  |
| Grade ≥3 ALT increased             | 9.9  |  |  |  |
| Any ALP increased                  | 11.0 |  |  |  |
| Grade ≥3 ALP increased             | 5.5  |  |  |  |
| Any LDH increased                  | 11.0 |  |  |  |
| Grade ≥3 LDH increased             | 1.1  |  |  |  |
| Any Weight increased               | 6.6  |  |  |  |
| Grade ≥3 Weight increased          | 0    |  |  |  |
| Any Dysgeusia                      | 26.4 |  |  |  |
| Grade ≥3 Dysgeusia                 | 0    |  |  |  |
| Any Headache                       | 22.0 |  |  |  |
| Grade ≥3 Headache                  | 1.1  |  |  |  |
| Any Dizziness                      | 13.2 |  |  |  |
| Grade ≥3 Dizziness                 | 1.1  |  |  |  |
| Any Paresthesia                    | 8.8  |  |  |  |

|                                                  |      |  |  |  |
|--------------------------------------------------|------|--|--|--|
| Grade $\geq 3$ Paresthesia                       | 0    |  |  |  |
| Any Memory impairment                            | 4.4  |  |  |  |
| Grade $\geq 3$ Memory impairment                 | 0    |  |  |  |
| Any Arthralgia                                   | 28.6 |  |  |  |
| Grade $\geq 3$ Arthralgia                        | 2.2  |  |  |  |
| Any Pain in extremity                            | 11.0 |  |  |  |
| Grade $\geq 3$ Pain in extremity                 | 0    |  |  |  |
| Any Periorbital edema                            | 20.0 |  |  |  |
| Grade $\geq 3$ Periorbital edema                 | 1.1  |  |  |  |
| Any Eyelid edema                                 | 6.6  |  |  |  |
| Grade $\geq 3$ Eyelid edema                      | 0    |  |  |  |
| Any Decreased appetite                           | 15.4 |  |  |  |
| Grade $\geq 3$ Decreased appetite                | 0    |  |  |  |
| Any Hypertension                                 | 13.1 |  |  |  |
| Grade $\geq 3$ Hypertension                      | 5.5  |  |  |  |
| Any Upper respiratory tract infection            | 8.8  |  |  |  |
| Grade $\geq 3$ Upper respiratory tract infection | 0    |  |  |  |
| Any Cough                                        | 7.7  |  |  |  |
| Grade $\geq 3$ Cough                             | 0    |  |  |  |
| Any Dyspnea                                      | 7.7  |  |  |  |
| Grade $\geq 3$ Dyspnea                           | 0    |  |  |  |
| Any Insomnia                                     | 6.6  |  |  |  |
| Grade $\geq 3$ Insomnia                          | 0    |  |  |  |
| Any Rash                                         | 26.4 |  |  |  |
| Grade $\geq 3$ Rash                              | 1.1  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR) Based on RECIST 1.1

|                 |                                                |
|-----------------|------------------------------------------------|
| End point title | Duration of Response (DOR) Based on RECIST 1.1 |
|-----------------|------------------------------------------------|

End point description:

Duration of response (DOR) based on RECIST 1.1 is defined from the date of the first recorded evidence of response to the first date of documented disease progression. DOR was assessed in the ITR population, specifically among the Pexidartinib Part 1, Pexidartinib Part 2; Pexidartinib Part 2 only. Participants randomized to Placebo Part 1 only were not analyzed. DOR was based on numbers of responders only.

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

End point timeframe:

Date of first documentation of objective response up to date of first documentation of progressive disease, assessed up to end of study (approximately 71 months)

| End point values                 | Pexidartinib (Parts 1 and 2) | Placebo (Part 1), Crossover Pexidartinib (Part 2) |  |  |
|----------------------------------|------------------------------|---------------------------------------------------|--|--|
| Subject group type               | Reporting group              | Reporting group                                   |  |  |
| Number of subjects analysed      | 37 <sup>[6]</sup>            | 18 <sup>[7]</sup>                                 |  |  |
| Units: months                    |                              |                                                   |  |  |
| median (confidence interval 95%) | 99.9 (31.01 to 99.9)         | 99.9 (39.0 to 99.9)                               |  |  |

Notes:

[6] - 99.9 = NA, median and 95% upper CI not estimable due to insufficient number of events

[7] - 99.9 = NA, median and 95% upper CI not estimable due to insufficient number of events

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DOR) Based on Tumor Volume Score (TVS)

|                 |                                                              |
|-----------------|--------------------------------------------------------------|
| End point title | Duration of Response (DOR) Based on Tumor Volume Score (TVS) |
|-----------------|--------------------------------------------------------------|

End point description:

Duration of response (DOR) based on TVS is defined from the date of the first recorded evidence of response to the first date of documented disease progression. DOR was assessed in the ITT population, specifically among the Pexidartinib Part 1, Pexidartinib Part 2; Pexidartinib Part 2 only. Participants randomized to Placebo Part 1 only were not analyzed. DOR was based on numbers of responders only.

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

End point timeframe:

Date of first documentation of objective response up to date of first documentation of progressive disease, assessed up to end of study (approximately 71 months)

| End point values                 | Pexidartinib (Parts 1 and 2) | Placebo (Part 1), Crossover Pexidartinib (Part 2) |  |  |
|----------------------------------|------------------------------|---------------------------------------------------|--|--|
| Subject group type               | Reporting group              | Reporting group                                   |  |  |
| Number of subjects analysed      | 41 <sup>[8]</sup>            | 21 <sup>[9]</sup>                                 |  |  |
| Units: months                    |                              |                                                   |  |  |
| median (confidence interval 95%) | 52.70 (38.60 to 99.9)        | 99.9 (99.9 to 99.9)                               |  |  |

Notes:

[8] - 99.9 = NA, 95% CI upper limit was not estimable due to insufficient number of events.

[9] - 99.9 = NA, median and 95% CIs were not estimable due to insufficient number of events.

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Percentage of Subjects With Symptomatic, Locally Advanced TGCT Achieving Complete or Partial Response to Pexidartinib Compared With That of Placebo per RECIST 1.1 by Week 49

|                 |                                                                                                                                                                               |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects With Symptomatic, Locally Advanced TGCT Achieving Complete or Partial Response to Pexidartinib Compared With That of Placebo per RECIST 1.1 by Week 49 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

CR and PR were assessed based on centrally-read MRI scans and RECIST 1.1. A CR was defined as disappearance of all tumors and a PR was defined as at least a 30% decrease in the sum of diameters of target tumors using the baseline sum diameters as the reference. Best overall response was assessed in the ITT population.

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

End point timeframe:

By Week 49

| End point values              | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|-------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type            | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed   | 91                       | 61                             | 30                                  |  |
| Units: Percentage of subjects |                          |                                |                                     |  |
| number (not applicable)       |                          |                                |                                     |  |
| CR                            | 24.2                     | 24.6                           | 23.3                                |  |
| PR                            | 29.7                     | 29.5                           | 30.0                                |  |
| Response (CR or PR)           | 53.8                     | 54.1                           | 53.3                                |  |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Mean Change From Baseline for ROM Score in Subjects Receiving Pexidartinib Compared with those on Placebo Up to Week 49

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline for ROM Score in Subjects Receiving Pexidartinib Compared with those on Placebo Up to Week 49 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Range of motion (ROM) of the joint was assessed by a qualified, independent, and blinded or third-party assessors at the clinical site. Measurements were recorded in degrees. At baseline, the plane of movement with the smallest relative value (worst) was identified and this plane was used for evaluating the relative change of motion subsequently. Only the plane with the worst impaired ROM at baseline was selected for subsequent analyses. ROM was assessed in the ITT population. ROM was assessed in the ITT population.

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

End point timeframe:

Baseline, Week 25, Week 49

| End point values                     | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|--------------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type                   | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed          | 91                       | 61                             | 30                                  |  |
| Units: Mean change from baseline     |                          |                                |                                     |  |
| arithmetic mean (standard deviation) |                          |                                |                                     |  |
| Baseline (N=61, 30, 91)              | 63.8 (± 24.2)            | 62.5 (± 24.8)                  | 66.5 (± 22.9)                       |  |

|                        |               |               |               |  |
|------------------------|---------------|---------------|---------------|--|
| Week 25 (N=45, 24, 69) | 14.8 (± 14.2) | 15.6 (± 14.9) | 13.1 (± 12.9) |  |
| Week 49 (N=33, 22, 55) | 13.4 (± 17.3) | 14.4 (± 19.5) | 12.0 (± 13.4) |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Mean Change From Baseline in the PROMIS Physical Function Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 49

|                                                                                                                                                                                       |                                                                                                                                                 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                       | Mean Change From Baseline in the PROMIS Physical Function Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 49 |
| End point description:<br>The PROMIS physical function scale was used to assess physical function of the upper and lower limbs. Physical function was assessed in the ITT population. |                                                                                                                                                 |
| End point type                                                                                                                                                                        | Other pre-specified                                                                                                                             |
| End point timeframe:<br>Baseline, Week 25, Week 49                                                                                                                                    |                                                                                                                                                 |

| End point values                                                      | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|-----------------------------------------------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type                                                    | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed                                           | 91                       | 61                             | 30                                  |  |
| Units: Mean change from baseline arithmetic mean (standard deviation) |                          |                                |                                     |  |
| Baseline (N=60, 30, 90)                                               | 37.9 (± 5.6)             | 37.5 (± 4.9)                   | 38.7 (± 6.9)                        |  |
| Week 25 (N=38, 16, 54)                                                | 4.0 (± 5.4)              | 3.6 (± 4.9)                    | 4.9 (± 6.3)                         |  |
| Week 49 (N=25, 14, 39)                                                | 5.8 (± 5.2)              | 4.7 (± 4.4)                    | 7.6 (± 6.3)                         |  |

## Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Mean Change From Baseline for Worst Stiffness Numeric Rating Scale Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 49

|                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                  | Mean Change From Baseline for Worst Stiffness Numeric Rating Scale Score in Subjects Receiving Pexidartinib Compared With Those on Placebo Up to Week 49 |
| End point description:<br>The Worst Stiffness Numeric Rating Scale (NRS) was a 1-item, self-administered questionnaire assessing the "worst" stiffness in the last 24 hours. The NRS for this item ranged from 0 (no stiffness) to 10 (stiffness as bad as you can imagine). Worst stiffness was assessed in the ITT population. |                                                                                                                                                          |
| End point type                                                                                                                                                                                                                                                                                                                   | Other pre-specified                                                                                                                                      |

End point timeframe:

Baseline, Week 25, Week 49

| End point values                                                      | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|-----------------------------------------------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type                                                    | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed                                           | 91                       | 61                             | 30                                  |  |
| Units: Mean change from baseline arithmetic mean (standard deviation) |                          |                                |                                     |  |
| Baseline (N=59, 26, 85)                                               | 5.6 (± 1.9)              | 5.6 (± 1.7)                    | 5.7 (± 2.3)                         |  |
| Week 25 (N=33, 18, 51)                                                | -2.8 (± 2.5)             | -2.7 (± 2.2)                   | -3.0 (± 3.1)                        |  |
| Week 49 (N=22, 10, 32)                                                | -3.1 (± 2.3)             | -3.5 (± 1.9)                   | -2.2 (± 2.8)                        |  |

### Statistical analyses

No statistical analyses for this end point

### Other pre-specified: Mean Change From Baseline for Worst Pain NRS in Subjects Receiving Pexidartinib Compared With Those on Placebo by Week 49

|                 |                                                                                                                           |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|
| End point title | Mean Change From Baseline for Worst Pain NRS in Subjects Receiving Pexidartinib Compared With Those on Placebo by Week 49 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------|

End point description:

The Brief Pain Inventory (BPI) Worst Pain NRS was a 1-item, self-administered questionnaire assessing the "worst" pain in the last 24 hours. The NRS for this item ranged from 0 (no pain) to 10 (pain as bad as you can imagine). Worst pain was assessed in the ITT population.

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

End point timeframe:

By Week 49

| End point values                                                      | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|-----------------------------------------------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type                                                    | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed                                           | 91                       | 61                             | 30                                  |  |
| Units: Mean change from baseline arithmetic mean (standard deviation) |                          |                                |                                     |  |
| Baseline (N=59, 26, 85)                                               | 5.5 (± 1.9)              | 5.6 (± 1.6)                    | 5.2 (± 2.5)                         |  |
| Week 25 (N=33, 18, 51)                                                | -2.7 (± 2.5)             | -2.7 (± 2.2)                   | -2.6 (± 3.1)                        |  |
| Week 49 (N=22, 10, 32)                                                | -3.2 (± 2.3)             | -3.3 (± 1.7)                   | -2.8 (± 3.4)                        |  |

### Statistical analyses



**Other pre-specified: Percentage of Subjects With Symptomatic, Locally Advanced TGCT Achieving Complete or Partial Response Based on TVS After Receiving Pexidartinib Compared With Those on Placebo by Week 49**

|                 |                                                                                                                                                                                           |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of Subjects With Symptomatic, Locally Advanced TGCT Achieving Complete or Partial Response Based on TVS After Receiving Pexidartinib Compared With Those on Placebo by Week 49 |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## End point description:

Best overall response (CR or PR) was assessed using tumor volume score (TVS) in the ITT population. TVS is a semi-quantitative MRI scoring system that describes tumor mass and is based on 10% increments of the estimated volume of the maximally distended synovial cavity or tendon sheath involved. A tumor that is equal in volume to that of a maximally distended synovial cavity or tendon sheath was scored 10; a score of 0 indicated no evidence of tumor.

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

## End point timeframe:

By Week 49

| End point values                 | All Pexidartinib Treated | Pexidartinib Part 1 and Part 2 | Placebo Part 1, Pexidartinib Part 2 |  |
|----------------------------------|--------------------------|--------------------------------|-------------------------------------|--|
| Subject group type               | Subject analysis set     | Subject analysis set           | Subject analysis set                |  |
| Number of subjects analysed      |                          |                                |                                     |  |
| Units: Percentage of subjects    |                          |                                |                                     |  |
| number (not applicable)          |                          |                                |                                     |  |
| Best overall response (CR or PR) | 64.8                     | 63.9                           | 66.7                                |  |

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event were monitored throughout the study from the time the subject signed the informed consent form to 28 days after the final treatment dose.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Pexidartinib (Part 1) |
|-----------------------|-----------------------|

Reporting group description:

Subjects randomized to pexidartinib for 24 weeks administered twice a day.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Placebo (Part 1) |
|-----------------------|------------------|

Reporting group description:

Subjects randomized to matching placebo for 24 weeks administered twice a day.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Pexidartinib (Parts 1 and 2) |
|-----------------------|------------------------------|

Reporting group description:

Subjects received pexidartinib in Part 1 and Part 2 at their prescribed dose.

|                       |                                                   |
|-----------------------|---------------------------------------------------|
| Reporting group title | Placebo (Part 1), Crossover Pexidartinib (Part 2) |
|-----------------------|---------------------------------------------------|

Reporting group description:

Subjects received placebo in Part 1 and pexidartinib in Part 2 at their prescribed dose.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | All Pexidartinib Treated |
|-----------------------|--------------------------|

Reporting group description:

Subjects received pexidartinib in Part 1 and Part 2 (placebo crossed over to pexidartinib).

| Serious adverse events                                              | Pexidartinib (Part 1) | Placebo (Part 1) | Pexidartinib (Parts 1 and 2) |
|---------------------------------------------------------------------|-----------------------|------------------|------------------------------|
| Total subjects affected by serious adverse events                   |                       |                  |                              |
| subjects affected / exposed                                         | 8 / 61 (13.11%)       | 1 / 59 (1.69%)   | 12 / 61 (19.67%)             |
| number of deaths (all causes)                                       | 0                     | 0                | 0                            |
| number of deaths resulting from adverse events                      | 0                     | 0                | 0                            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                       |                  |                              |
| Adenosquamous carcinoma of the cervix                               |                       |                  |                              |
| subjects affected / exposed                                         | 0 / 61 (0.00%)        | 0 / 59 (0.00%)   | 0 / 61 (0.00%)               |
| occurrences causally related to treatment / all                     | 0 / 0                 | 0 / 0            | 0 / 0                        |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0            | 0 / 0                        |
| Rectal adenocarcinoma                                               |                       |                  |                              |
| subjects affected / exposed                                         | 0 / 61 (0.00%)        | 0 / 59 (0.00%)   | 0 / 61 (0.00%)               |
| occurrences causally related to treatment / all                     | 0 / 0                 | 0 / 0            | 0 / 0                        |
| deaths causally related to treatment / all                          | 0 / 0                 | 0 / 0            | 0 / 0                        |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Endometrial cancer                              |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 0 / 61 (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          |
| Squamous cell carcinoma of skin                 |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lipoma                                          |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rectal cancer stage II                          |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Transaminases increased                         |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Liver function test abnormal                    |                |                |                |
| subjects affected / exposed                     | 2 / 61 (3.28%) | 0 / 59 (0.00%) | 2 / 61 (3.28%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatic enzyme abnormal                         |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| complications                                   |                |                |                |
| Joint injury                                    |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post procedural complication                    |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rib fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal fracture                                 |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Wound dehiscence                                |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Cardiac arrest                                  |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Migraine                                        |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pregnancy, puerperium and perinatal conditions  |                |                |                |
| Abortion spontaneous                            |                |                |                |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Local swelling                                       |                |                |                |
| subjects affected / exposed                          | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                               |                |                |                |
| subjects affected / exposed                          | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                              |                |                |                |
| Hepatotoxicity                                       |                |                |                |
| subjects affected / exposed                          | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Liver disorder                                       |                |                |                |
| subjects affected / exposed                          | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatotoxicity                                       |                |                |                |
| subjects affected / exposed                          | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders      |                |                |                |
| Asthma                                               |                |                |                |
| subjects affected / exposed                          | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders               |                |                |                |
| Rash papular                                         |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rash                                            |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Neck pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spondylolisthesis                               |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Hepatitis A                                     |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatitis E                                     |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lymphangitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Bronchopneumonia                                |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Paronychia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Placebo (Part 1),<br>Crossover<br>Pexidartinib (Part 2) | All Pexidartinib<br>Treated |  |
|---------------------------------------------------------------------|---------------------------------------------------------|-----------------------------|--|
| Total subjects affected by serious adverse events                   |                                                         |                             |  |
| subjects affected / exposed                                         | 9 / 30 (30.00%)                                         | 21 / 91 (23.08%)            |  |
| number of deaths (all causes)                                       | 1                                                       | 1                           |  |
| number of deaths resulting from adverse events                      | 0                                                       | 0                           |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                         |                             |  |
| Adenosquamous carcinoma of the cervix                               |                                                         |                             |  |
| subjects affected / exposed                                         | 1 / 30 (3.33%)                                          | 1 / 91 (1.10%)              |  |
| occurrences causally related to treatment / all                     | 0 / 1                                                   | 0 / 1                       |  |
| deaths causally related to treatment / all                          | 0 / 0                                                   | 0 / 0                       |  |
| Rectal adenocarcinoma                                               |                                                         |                             |  |
| subjects affected / exposed                                         | 1 / 30 (3.33%)                                          | 1 / 91 (1.10%)              |  |
| occurrences causally related to treatment / all                     | 0 / 1                                                   | 0 / 1                       |  |
| deaths causally related to treatment / all                          | 0 / 0                                                   | 0 / 0                       |  |
| Endometrial cancer                                                  |                                                         |                             |  |
| subjects affected / exposed                                         | 0 / 30 (0.00%)                                          | 0 / 91 (0.00%)              |  |
| occurrences causally related to treatment / all                     | 0 / 0                                                   | 0 / 0                       |  |
| deaths causally related to treatment / all                          | 0 / 0                                                   | 0 / 0                       |  |
| Squamous cell carcinoma of skin                                     |                                                         |                             |  |
| subjects affected / exposed                                         | 1 / 30 (3.33%)                                          | 1 / 91 (1.10%)              |  |
| occurrences causally related to treatment / all                     | 0 / 1                                                   | 0 / 1                       |  |
| deaths causally related to treatment / all                          | 0 / 0                                                   | 0 / 0                       |  |
| Lipoma                                                              |                                                         |                             |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Rectal cancer stage II                          |                |                |  |
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Investigations                                  |                |                |  |
| Transaminases increased                         |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Liver function test abnormal                    |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 2 / 91 (2.20%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatic enzyme abnormal                         |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood bilirubin increased                       |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| 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  |                |                |  |
| Joint injury                                    |                |                |  |
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Post procedural complication                    |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |



|                                                      |                |                |  |
|------------------------------------------------------|----------------|----------------|--|
| Rib fracture                                         |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Spinal fracture                                      |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Wound dehiscence                                     |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                                    |                |                |  |
| Cardiac arrest                                       |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 1          |  |
| Nervous system disorders                             |                |                |  |
| Migraine                                             |                |                |  |
| subjects affected / exposed                          | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Pregnancy, puerperium and perinatal conditions       |                |                |  |
| Abortion spontaneous                                 |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Local swelling                                       |                |                |  |
| subjects affected / exposed                          | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Non-cardiac chest pain                               |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Hepatotoxicity                                  |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Liver disorder                                  |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatotoxicity                                  |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Asthma                                          |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Skin and subcutaneous tissue disorders          |                |                |  |
| Rash papular                                    |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Rash                                            |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Neck pain                                       |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Osteoarthritis                                  |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Spondylolisthesis                               |                |                |  |
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Hepatitis A                                     |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatitis E                                     |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Lymphangitis                                    |                |                |  |
| subjects affected / exposed                     | 1 / 30 (3.33%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchopneumonia                                |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Paronychia                                      |                |                |  |
| subjects affected / exposed                     | 0 / 30 (0.00%) | 1 / 91 (1.10%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| Non-serious adverse events                                          | Pexidartinib (Part 1) | Placebo (Part 1) | Pexidartinib (Parts 1 and 2) |
|---------------------------------------------------------------------|-----------------------|------------------|------------------------------|
| Total subjects affected by non-serious adverse events               |                       |                  |                              |
| subjects affected / exposed                                         | 60 / 61 (98.36%)      | 55 / 59 (93.22%) | 61 / 61 (100.00%)            |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                       |                  |                              |
| Tumor pain                                                          |                       |                  |                              |
| alternative assessment type: Non-systematic                         |                       |                  |                              |
| subjects affected / exposed                                         | 4 / 61 (6.56%)        | 4 / 59 (6.78%)   | 4 / 61 (6.56%)               |
| occurrences (all)                                                   | 7                     | 6                | 7                            |
| Vascular disorders                                                  |                       |                  |                              |
| Hypertension                                                        |                       |                  |                              |
| alternative assessment type: Non-systematic                         |                       |                  |                              |
| subjects affected / exposed                                         | 9 / 61 (14.75%)       | 6 / 59 (10.17%)  | 14 / 61 (22.95%)             |
| occurrences (all)                                                   | 15                    | 6                | 24                           |
| Hypotension                                                         |                       |                  |                              |
| alternative assessment type: Non-systematic                         |                       |                  |                              |
| subjects affected / exposed                                         | 0 / 61 (0.00%)        | 0 / 59 (0.00%)   | 0 / 61 (0.00%)               |
| occurrences (all)                                                   | 0                     | 0                | 0                            |
| General disorders and administration site conditions                |                       |                  |                              |
| Fatigue                                                             |                       |                  |                              |
| subjects affected / exposed                                         | 33 / 61 (54.10%)      | 21 / 59 (35.59%) | 35 / 61 (57.38%)             |
| occurrences (all)                                                   | 49                    | 26               | 57                           |
| Face oedema                                                         |                       |                  |                              |
| alternative assessment type: Non-systematic                         |                       |                  |                              |
| subjects affected / exposed                                         | 8 / 61 (13.11%)       | 1 / 59 (1.69%)   | 9 / 61 (14.75%)              |
| occurrences (all)                                                   | 8                     | 1                | 11                           |
| Oedema peripheral                                                   |                       |                  |                              |
| alternative assessment type: Non-systematic                         |                       |                  |                              |
| subjects affected / exposed                                         | 8 / 61 (13.11%)       | 2 / 59 (3.39%)   | 15 / 61 (24.59%)             |
| occurrences (all)                                                   | 9                     | 2                | 18                           |
| Asthenia                                                            |                       |                  |                              |
| alternative assessment type: Non-systematic                         |                       |                  |                              |

|                                                 |                |                |                 |
|-------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                     | 6 / 61 (9.84%) | 3 / 59 (5.08%) | 9 / 61 (14.75%) |
| occurrences (all)                               | 7              | 5              | 16              |
| Pyrexia                                         |                |                |                 |
| alternative assessment type: Non-systematic     |                |                |                 |
| subjects affected / exposed                     | 4 / 61 (6.56%) | 1 / 59 (1.69%) | 8 / 61 (13.11%) |
| occurrences (all)                               | 4              | 1              | 8               |
| Influenza like illness                          |                |                |                 |
| alternative assessment type: Non-systematic     |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 5 / 61 (8.20%)  |
| occurrences (all)                               | 0              | 0              | 6               |
| Chest pain                                      |                |                |                 |
| alternative assessment type: Non-systematic     |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Malaise                                         |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 1 / 61 (1.64%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Peripheral swelling                             |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 0 / 61 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0               |
| Respiratory, thoracic and mediastinal disorders |                |                |                 |
| Cough                                           |                |                |                 |
| alternative assessment type: Non-systematic     |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 3 / 59 (5.08%) | 4 / 61 (6.56%)  |
| occurrences (all)                               | 0              | 3              | 6               |
| Dyspnoea                                        |                |                |                 |
| alternative assessment type: Non-systematic     |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 3 / 61 (4.92%)  |
| occurrences (all)                               | 0              | 0              | 4               |
| Oropharyngeal pain                              |                |                |                 |
| alternative assessment type: Non-systematic     |                |                |                 |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 2 / 59 (3.39%) | 4 / 61 (6.56%)  |
| occurrences (all)                               | 0              | 3              | 4               |
| Psychiatric disorders                           |                |                |                 |

|                                                                                                                                                           |                        |                     |                        |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|---------------------|------------------------|
| Insomnia<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 61 (0.00%)<br>0    | 2 / 59 (3.39%)<br>2 | 4 / 61 (6.56%)<br>4    |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                                                                                               | 0 / 61 (0.00%)<br>0    | 1 / 59 (1.69%)<br>1 | 1 / 61 (1.64%)<br>1    |
| Investigations<br>Aspartate aminotransferase increased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 24 / 61 (39.34%)<br>48 | 0 / 59 (0.00%)<br>0 | 28 / 61 (45.90%)<br>63 |
| Alanine aminotransferase increased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                     | 17 / 61 (27.87%)<br>44 | 1 / 59 (1.69%)<br>1 | 19 / 61 (31.15%)<br>53 |
| Blood alkaline phosphatase increased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                   | 9 / 61 (14.75%)<br>26  | 0 / 59 (0.00%)<br>0 | 9 / 61 (14.75%)<br>30  |
| Blood lactate dehydrogenase increased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                  | 7 / 61 (11.48%)<br>12  | 0 / 59 (0.00%)<br>0 | 7 / 61 (11.48%)<br>17  |
| White blood cell count decreased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 61 (0.00%)<br>0    | 1 / 59 (1.69%)<br>1 | 6 / 61 (9.84%)<br>11   |
| Weight increased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 61 (0.00%)<br>0    | 0 / 59 (0.00%)<br>0 | 3 / 61 (4.92%)<br>4    |
| Blood bilirubin increased<br>alternative assessment type: Non-systematic                                                                                  |                        |                     |                        |

|                                                                                                                                           |                        |                        |                        |
|-------------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                                                                          | 0 / 61 (0.00%)<br>0    | 1 / 59 (1.69%)<br>2    | 4 / 61 (6.56%)<br>8    |
| Blood creatine phosphokinase increased<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 0 / 61 (0.00%)<br>0    | 0 / 59 (0.00%)<br>0    | 6 / 61 (9.84%)<br>16   |
| Blood triglycerides increased<br>subjects affected / exposed<br>occurrences (all)                                                         | 1 / 61 (1.64%)<br>1    | 0 / 59 (0.00%)<br>0    | 1 / 61 (1.64%)<br>3    |
| Cardiac disorders<br>Bradycardia<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)       | 0 / 61 (0.00%)<br>0    | 0 / 59 (0.00%)<br>0    | 0 / 61 (0.00%)<br>0    |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                                                          | 2 / 61 (3.28%)<br>2    | 0 / 59 (0.00%)<br>0    | 4 / 61 (6.56%)<br>5    |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                                                           | 0 / 61 (0.00%)<br>0    | 0 / 59 (0.00%)<br>0    | 1 / 61 (1.64%)<br>3    |
| Nervous system disorders<br>Dysgeusia<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)  | 15 / 61 (24.59%)<br>24 | 1 / 59 (1.69%)<br>1    | 18 / 61 (29.51%)<br>29 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                                                                              | 11 / 61 (18.03%)<br>16 | 11 / 59 (18.64%)<br>15 | 15 / 61 (24.59%)<br>25 |
| Dizziness<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                              | 6 / 61 (9.84%)<br>7    | 9 / 59 (15.25%)<br>12  | 10 / 61 (16.39%)<br>14 |
| Paresthesia<br>alternative assessment type: Non-systematic                                                                                |                        |                        |                        |

|                                             |                |                |                 |
|---------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                 | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 6 / 61 (9.84%)  |
| occurrences (all)                           | 0              | 1              | 7               |
| Memory impairment                           |                |                |                 |
| alternative assessment type: Non-systematic |                |                |                 |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 2 / 61 (3.28%)  |
| occurrences (all)                           | 0              | 1              | 2               |
| Neuropathy peripheral                       |                |                |                 |
| alternative assessment type: Non-systematic |                |                |                 |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 4 / 61 (6.56%)  |
| occurrences (all)                           | 0              | 0              | 5               |
| Hypoaesthesia                               |                |                |                 |
| subjects affected / exposed                 | 1 / 61 (1.64%) | 2 / 59 (3.39%) | 1 / 61 (1.64%)  |
| occurrences (all)                           | 1              | 2              | 1               |
| Sciatica                                    |                |                |                 |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 0 / 61 (0.00%)  |
| occurrences (all)                           | 0              | 1              | 0               |
| Blood and lymphatic system disorders        |                |                |                 |
| Anaemia                                     |                |                |                 |
| alternative assessment type: Non-systematic |                |                |                 |
| subjects affected / exposed                 | 3 / 61 (4.92%) | 1 / 59 (1.69%) | 7 / 61 (11.48%) |
| occurrences (all)                           | 3              | 2              | 12              |
| Neutropenia                                 |                |                |                 |
| alternative assessment type: Non-systematic |                |                |                 |
| subjects affected / exposed                 | 3 / 61 (4.92%) | 0 / 59 (0.00%) | 4 / 61 (6.56%)  |
| occurrences (all)                           | 3              | 0              | 13              |
| Leukopenia                                  |                |                |                 |
| alternative assessment type: Non-systematic |                |                |                 |
| subjects affected / exposed                 | 2 / 61 (3.28%) | 0 / 59 (0.00%) | 4 / 61 (6.56%)  |
| occurrences (all)                           | 2              | 0              | 7               |
| Thrombocytopenia                            |                |                |                 |
| alternative assessment type: Non-systematic |                |                |                 |
| subjects affected / exposed                 | 2 / 61 (3.28%) | 0 / 59 (0.00%) | 2 / 61 (3.28%)  |
| occurrences (all)                           | 2              | 0              | 2               |
| Ear and labyrinth disorders                 |                |                |                 |



|                                                                                                                                       |                        |                        |                        |
|---------------------------------------------------------------------------------------------------------------------------------------|------------------------|------------------------|------------------------|
| Tinnitus<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 61 (1.64%)<br>1    | 0 / 59 (0.00%)<br>0    | 2 / 61 (3.28%)<br>2    |
| Vertigo<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 61 (1.64%)<br>1    | 0 / 59 (0.00%)<br>0    | 4 / 61 (6.56%)<br>4    |
| Eye disorders<br>Periorbital edema<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all) | 11 / 61 (18.03%)<br>13 | 1 / 59 (1.69%)<br>1    | 17 / 61 (27.87%)<br>23 |
| Eye oedema<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                         | 6 / 61 (9.84%)<br>6    | 2 / 59 (3.39%)<br>2    | 6 / 61 (9.84%)<br>6    |
| Eyelid oedema<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 61 (0.00%)<br>0    | 0 / 59 (0.00%)<br>0    | 3 / 61 (4.92%)<br>5    |
| Vision blurred<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 61 (0.00%)<br>0    | 0 / 59 (0.00%)<br>0    | 5 / 61 (8.20%)<br>5    |
| Lacrimation increased<br>subjects affected / exposed<br>occurrences (all)                                                             | 3 / 61 (4.92%)<br>3    | 0 / 59 (0.00%)<br>0    | 4 / 61 (6.56%)<br>4    |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)                                              | 23 / 61 (37.70%)<br>40 | 24 / 59 (40.68%)<br>27 | 28 / 61 (45.90%)<br>66 |
| Diarrhea<br>subjects affected / exposed<br>occurrences (all)                                                                          | 13 / 61 (21.31%)<br>17 | 15 / 59 (25.42%)<br>18 | 19 / 61 (31.15%)<br>34 |
| Vomiting                                                                                                                              |                        |                        |                        |

|                                             |                  |                 |                  |
|---------------------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed                 | 12 / 61 (19.67%) | 3 / 59 (5.08%)  | 16 / 61 (26.23%) |
| occurrences (all)                           | 16               | 3               | 23               |
| Abdominal pain                              |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 10 / 61 (16.39%) | 6 / 59 (10.17%) | 13 / 61 (21.31%) |
| occurrences (all)                           | 12               | 8               | 15               |
| Constipation                                |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 7 / 61 (11.48%)  | 3 / 59 (5.08%)  | 10 / 61 (16.39%) |
| occurrences (all)                           | 8                | 3               | 13               |
| Dry mouth                                   |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 6 / 61 (9.84%)   | 2 / 59 (3.39%)  | 8 / 61 (13.11%)  |
| occurrences (all)                           | 6                | 2               | 10               |
| Stomatitis                                  |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 4 / 61 (6.56%)   | 1 / 59 (1.69%)  | 5 / 61 (8.20%)   |
| occurrences (all)                           | 4                | 2               | 5                |
| Abdominal pain upper                        |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 4 / 59 (6.78%)  | 3 / 61 (4.92%)   |
| occurrences (all)                           | 0                | 4               | 3                |
| Skin and subcutaneous tissue disorders      |                  |                 |                  |
| Hair color changes                          |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 41 / 61 (67.21%) | 2 / 59 (3.39%)  | 44 / 61 (72.13%) |
| occurrences (all)                           | 46               | 2               | 53               |
| Pruritis                                    |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 10 / 61 (16.39%) | 2 / 59 (3.39%)  | 10 / 61 (16.39%) |
| occurrences (all)                           | 11               | 2               | 10               |
| Rash                                        |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 8 / 61 (13.11%)  | 3 / 59 (5.08%)  | 17 / 61 (27.87%) |
| occurrences (all)                           | 9                | 4               | 28               |
| Rash maculo-papular                         |                  |                 |                  |

|                                             |                |                |                  |
|---------------------------------------------|----------------|----------------|------------------|
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 6 / 61 (9.84%) | 1 / 59 (1.69%) | 10 / 61 (16.39%) |
| occurrences (all)                           | 8              | 1              | 17               |
| Erythema                                    |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 2 / 61 (3.28%)   |
| occurrences (all)                           | 0              | 0              | 3                |
| Pruritis generalized                        |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 6 / 61 (9.84%)   |
| occurrences (all)                           | 0              | 0              | 7                |
| Dry skin                                    |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 2 / 59 (3.39%) | 5 / 61 (8.20%)   |
| occurrences (all)                           | 0              | 2              | 6                |
| Alopecia                                    |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 4 / 61 (6.56%)   |
| occurrences (all)                           | 0              | 0              | 4                |
| Skin hypopigmentation                       |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 5 / 61 (8.20%)   |
| occurrences (all)                           | 0              | 1              | 7                |
| Photosensitivity reaction                   |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 3 / 61 (4.92%)   |
| occurrences (all)                           | 0              | 0              | 3                |
| Rash pruritic                               |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 1 / 61 (1.64%)   |
| occurrences (all)                           | 0              | 1              | 1                |
| Dermatitis                                  |                |                |                  |
| alternative assessment type: Non-systematic |                |                |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%) | 0 / 59 (0.00%) | 0 / 61 (0.00%)   |
| occurrences (all)                           | 0              | 0              | 0                |

|                                                 |                  |                  |                  |
|-------------------------------------------------|------------------|------------------|------------------|
| Renal and urinary disorders                     |                  |                  |                  |
| Haematuria                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 61 (0.00%)   | 2 / 59 (3.39%)   | 0 / 61 (0.00%)   |
| occurrences (all)                               | 0                | 2                | 0                |
| Musculoskeletal and connective tissue disorders |                  |                  |                  |
| Arthralgia                                      |                  |                  |                  |
| alternative assessment type: Non-systematic     |                  |                  |                  |
| subjects affected / exposed                     | 14 / 61 (22.95%) | 15 / 59 (25.42%) | 19 / 61 (31.15%) |
| occurrences (all)                               | 17               | 18               | 29               |
| Pain in extremity                               |                  |                  |                  |
| alternative assessment type: Non-systematic     |                  |                  |                  |
| subjects affected / exposed                     | 4 / 61 (6.56%)   | 3 / 59 (5.08%)   | 9 / 61 (14.75%)  |
| occurrences (all)                               | 6                | 3                | 11               |
| Back pain                                       |                  |                  |                  |
| alternative assessment type: Non-systematic     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 61 (0.00%)   | 0 / 59 (0.00%)   | 6 / 61 (9.84%)   |
| occurrences (all)                               | 0                | 0                | 7                |
| Muscle spasms                                   |                  |                  |                  |
| subjects affected / exposed                     | 2 / 61 (3.28%)   | 1 / 59 (1.69%)   | 4 / 61 (6.56%)   |
| occurrences (all)                               | 2                | 1                | 6                |
| Myalgia                                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 61 (1.64%)   | 2 / 59 (3.39%)   | 2 / 61 (3.28%)   |
| occurrences (all)                               | 1                | 2                | 2                |
| Infections and infestations                     |                  |                  |                  |
| Nasopharyngitis                                 |                  |                  |                  |
| alternative assessment type: Non-systematic     |                  |                  |                  |
| subjects affected / exposed                     | 4 / 61 (6.56%)   | 3 / 59 (5.08%)   | 5 / 61 (8.20%)   |
| occurrences (all)                               | 5                | 3                | 7                |
| Upper respiratory tract infection               |                  |                  |                  |
| alternative assessment type: Non-systematic     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 61 (0.00%)   | 0 / 59 (0.00%)   | 8 / 61 (13.11%)  |
| occurrences (all)                               | 0                | 0                | 11               |
| Sinusitis                                       |                  |                  |                  |
| alternative assessment type: Non-systematic     |                  |                  |                  |

|                                             |                  |                 |                  |
|---------------------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 0 / 59 (0.00%)  | 5 / 61 (8.20%)   |
| occurrences (all)                           | 0                | 0               | 9                |
| Cellulitis                                  |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 0 / 59 (0.00%)  | 1 / 61 (1.64%)   |
| occurrences (all)                           | 0                | 0               | 1                |
| Cystitis                                    |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 1 / 59 (1.69%)  | 0 / 61 (0.00%)   |
| occurrences (all)                           | 0                | 1               | 0                |
| Herpes zoster                               |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 0 / 59 (0.00%)  | 0 / 61 (0.00%)   |
| occurrences (all)                           | 0                | 0               | 0                |
| Influenza                                   |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 2 / 59 (3.39%)  | 2 / 61 (3.28%)   |
| occurrences (all)                           | 0                | 2               | 3                |
| Urinary tract infection                     |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 4 / 59 (6.78%)  | 2 / 61 (3.28%)   |
| occurrences (all)                           | 0                | 5               | 2                |
| Metabolism and nutrition disorders          |                  |                 |                  |
| Decreased appetite                          |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 10 / 61 (16.39%) | 6 / 59 (10.17%) | 11 / 61 (18.03%) |
| occurrences (all)                           | 13               | 6               | 15               |
| Hypercholesterolemia                        |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 5 / 61 (8.20%)   | 0 / 59 (0.00%)  | 7 / 61 (11.48%)  |
| occurrences (all)                           | 8                | 0               | 20               |
| Fluid retention                             |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |
| subjects affected / exposed                 | 0 / 61 (0.00%)   | 0 / 59 (0.00%)  | 3 / 61 (4.92%)   |
| occurrences (all)                           | 0                | 0               | 6                |
| Hyperglycemia                               |                  |                 |                  |
| alternative assessment type: Non-systematic |                  |                 |                  |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 61 (0.00%) | 1 / 59 (1.69%) | 1 / 61 (1.64%) |
| occurrences (all)           | 0              | 1              | 1              |
| Hypertriglyceridaemia       |                |                |                |
| subjects affected / exposed | 0 / 61 (0.00%) | 4 / 59 (6.78%) | 2 / 61 (3.28%) |
| occurrences (all)           | 0              | 5              | 4              |
| Hypophosphataemia           |                |                |                |
| subjects affected / exposed | 3 / 61 (4.92%) | 1 / 59 (1.69%) | 3 / 61 (4.92%) |
| occurrences (all)           | 3              | 1              | 6              |

| <b>Non-serious adverse events</b>                                   | Placebo (Part 1),<br>Crossover<br>Pexidartinib (Part 2) | All Pexidartinib<br>Treated |  |
|---------------------------------------------------------------------|---------------------------------------------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events               |                                                         |                             |  |
| subjects affected / exposed                                         | 30 / 30 (100.00%)                                       | 91 / 91 (100.00%)           |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                                         |                             |  |
| Tumor pain                                                          |                                                         |                             |  |
| alternative assessment type: Non-systematic                         |                                                         |                             |  |
| subjects affected / exposed                                         | 2 / 30 (6.67%)                                          | 6 / 91 (6.59%)              |  |
| occurrences (all)                                                   | 2                                                       | 9                           |  |
| Vascular disorders                                                  |                                                         |                             |  |
| Hypertension                                                        |                                                         |                             |  |
| alternative assessment type: Non-systematic                         |                                                         |                             |  |
| subjects affected / exposed                                         | 12 / 30 (40.00%)                                        | 26 / 91 (28.57%)            |  |
| occurrences (all)                                                   | 21                                                      | 45                          |  |
| Hypotension                                                         |                                                         |                             |  |
| alternative assessment type: Non-systematic                         |                                                         |                             |  |
| subjects affected / exposed                                         | 2 / 30 (6.67%)                                          | 2 / 91 (2.20%)              |  |
| occurrences (all)                                                   | 2                                                       | 2                           |  |
| General disorders and administration site conditions                |                                                         |                             |  |
| Fatigue                                                             |                                                         |                             |  |
| subjects affected / exposed                                         | 8 / 30 (26.67%)                                         | 43 / 91 (47.25%)            |  |
| occurrences (all)                                                   | 13                                                      | 70                          |  |
| Face oedema                                                         |                                                         |                             |  |
| alternative assessment type: Non-systematic                         |                                                         |                             |  |
| subjects affected / exposed                                         | 6 / 30 (20.00%)                                         | 15 / 91 (16.48%)            |  |
| occurrences (all)                                                   | 13                                                      | 24                          |  |
| Oedema peripheral                                                   |                                                         |                             |  |

|                                                 |                 |                  |  |
|-------------------------------------------------|-----------------|------------------|--|
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 9 / 30 (30.00%) | 24 / 91 (26.37%) |  |
| occurrences (all)                               | 11              | 29               |  |
| Asthenia                                        |                 |                  |  |
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 7 / 30 (23.33%) | 16 / 91 (17.58%) |  |
| occurrences (all)                               | 18              | 34               |  |
| Pyrexia                                         |                 |                  |  |
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 6 / 30 (20.00%) | 14 / 91 (15.38%) |  |
| occurrences (all)                               | 6               | 14               |  |
| Influenza like illness                          |                 |                  |  |
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 1 / 30 (3.33%)  | 6 / 91 (6.59%)   |  |
| occurrences (all)                               | 1               | 7                |  |
| Chest pain                                      |                 |                  |  |
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)  | 3 / 91 (3.30%)   |  |
| occurrences (all)                               | 2               | 3                |  |
| Malaise                                         |                 |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)  | 3 / 91 (3.30%)   |  |
| occurrences (all)                               | 3               | 4                |  |
| Peripheral swelling                             |                 |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)  | 2 / 91 (2.20%)   |  |
| occurrences (all)                               | 2               | 2                |  |
| Respiratory, thoracic and mediastinal disorders |                 |                  |  |
| Cough                                           |                 |                  |  |
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 5 / 30 (16.67%) | 9 / 91 (9.89%)   |  |
| occurrences (all)                               | 7               | 13               |  |
| Dyspnoea                                        |                 |                  |  |
| alternative assessment type: Non-systematic     |                 |                  |  |
| subjects affected / exposed                     | 4 / 30 (13.33%) | 7 / 91 (7.69%)   |  |
| occurrences (all)                               | 4               | 8                |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                 |                                                                                                                                                                         |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| <p>Oropharyngeal pain</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <p>1 / 30 (3.33%)</p> <p>1</p>                                                                                                                                  | <p>5 / 91 (5.49%)</p> <p>5</p>                                                                                                                                          |  |
| <p>Psychiatric disorders</p> <p>Insomnia</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Anxiety</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <p>3 / 30 (10.00%)</p> <p>4</p> <p>2 / 30 (6.67%)</p> <p>2</p>                                                                                                  | <p>7 / 91 (7.69%)</p> <p>8</p> <p>3 / 91 (3.30%)</p> <p>3</p>                                                                                                           |  |
| <p>Investigations</p> <p>Aspartate aminotransferase increased</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Alanine aminotransferase increased</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood alkaline phosphatase increased</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Blood lactate dehydrogenase increased</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>White blood cell count decreased</p> <p>alternative assessment type: Non-systematic</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Weight increased</p> <p>alternative assessment type: Non-</p> | <p>6 / 30 (20.00%)</p> <p>11</p> <p>7 / 30 (23.33%)</p> <p>13</p> <p>1 / 30 (3.33%)</p> <p>1</p> <p>3 / 30 (10.00%)</p> <p>6</p> <p>1 / 30 (3.33%)</p> <p>2</p> | <p>34 / 91 (37.36%)</p> <p>74</p> <p>26 / 91 (28.57%)</p> <p>66</p> <p>10 / 91 (10.99%)</p> <p>31</p> <p>10 / 91 (10.99%)</p> <p>23</p> <p>7 / 91 (7.69%)</p> <p>13</p> |  |



|                                             |                 |                  |  |
|---------------------------------------------|-----------------|------------------|--|
| systematic                                  |                 |                  |  |
| subjects affected / exposed                 | 4 / 30 (13.33%) | 7 / 91 (7.69%)   |  |
| occurrences (all)                           | 4               | 8                |  |
| Blood bilirubin increased                   |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 1 / 30 (3.33%)  | 5 / 91 (5.49%)   |  |
| occurrences (all)                           | 1               | 9                |  |
| Blood creatine phosphokinase increased      |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 4 / 30 (13.33%) | 10 / 91 (10.99%) |  |
| occurrences (all)                           | 27              | 43               |  |
| Blood triglycerides increased               |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 3 / 91 (3.30%)   |  |
| occurrences (all)                           | 2               | 5                |  |
| Cardiac disorders                           |                 |                  |  |
| Bradycardia                                 |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 2 / 91 (2.20%)   |  |
| occurrences (all)                           | 3               | 3                |  |
| Palpitations                                |                 |                  |  |
| subjects affected / exposed                 | 0 / 30 (0.00%)  | 4 / 91 (4.40%)   |  |
| occurrences (all)                           | 0               | 5                |  |
| Tachycardia                                 |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 3 / 91 (3.30%)   |  |
| occurrences (all)                           | 2               | 5                |  |
| Nervous system disorders                    |                 |                  |  |
| Dysgeusia                                   |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 7 / 30 (23.33%) | 25 / 91 (27.47%) |  |
| occurrences (all)                           | 10              | 39               |  |
| Headache                                    |                 |                  |  |
| subjects affected / exposed                 | 6 / 30 (20.00%) | 21 / 91 (23.08%) |  |
| occurrences (all)                           | 8               | 33               |  |
| Dizziness                                   |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |

|                                             |                 |                  |  |
|---------------------------------------------|-----------------|------------------|--|
| subjects affected / exposed                 | 5 / 30 (16.67%) | 12 / 91 (13.19%) |  |
| occurrences (all)                           | 5               | 16               |  |
| Paresthesia                                 |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 9 / 91 (9.89%)   |  |
| occurrences (all)                           | 6               | 13               |  |
| Memory impairment                           |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 5 / 91 (5.49%)   |  |
| occurrences (all)                           | 7               | 9                |  |
| Neuropathy peripheral                       |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 1 / 30 (3.33%)  | 5 / 91 (5.49%)   |  |
| occurrences (all)                           | 1               | 6                |  |
| Hypoaesthesia                               |                 |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 4 / 91 (4.40%)   |  |
| occurrences (all)                           | 5               | 6                |  |
| Sciatica                                    |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 2 / 91 (2.20%)   |  |
| occurrences (all)                           | 2               | 2                |  |
| Blood and lymphatic system disorders        |                 |                  |  |
| Anaemia                                     |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 1 / 30 (3.33%)  | 8 / 91 (8.79%)   |  |
| occurrences (all)                           | 1               | 13               |  |
| Neutropenia                                 |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 6 / 91 (6.59%)   |  |
| occurrences (all)                           | 3               | 16               |  |
| Leukopenia                                  |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 6 / 91 (6.59%)   |  |
| occurrences (all)                           | 10              | 17               |  |
| Thrombocytopenia                            |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                       |                                                                                                                                        |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 2 / 30 (6.67%)<br>5                                                                                                                   | 4 / 91 (4.40%)<br>7                                                                                                                    |  |
| Ear and labyrinth disorders<br>Tinnitus<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Vertigo<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)                                                                                                                                                                                                                                                                                                                                 | <br><br>3 / 30 (10.00%)<br>6<br><br>4 / 30 (13.33%)<br>4                                                                              | <br><br>5 / 91 (5.49%)<br>8<br><br>8 / 91 (8.79%)<br>8                                                                                 |  |
| Eye disorders<br>Periorbital edema<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Eye oedema<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Eyelid oedema<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Vision blurred<br>alternative assessment type: Non-systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Lacrimation increased<br>subjects affected / exposed<br>occurrences (all) | <br>5 / 30 (16.67%)<br>6<br><br>0 / 30 (0.00%)<br>0<br><br>3 / 30 (10.00%)<br>4<br><br>2 / 30 (6.67%)<br>3<br><br>1 / 30 (3.33%)<br>1 | <br>22 / 91 (24.18%)<br>29<br><br>6 / 91 (6.59%)<br>6<br><br>6 / 91 (6.59%)<br>9<br><br>7 / 91 (7.69%)<br>8<br><br>5 / 91 (5.49%)<br>5 |  |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <br>7 / 30 (23.33%)<br>10                                                                                                             | <br>35 / 91 (38.46%)<br>76                                                                                                             |  |

|                                             |                  |                  |  |
|---------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                 | 10 / 30 (33.33%) | 29 / 91 (31.87%) |  |
| occurrences (all)                           | 23               | 57               |  |
| Vomiting                                    |                  |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%)  | 19 / 91 (20.88%) |  |
| occurrences (all)                           | 3                | 26               |  |
| Abdominal pain                              |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%)  | 16 / 91 (17.58%) |  |
| occurrences (all)                           | 3                | 18               |  |
| Constipation                                |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%)  | 13 / 91 (14.29%) |  |
| occurrences (all)                           | 5                | 18               |  |
| Dry mouth                                   |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |
| subjects affected / exposed                 | 4 / 30 (13.33%)  | 12 / 91 (13.19%) |  |
| occurrences (all)                           | 4                | 14               |  |
| Stomatitis                                  |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%)  | 8 / 91 (8.79%)   |  |
| occurrences (all)                           | 5                | 10               |  |
| Abdominal pain upper                        |                  |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)   | 5 / 91 (5.49%)   |  |
| occurrences (all)                           | 2                | 5                |  |
| Skin and subcutaneous tissue disorders      |                  |                  |  |
| Hair color changes                          |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |
| subjects affected / exposed                 | 25 / 30 (83.33%) | 69 / 91 (75.82%) |  |
| occurrences (all)                           | 39               | 92               |  |
| Pruritis                                    |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |
| subjects affected / exposed                 | 9 / 30 (30.00%)  | 19 / 91 (20.88%) |  |
| occurrences (all)                           | 15               | 25               |  |
| Rash                                        |                  |                  |  |
| alternative assessment type: Non-systematic |                  |                  |  |

|                                             |                 |                  |
|---------------------------------------------|-----------------|------------------|
| subjects affected / exposed                 | 8 / 30 (26.67%) | 25 / 91 (27.47%) |
| occurrences (all)                           | 13              | 41               |
| Rash maculo-papular                         |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 4 / 30 (13.33%) | 14 / 91 (15.38%) |
| occurrences (all)                           | 5               | 22               |
| Erythema                                    |                 |                  |
| subjects affected / exposed                 | 6 / 30 (20.00%) | 8 / 91 (8.79%)   |
| occurrences (all)                           | 10              | 13               |
| Pruritis generalized                        |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 5 / 30 (16.67%) | 11 / 91 (12.09%) |
| occurrences (all)                           | 5               | 12               |
| Dry skin                                    |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 8 / 91 (8.79%)   |
| occurrences (all)                           | 4               | 10               |
| Alopecia                                    |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 6 / 91 (6.59%)   |
| occurrences (all)                           | 2               | 6                |
| Skin hypopigmentation                       |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 1 / 30 (3.33%)  | 6 / 91 (6.59%)   |
| occurrences (all)                           | 1               | 8                |
| Photosensitivity reaction                   |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 6 / 91 (6.59%)   |
| occurrences (all)                           | 4               | 7                |
| Rash pruritic                               |                 |                  |
| alternative assessment type: Non-systematic |                 |                  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 3 / 91 (3.30%)   |
| occurrences (all)                           | 3               | 4                |
| Dermatitis                                  |                 |                  |
| alternative assessment type: Non-           |                 |                  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| systematic                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)   | 2 / 91 (2.20%)   |  |
| occurrences (all)                               | 3                | 3                |  |
| Renal and urinary disorders                     |                  |                  |  |
| Haematuria                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)   | 2 / 91 (2.20%)   |  |
| occurrences (all)                               | 2                | 2                |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |
| Arthralgia                                      |                  |                  |  |
| alternative assessment type: Non-systematic     |                  |                  |  |
| subjects affected / exposed                     | 15 / 30 (50.00%) | 34 / 91 (37.36%) |  |
| occurrences (all)                               | 33               | 62               |  |
| Pain in extremity                               |                  |                  |  |
| alternative assessment type: Non-systematic     |                  |                  |  |
| subjects affected / exposed                     | 6 / 30 (20.00%)  | 15 / 91 (16.48%) |  |
| occurrences (all)                               | 17               | 28               |  |
| Back pain                                       |                  |                  |  |
| alternative assessment type: Non-systematic     |                  |                  |  |
| subjects affected / exposed                     | 4 / 30 (13.33%)  | 10 / 91 (10.99%) |  |
| occurrences (all)                               | 8                | 15               |  |
| Muscle spasms                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 30 (3.33%)   | 5 / 91 (5.49%)   |  |
| occurrences (all)                               | 1                | 7                |  |
| Myalgia                                         |                  |                  |  |
| subjects affected / exposed                     | 4 / 30 (13.33%)  | 6 / 91 (6.59%)   |  |
| occurrences (all)                               | 7                | 9                |  |
| Infections and infestations                     |                  |                  |  |
| Nasopharyngitis                                 |                  |                  |  |
| alternative assessment type: Non-systematic     |                  |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)   | 7 / 91 (7.69%)   |  |
| occurrences (all)                               | 2                | 9                |  |
| Upper respiratory tract infection               |                  |                  |  |
| alternative assessment type: Non-systematic     |                  |                  |  |
| subjects affected / exposed                     | 2 / 30 (6.67%)   | 10 / 91 (10.99%) |  |
| occurrences (all)                               | 2                | 13               |  |

|                                             |                 |                  |  |
|---------------------------------------------|-----------------|------------------|--|
| Sinusitis                                   |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 1 / 30 (3.33%)  | 6 / 91 (6.59%)   |  |
| occurrences (all)                           | 1               | 10               |  |
| Cellulitis                                  |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 4 / 91 (4.40%)   |  |
| occurrences (all)                           | 3               | 4                |  |
| Cystitis                                    |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 2 / 91 (2.20%)   |  |
| occurrences (all)                           | 3               | 3                |  |
| Herpes zoster                               |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 2 / 91 (2.20%)   |  |
| occurrences (all)                           | 2               | 2                |  |
| Influenza                                   |                 |                  |  |
| subjects affected / exposed                 | 4 / 30 (13.33%) | 6 / 91 (6.59%)   |  |
| occurrences (all)                           | 5               | 8                |  |
| Urinary tract infection                     |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 4 / 91 (4.40%)   |  |
| occurrences (all)                           | 6               | 8                |  |
| Metabolism and nutrition disorders          |                 |                  |  |
| Decreased appetite                          |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 3 / 30 (10.00%) | 14 / 91 (15.38%) |  |
| occurrences (all)                           | 4               | 19               |  |
| Hypercholesterolemia                        |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 4 / 30 (13.33%) | 11 / 91 (12.09%) |  |
| occurrences (all)                           | 7               | 27               |  |
| Fluid retention                             |                 |                  |  |
| alternative assessment type: Non-systematic |                 |                  |  |
| subjects affected / exposed                 | 2 / 30 (6.67%)  | 5 / 91 (5.49%)   |  |
| occurrences (all)                           | 5               | 11               |  |
| Hyperglycemia                               |                 |                  |  |

|                                             |                |                |  |
|---------------------------------------------|----------------|----------------|--|
| alternative assessment type: Non-systematic |                |                |  |
| subjects affected / exposed                 | 2 / 30 (6.67%) | 3 / 91 (3.30%) |  |
| occurrences (all)                           | 2              | 3              |  |
| Hypertriglyceridaemia                       |                |                |  |
| subjects affected / exposed                 | 2 / 30 (6.67%) | 4 / 91 (4.40%) |  |
| occurrences (all)                           | 3              | 7              |  |
| Hypophosphataemia                           |                |                |  |
| subjects affected / exposed                 | 2 / 30 (6.67%) | 5 / 91 (5.49%) |  |
| occurrences (all)                           | 3              | 9              |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                             |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 05 December 2014  | Clarified treatment procedures (e.g. maximum number of cycles) of pexidartinib, revised inclusion and exclusion criteria, modified sample size, updated treatment composition, and clarified dose modification guidelines.                            |
| 11 February 2015  | Revised inclusion criteria, clarified blinding/unblinding procedures, updated list of participating countries, clarified location of Schedule of Events, updated medical monitor, and updated assessment methods.                                     |
| 25 March 2016     | Updated formulation of pexidartinib, clarified inclusion and exclusion criteria, revised study assessments, clarified study procedures, and updated efficacy endpoints and dose modification guidelines.                                              |
| 19 July 2016      | Revised study procedures and statistical analyses, updated efficacy endpoints, and clarified unblinding procedures.                                                                                                                                   |
| 10 October 2016   | Updated Risk Information and Change in Study Conduct section and new safety data and measures were included.                                                                                                                                          |
| 10 February 2017  | Clarified study inclusion and exclusion criteria, updated methods for pharmacogenomics analysis, clarified criteria of completion for assessments, clarified study procedures for subjects who complete Part 2, and updated MedDRA version reference. |
| 11 September 2017 | Sequential hierarchy of the secondary efficacy endpoints was changed and the medical monitor was updated.                                                                                                                                             |
| 15 December 2017  | Updated safety data for pexidartinib and revised the criteria for pexidartinib dose modification.                                                                                                                                                     |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date              | Interruption                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Restart date |
|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| 30 September 2016 | Enrollment was stopped; no new subjects were permitted to start the study drug. Subjects on placebo in Part 1 were no longer allowed to enter Part 2 to receive open-label pexidartinib. After Part 1 was completed, subjects who wished to continue onto the open-label part of the study (Part 2) were unblinded and those on placebo were discontinued. Investigators and subjects were informed of the new safety information and decided whether to continue in the study. The frequency of liver function testing was increased and gamma-glutamyl transpeptidase was added to the laboratory panel. These changes were implemented in the protocol version 6.0 dated 10 Oct 2016. | -            |

Notes:

### Limitations and caveats

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

Enrollment was stopped on 30 Sep 2016; no new subjects received the study drug. After Part 1, those who wished to continue were un-blinded; those on placebo were discontinued.

Notes: