



## Clinical trial results:

**A multi-centre Phase IIa double-blind, placebo-controlled study to investigate the efficacy and safety of GSK3196165 in subjects with inflammatory hand osteoarthritis.**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-003089-96   |
| Trial protocol           | GB DE NL PL      |
| Global end of trial date | 29 November 2017 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 12 April 2019    |
| First version publication date | 12 December 2018 |
| Version creation reason        |                  |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 204851 |
|-----------------------|--------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline  |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |

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:

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**Results analysis stage**

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 13 April 2018 |
| Is this the analysis of the primary completion data? | No            |

|                                  |                  |
|----------------------------------|------------------|
| Global end of trial reached?     | Yes              |
| Global end of trial date         | 29 November 2017 |
| Was the trial ended prematurely? | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

To assess the efficacy potential of GSK3196165 on pain in inflammatory hand osteoarthritis.

Protection of trial subjects:

Paracetamol (acetaminophen) was a permitted concomitant medication for hand pain, for the duration of this study and could be taken on an as needed basis up to 4gram per day or to the maximum permitted under local label.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 17 March 2016 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Germany: 11        |
| Country: Number of subjects enrolled | Netherlands: 8     |
| Country: Number of subjects enrolled | Poland: 8          |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | United States: 7   |
| Worldwide total number of subjects   | 44                 |
| EEA total number of subjects         | 37                 |

Notes:

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**Subjects enrolled per age group**

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 36 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 8 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This was a multi-center, double-blind, placebo-controlled study to investigate the efficacy and safety of GSK3196165 in participants with inflammatory hand osteoarthritis. The study was conducted in five countries in Poland, United Kingdom, Netherlands, Germany and United States.

### Pre-assignment

Screening details:

A total 121 participants were screened of which 77 were screen failures and 44 participants were enrolled in the study.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall Study (overall period)                                |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

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

Arm description:

Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

|  |                        |
|--|------------------------|
| Arm type                               | Placebo                |
| Investigational medicinal product name | Placebo                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Participants were administered sterile 0.9 percentage (w/v) sodium chloride solution.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | GSK3196165 180mg |
|------------------|------------------|

Arm description:

Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | GSK3196165             |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Participants were administered 180 milligram (1.2 milliliter) of GSK3196165 aqueous solution of purified monoclonal antibody.

| <b>Number of subjects in period 1</b> | Placebo | GSK3196165 180mg |
|---------------------------------------|---------|------------------|
| Started                               | 22      | 22               |
| Completed                             | 21      | 18               |
| Not completed                         | 1       | 4                |
| Consent withdrawn by subject          | 1       | 1                |
| Adverse event, non-fatal              | -       | 2                |
| Lost to follow-up                     | -       | 1                |

## Baseline characteristics

### Reporting groups

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

Reporting group description:

Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

|                       |                  |
|-----------------------|------------------|
| Reporting group title | GSK3196165 180mg |
|-----------------------|------------------|

Reporting group description:

Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

| Reporting group values                                | Placebo | GSK3196165 180mg | Total |
|---|---------|------------------|-------|
| Number of subjects                                    | 22      | 22               | 44    |
| 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 months)              | 0       | 0                | 0     |
| Children (2-11 years)                                 | 0       | 0                | 0     |
| Adolescents (12-17 years)                             | 0       | 0                | 0     |
| Adults (18-64 years)                                  | 19      | 17               | 36    |
| From 65-84 years                                      | 3       | 5                | 8     |
| 85 years and over                                     | 0       | 0                | 0     |
| Age Continuous<br>Units: Years                        |         |                  |       |
| arithmetic mean                                       | 56.7    | 60.9             |       |
| standard deviation                                    | ± 6.80  | ± 6.25           | -     |
| Sex: Female, Male<br>Units: Subjects                  |         |                  |       |
| Female  | 20      | 20               | 40    |
| Male  | 2       | 2                | 4     |
| Race/Ethnicity, Customized<br>Units: Subjects         |         |                  |       |

## End points

### End points reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | Placebo          |
| Reporting group description:<br>Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71). |                  |
| Reporting group title   | GSK3196165 180mg |
| Reporting group description:<br>Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).             |                  |

### Primary: Change from Baseline in 24-hour average hand pain intensity, averaged over the 7 days prior to Week 6

|   |   |
|---|---|
| End point title   | Change from Baseline in 24-hour average hand pain intensity, averaged over the 7 days prior to Week 6 |
| End point description:<br>Participants were required to complete a daily pain NRS based on their 24-hour average hand pain intensity with the anchors "0" (no pain) and "10" (worst imaginable pain), which was averaged over the 7 days prior to assessment visit. The 7 day average score was calculated as sum of daily 24 hours average hand pain NRS scores in the 7 days prior to assessment visit, divided by number of entries recorded in those 7 days. Baseline visit was at Day 1 and Baseline value was defined as the average of the 7 days prior to baseline visit (Day 1 pre-dose). Change from Baseline is equal to post-dose visit value minus Baseline value. Intent-To-Treat Population comprised of all randomized participants who received at least one dose of study treatment (GSK3196165 or placebo). n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model. |   |
| End point type  | Primary   |
| End point timeframe:<br>Baseline (Day 1 Pre-dose) and Week 6  |   |

| End point values                    | Placebo           | GSK3196165 180mg  |  |  |
|-------------------------------------|-------------------|-------------------|--|--|
| Subject group type                  | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed         | 21 <sup>[1]</sup> | 20 <sup>[2]</sup> |  |  |
| Units: Scores on scale              |                   |                   |  |  |
| least squares mean (standard error) | -1.34 (± 0.325)   | -1.70 (± 0.334)   |  |  |

Notes:

[1] - Intent To Treat Population.

[2] - Intent To Treat Population.

### Statistical analyses

|                            |   |
|----------------------------|---|
| Statistical analysis title | Difference from placebo for Week 6 is presented |
| Comparison groups          | Placebo v GSK3196165 180mg                      |

|   |  |
|---|--|
| Number of subjects included in analysis | 41                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.442 <sup>[3]</sup>                 |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.36                                  |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.31                                  |
| upper limit                             | 0.58                                   |

Notes:

[3] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

### Secondary: Change from Baseline in 24 hours average hand pain intensity averaged over the 7 days prior to each visit

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in 24 hours average hand pain intensity averaged over the 7 days prior to each visit |
|-----------------|---|

End point description:

Participants were required to complete a daily pain NRS based on their 24-hour average hand pain intensity with the anchors "0" (no pain) and "10" (worst imaginable pain), which was averaged over the 7 days prior to assessment visit. The 7 day average score is calculated by sum of daily 24 hours average hand pain NRS scores in the 7 days prior to assessment visit, divided by number of entries recorded in those 7 days. Baseline visit was at Day 1 and Baseline value was defined as the average of the 7 days prior to baseline visit (Day 1 pre-dose). Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

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

End point timeframe:

Baseline (Pre-dose Day 1), Weeks 1, 2, 3, 4, 6, 8, 10 and 12

| End point values                    | Placebo            | GSK3196165<br>180mg |  |  |
|-------------------------------------|--------------------|---------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed         | 22 <sup>[4]</sup>  | 22 <sup>[5]</sup>   |  |  |
| Units: Scores on scale              |                    |                     |  |  |
| least squares mean (standard error) |                    |                     |  |  |
| Week 1, n=22, 20                    | -0.13 (±<br>0.152) | -0.59 (±<br>0.160)  |  |  |
| Week 2, n=21, 20                    | -0.48 (±<br>0.230) | -0.86 (±<br>0.239)  |  |  |
| Week 3, n=21, 20                    | -0.74 (±<br>0.279) | -1.24 (±<br>0.289)  |  |  |
| Week 4, n=21, 20                    | -0.91 (±<br>0.291) | -1.65 (±<br>0.301)  |  |  |
| Week 6, n=21, 20                    | -1.34 (±<br>0.325) | -1.70 (±<br>0.334)  |  |  |
| Week 8, n=20, 19                    | -1.27 (±<br>0.382) | -2.10 (±<br>0.393)  |  |  |
| Week 10, n=20, 19                   | -1.18 (±<br>0.376) | -2.09 (±<br>0.389)  |  |  |

|                   |                      |                      |  |  |
|-------------------|----------------------|----------------------|--|--|
| Week 12, n=19, 18 | -1.35 ( $\pm$ 0.402) | -2.24 ( $\pm$ 0.416) |  |  |
|-------------------|----------------------|----------------------|--|--|

Notes:

[4] - Intent-to-Treat Population.

[5] - Intent-to-Treat Population.

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 1 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.046 <sup>[6]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.46   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.9  |
| upper limit                             | -0.01   |

Notes:

[6] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 2 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.257 <sup>[7]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.38   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.05   |
| upper limit                             | 0.29  |

Notes:

[7] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Difference from placebo for Week 3 is presented |
| Comparison groups                 | Placebo v GSK3196165 180mg                      |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.22 <sup>[8]</sup>                  |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.5                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.31                                  |
| upper limit                             | 0.31                                   |

Notes:

[8] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 4 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.085 <sup>[9]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.74   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.59   |
| upper limit                             | 0.11  |

Notes:

[9] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 6 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.442 <sup>[10]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.36   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.31   |
| upper limit                             | 0.58  |

Notes:

[10] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 8 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.139 <sup>[11]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.83   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.93   |
| upper limit                             | 0.28  |

Notes:

[11] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 10 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.103 <sup>[12]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.9   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -2   |
| upper limit                             | 0.19   |

Notes:

[12] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 12 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.132 <sup>[13]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.89  |

| Confidence interval |         |
|---------------------|---------|
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -2.06   |
| upper limit         | 0.28    |

Notes:

[13] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

### Secondary: Change from Baseline of worst hand pain intensity over 24 hours averaged over the 7 days prior to each visit

|                 |  |
|-----------------|--|
| End point title | Change from Baseline of worst hand pain intensity over 24 hours averaged over the 7 days prior to each visit |
|-----------------|--|

End point description:

Participants were required to complete a daily pain NRS based on their 24-hour worst hand pain intensity with the anchors "0" (no pain) and "10" (worst imaginable pain), which was averaged over the 7 days prior to assessment visit. The score is calculated as sum of daily 24 hours worst hand pain NRS scores in the 7 days prior to assessment visit, divided by number of entries recorded in those 7 days. Baseline visit was at Day 1 and Baseline value was defined as the average of the 7 days prior to baseline visit (Day 1 pre-dose). Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

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

End point timeframe:

Baseline (Pre-dose Day 1), Weeks 1, 2, 3, 4, 6, 8, 10 and 12

| End point values                    | Placebo            | GSK3196165<br>180mg |  |  |
|-------------------------------------|--------------------|---------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed         | 22 <sup>[14]</sup> | 22 <sup>[15]</sup>  |  |  |
| Units: Scores on scale              |                    |                     |  |  |
| least squares mean (standard error) |                    |                     |  |  |
| Week 1, n=22, 20                    | 0.01 (± 0.174)     | -0.45 (± 0.183)     |  |  |
| Week 2, n=21, 20                    | -0.42 (± 0.235)    | -0.69 (± 0.245)     |  |  |
| Week 3, n=21, 20                    | -0.63 (± 0.269)    | -1.23 (± 0.278)     |  |  |
| Week 4, n= 21, 20                   | -0.72 (± 0.289)    | -1.51 (± 0.299)     |  |  |
| Week 6, n= 21, 20                   | -1.30 (± 0.328)    | -1.63 (± 0.337)     |  |  |
| Week 8, n= 20, 19                   | -1.18 (± 0.394)    | -2.11 (± 0.406)     |  |  |
| Week 10, n= 20, 19                  | -1.15 (± 0.394)    | -2.13 (± 0.407)     |  |  |
| Week 12, n= 19, 18                  | -1.32 (± 0.415)    | -2.34 (± 0.430)     |  |  |

Notes:

[14] - Intent-to-Treat Population.

[15] - Intent-to-Treat Population.

### Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 1 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.082 <sup>[16]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.45   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.97   |
| upper limit                             | 0.06  |

Notes:

[16] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 2 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.426 <sup>[17]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.27   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -0.96   |
| upper limit                             | 0.41  |

Notes:

[17] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 3 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.129 <sup>[18]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.6  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.38   |
| upper limit                             | 0.18  |

Notes:

[18] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 4 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.067 <sup>[19]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.78   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.63   |
| upper limit                             | 0.06  |

Notes:

[19] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 6 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.494 <sup>[20]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.33   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.28   |
| upper limit                             | 0.63  |

Notes:

[20] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 8 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.107 <sup>[21]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.94   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -2.08   |
| upper limit         | 0.21    |

Notes:

[21] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 10 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.092 <sup>[22]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.98  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -2.13  |
| upper limit                             | 0.17   |

Notes:

[22] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 12 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.098 <sup>[23]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -1.01  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -2.22  |
| upper limit                             | 0.2  |

Notes:

[23] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

### **Secondary: Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit**

|                 |  |
|-----------------|--|
| End point title | Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit |
|-----------------|--|

End point description:

Participants were required to complete average pain NRS daily and rate the average hand pain over last

24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants who achieved at least 30 percentage reduction from Baseline in the 24-hours average hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is reported. Participants with missing data at a particular visit had been assumed to be non-responders.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22) |           |

| End point values                  | Placebo            | GSK3196165<br>180mg |  |  |
|-----------------------------------|--------------------|---------------------|--|--|
| Subject group type                | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed       | 22 <sup>[24]</sup> | 22 <sup>[25]</sup>  |  |  |
| Units: Percentage of participants |                    |                     |  |  |
| Week 1                            | 0                  | 9                   |  |  |
| Week 2                            | 0                  | 18                  |  |  |
| Week 3                            | 5                  | 23                  |  |  |
| Week 4                            | 14                 | 41                  |  |  |
| Week 6                            | 23                 | 45                  |  |  |
| Week 8                            | 18                 | 50                  |  |  |
| Week 10                           | 18                 | 50                  |  |  |
| Week 12                           | 23                 | 45                  |  |  |
| Follow up (Week 22)               | 23                 | 27                  |  |  |

Notes:

[24] - Intent-to-Treat Population.

[25] - Intent-to-Treat Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit

|                 |  |
|-----------------|--|
| End point title | Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours average hand pain intensity at each visit |
|-----------------|--|

End point description:

Participants were required to complete average pain NRS daily and rate the average hand pain over last 24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants who achieved at least 50 percentage reduction from Baseline in the 24-hours average hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is presented. Participants with missing data at a particular visit had been assumed to be non-responders.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22) |           |

| End point values                  | Placebo            | GSK3196165<br>180mg |  |  |
|-----------------------------------|--------------------|---------------------|--|--|
| Subject group type                | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed       | 22 <sup>[26]</sup> | 22 <sup>[27]</sup>  |  |  |
| Units: Percentage of participants |                    |                     |  |  |
| Week 1                            | 0                  | 0                   |  |  |
| Week 2                            | 0                  | 9                   |  |  |
| Week 3                            | 0                  | 18                  |  |  |
| Week 4                            | 0                  | 23                  |  |  |
| Week 6                            | 14                 | 27                  |  |  |
| Week 8                            | 14                 | 41                  |  |  |
| Week 10                           | 9                  | 36                  |  |  |
| Week 12                           | 14                 | 41                  |  |  |
| Follow up (Week 22)               | 9                  | 23                  |  |  |

Notes:

[26] - Intent-to-Treat Population.

[27] - Intent-to-Treat Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit

|                 |  |
|-----------------|--|
| End point title | Percentage of participants achieving a 30 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit |
|-----------------|--|

End point description:

Participants were required to complete worst pain NRS daily and rate the hand pain at its worst over last 24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants achieving at least 30 percentage reduction from Baseline in the 24-hours worst hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is presented. Participants with missing data at a particular visit had been assumed to be non-responders.

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

End point timeframe:

Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22)

| End point values                  | Placebo            | GSK3196165<br>180mg |  |  |
|-----------------------------------|--------------------|---------------------|--|--|
| Subject group type                | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed       | 22 <sup>[28]</sup> | 22 <sup>[29]</sup>  |  |  |
| Units: Percentage of participants |                    |                     |  |  |
| Week 1                            | 0                  | 9                   |  |  |
| Week 2                            | 0                  | 18                  |  |  |
| Week 3                            | 0                  | 23                  |  |  |
| Week 4                            | 0                  | 32                  |  |  |
| Week 6                            | 9                  | 36                  |  |  |
| Week 8                            | 9                  | 45                  |  |  |
| Week 10                           | 14                 | 45                  |  |  |
| Week 12                           | 14                 | 45                  |  |  |
| Follow up (Week 22)               | 14                 | 32                  |  |  |

Notes:

[28] - Intent-to-Treat Population.

[29] - Intent-to-Treat Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit

|                 |  |
|-----------------|--|
| End point title | Percentage of participants achieving a 50 percentage reduction from Baseline in 24 hours worst hand pain intensity at each visit |
|-----------------|--|

End point description:

Participants were required to complete worst pain NRS daily and rate the hand pain at its worst over last 24 hours on a scale of 0 (no pain) to 10 (worst imaginable pain). The percentage of participants achieving at least 50 percentage reduction from Baseline in the 24-hours worst hand pain intensity as measured by daily NRS and averaged over 7 days prior to each visit is presented. Participants with missing data at a particular visit had been assumed to be non-responders.

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

End point timeframe:

Baseline (Pre-dose, Day 1), Weeks 1, 2, 3, 4, 6, 8, 10, 12 and follow up (Week 22)

| End point values                  | Placebo            | GSK3196165<br>180mg |  |  |
|-----------------------------------|--------------------|---------------------|--|--|
| Subject group type                | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed       | 22 <sup>[30]</sup> | 22 <sup>[31]</sup>  |  |  |
| Units: Percentage of participants |                    |                     |  |  |
| Week 1                            | 0                  | 0                   |  |  |
| Week 2                            | 0                  | 5                   |  |  |
| Week 3                            | 0                  | 14                  |  |  |
| Week 4                            | 0                  | 18                  |  |  |
| Week 6                            | 5                  | 18                  |  |  |
| Week 8                            | 5                  | 32                  |  |  |
| Week 10                           | 5                  | 27                  |  |  |
| Week 12                           | 9                  | 36                  |  |  |
| Follow up (Week 22)               | 5                  | 23                  |  |  |

Notes:

[30] - Intent-to-Treat Population.

[31] - Intent-to-Treat Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Australian Canadian Hand Osteoarthritis Index (AUSCAN) 3.1 NRS scores at each visit.

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Australian Canadian Hand Osteoarthritis Index (AUSCAN) 3.1 NRS scores at each visit. |
|-----------------|--|

# End point description:

The AUSCAN Index is a self-administered questionnaire consisting of a 15-item scale which measures pain (5 items), stiffness (1 item) and degree of disability/physical function (9 items) during the preceding 48 hours. All items are rated on NRS scale with anchors "0" (none) to "10" (extreme). The scores for the pain and physical function components were calculated as simple summation of the item scores relating to that domain, so the Pain component ranges from 0 (i.e. all pain item scores are scored 0 [none]) to 50 (i.e. all pain item scores are scored 10 [extreme]), and the Physical Function component ranges from 0 (i.e. all physical function item scores are scored 0 [none]) to 90 (i.e. all physical function item scores are scored 10 [extreme]). The total AUSCAN score was calculated as simple summation of the 15 item scores and therefore ranges from 0 to 150. Baseline is defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value.

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

# End point timeframe:

Baseline (Day 1 Pre-dose), Weeks 1, 2, 4, 6, 8, 10, and 12

| End point values                     | Placebo            | GSK3196165<br>180mg |  |  |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type                   | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed          | 22 <sup>[32]</sup> | 22 <sup>[33]</sup>  |  |  |
| Units: Scores on scale               |                    |                     |  |  |
| least squares mean (standard error)  |                    |                     |  |  |
| Pain, Week 1, n=22, 20               | 0.8 (± 0.98)       | -1.9 (± 1.03)       |  |  |
| Pain, Week 2, n=21, 21               | -1.8 (± 1.27)      | -3.7 (± 1.28)       |  |  |
| Pain, Week 4, n=22, 21               | -3.5 (± 1.61)      | -7.2 (± 1.64)       |  |  |
| Pain, Week 6, n=22, 21               | -6.6 (± 1.72)      | -7.6 (± 1.76)       |  |  |
| Pain, Week 8, n=20, 20               | -4.9 (± 1.93)      | -8.7 (± 1.97)       |  |  |
| Pain, Week 10, n=20, 20              | -5.3 (± 1.82)      | -10.9 (± 1.87)      |  |  |
| Pain, Week 12, n=21,19               | -4.6 (± 1.84)      | -9.3 (± 1.91)       |  |  |
| Stiffness, Week 1, n= 22, 20         | -0.4 (± 0.29)      | -0.6 (± 0.31)       |  |  |
| Stiffness, Week 2, n= 21, 21         | -0.8 (± 0.33)      | -1.1 (± 0.33)       |  |  |
| Stiffness, Week 4, n= 22, 21         | -1.2 (± 0.41)      | -1.8 (± 0.42)       |  |  |
| Stiffness, Week 6, n= 22, 21         | -1.4 (± 0.39)      | -1.6 (± 0.40)       |  |  |
| Stiffness, Week 8, n= 20, 20         | -1.2 (± 0.41)      | -1.9 (± 0.42)       |  |  |
| Stiffness, Week 10, n= 20, 20        | -1.6 (± 0.44)      | -2.2 (± 0.45)       |  |  |
| Stiffness, Week 12, n= 21, 19        | -1.5 (± 0.45)      | -2.2 (± 0.47)       |  |  |
| Physical function, Week 1, n=22, 20  | -0.7 (± 2.08)      | -3.6 (± 2.16)       |  |  |
| Physical function, Week 2, n=21,21   | -2.8 (± 2.35)      | -5.7 (± 2.37)       |  |  |
| Physical function, Week 4, n=22, 21  | -6.4 (± 3.01)      | -11.3 (± 3.07)      |  |  |
| Physical function, Week 6, n=22, 21  | -9.1 (± 3.25)      | -11.8 (± 3.32)      |  |  |
| Physical function, Week 8, n=20, 20  | -8.3 (± 3.57)      | -13.2 (± 3.64)      |  |  |
| Physical function, Week 10, n=20, 20 | -9.0 (± 3.82)      | -15.2 (± 3.92)      |  |  |
| Physical function, Week 12, n=21, 19 | -7.2 (± 3.74)      | -15.4 (± 3.87)      |  |  |
| Total, Week 1, n= 22, 20             | -0.5 (± 3.07)      | -6.0 (± 3.20)       |  |  |
| Total, Week 2, n= 21, 21             | -5.7 (± 3.66)      | -10.4 (± 3.70)      |  |  |
| Total, Week 4, n= 22, 21             | -11.4 (± 4.72)     | -20.1 (± 4.83)      |  |  |
| Total, Week 6, n= 22, 21             | -17.3 (± 5.17)     | -20.7 (± 5.28)      |  |  |
| Total, Week 8, n= 20, 20             | -14.6 (± 5.70)     | -23.6 (± 5.81)      |  |  |
| Total, Week 10, n= 20, 20            | -16.1 (± 5.88)     | -28.2 (± 6.04)      |  |  |
| Total, Week 12, n= 21, 19            | -13.5 (± 5.92)     | -26.7 (± 6.12)      |  |  |

Notes:

[32] - Intent-to-Treat Population.

[33] - Intent-to-Treat Population.

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Pain component, Week 1             |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.061 <sup>[34]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -2.8                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -5.6                                   |
| upper limit                             | 0.1                                    |

Notes:

[34] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Pain component, Week 2             |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.282 <sup>[35]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -2                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -5.6                                   |
| upper limit                             | 1.7                                    |

Notes:

[35] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | For Pain componentWeek 4   |
| Comparison groups                 | Placebo v GSK3196165 180mg |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.113 <sup>[36]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -3.7                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -8.4                                   |
| upper limit                             | 0.9                                    |

Notes:

[36] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Pain component, Week 6             |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.695 <sup>[37]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -1                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -5.9                                   |
| upper limit                             | 4                                      |

Notes:

[37] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Pain component, Week 8             |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.176 <sup>[38]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -3.8                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -9.4                                   |
| upper limit                             | 1.8                                    |

Notes:

[38] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Pain component, Week 10            |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.041 <sup>[39]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -5.5                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -10.8                                  |
| upper limit                             | -0.2                                   |

Notes:

[39] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Pain component, Week 12            |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.082 <sup>[40]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -4.7                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -10.1                                  |
| upper limit                             | 0.6                                    |

Notes:

[40] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Stiffness component, Week 1        |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.587 <sup>[41]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.2                                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -1.1    |
| upper limit         | 0.6     |

Notes:

[41] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Stiffness component, Week 2        |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.457 <sup>[42]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.4                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.3                                   |
| upper limit                             | 0.6                                    |

Notes:

[42] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Stiffness component, Week 4        |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.298 <sup>[43]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.6                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.8                                   |
| upper limit                             | 0.6                                    |

Notes:

[43] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|                                   |                                 |
|-----------------------------------|---------------------------------|
| <b>Statistical analysis title</b> | For Stiffness component, Week 6 |
| Comparison groups                 | Placebo v GSK3196165 180mg      |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.726 <sup>[44]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.2                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.3                                   |
| upper limit                             | 0.9                                    |

Notes:

[44] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Stiffness component, Week 8        |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.213 <sup>[45]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.7                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.9                                   |
| upper limit                             | 0.4                                    |

Notes:

[45] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Stiffness component, Week 10       |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.331 <sup>[46]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.6                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.9                                   |
| upper limit                             | 0.7                                    |

Notes:

[46] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Stiffness component, Week 12       |
| Comparison groups                       | Placebo v GSK3196165 180mg             |
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.248 <sup>[47]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.8                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -2.1                                   |
| upper limit                             | 0.6                                    |

Notes:

[47] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Physical Function component, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180mg              |
| Number of subjects included in analysis | 44                                      |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | other                                   |
| P-value                                 | = 0.35 <sup>[48]</sup>                  |
| Method                                  | Mixed Model Repeated Measures Analysis  |
| Parameter estimate                      | Mean difference (net)                   |
| Point estimate                          | -2.9                                    |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -9                                      |
| upper limit                             | 3.3                                     |

Notes:

[48] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Physical Function component, Week 2 |
| Comparison groups                       | Placebo v GSK3196165 180mg              |
| Number of subjects included in analysis | 44                                      |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | other                                   |
| P-value                                 | = 0.383 <sup>[49]</sup>                 |
| Method                                  | Mixed Model Repeated Measures Analysis  |
| Parameter estimate                      | Mean difference (net)                   |
| Point estimate                          | -3                                      |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -9.8    |
| upper limit         | 3.8     |

Notes:

[49] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Physical Function component, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180mg              |
| Number of subjects included in analysis | 44                                      |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | other                                   |
| P-value                                 | = 0.271 <sup>[50]</sup>                 |
| Method                                  | Mixed Model Repeated Measures Analysis  |
| Parameter estimate                      | Mean difference (net)                   |
| Point estimate                          | -4.8                                    |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -13.5                                   |
| upper limit                             | 3.9                                     |

Notes:

[50] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Physical Function component, Week 6 |
| Comparison groups                       | Placebo v GSK3196165 180mg              |
| Number of subjects included in analysis | 44                                      |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | other                                   |
| P-value                                 | = 0.565 <sup>[51]</sup>                 |
| Method                                  | Mixed Model Repeated Measures Analysis  |
| Parameter estimate                      | Mean difference (net)                   |
| Point estimate                          | -2.7                                    |
| Confidence interval                     |   |
| level                                   | 95 %                                    |
| sides                                   | 2-sided                                 |
| lower limit                             | -12.1                                   |
| upper limit                             | 6.7                                     |

Notes:

[51] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | For Physical Function component, Week 8 |
| Comparison groups                 | Placebo v GSK3196165 180mg              |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.343 <sup>[52]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -4.9                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -15.2                                  |
| upper limit                             | 5.4                                    |

Notes:

[52] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Physical Function component, Week 10 |
| Comparison groups                       | Placebo v GSK3196165 180mg               |
| Number of subjects included in analysis | 44                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.266 <sup>[53]</sup>                  |
| Method                                  | Mixed Model Repeated Measures Analysis   |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -6.2                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -17.3                                    |
| upper limit                             | 4.9                                      |

Notes:

[53] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Physical Function component, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180mg               |
| Number of subjects included in analysis | 44                                       |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | other                                    |
| P-value                                 | = 0.136 <sup>[54]</sup>                  |
| Method                                  | Mixed Model Repeated Measures Analysis   |
| Parameter estimate                      | Mean difference (net)                    |
| Point estimate                          | -8.2                                     |
| Confidence interval                     |  |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | -19.1                                    |
| upper limit                             | 2.7                                      |

Notes:

[54] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Total of all component scores, Week 1 |
| Comparison groups                       | Placebo v GSK3196165 180mg                |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           | other                                     |
| P-value                                 | = 0.23 <sup>[55]</sup>                    |
| Method                                  | Mixed Model Repeated Measures Analysis    |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -5.5                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | -14.5                                     |
| upper limit                             | 3.6                                       |

Notes:

[55] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Total of all component scores, Week 2 |
| Comparison groups                       | Placebo v GSK3196165 180mg                |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           | other                                     |
| P-value                                 | = 0.381 <sup>[56]</sup>                   |
| Method                                  | Mixed Model Repeated Measures Analysis    |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -4.6                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | -15.2                                     |
| upper limit                             | 5.9                                       |

Notes:

[56] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Total of all component scores, Week 4 |
| Comparison groups                       | Placebo v GSK3196165 180mg                |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           | other                                     |
| P-value                                 | = 0.207 <sup>[57]</sup>                   |
| Method                                  | Mixed Model Repeated Measures Analysis    |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -8.7                                      |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -22.4   |
| upper limit         | 5       |

Notes:

[57] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Total of all component scores, Week 6 |
| Comparison groups                       | Placebo v GSK3196165 180mg                |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           | other                                     |
| P-value                                 | = 0.648 <sup>[58]</sup>                   |
| Method                                  | Mixed Model Repeated Measures Analysis    |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -3.4                                      |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | -18.4                                     |
| upper limit                             | 11.6                                      |

Notes:

[58] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | For Total of all component scores, Week 8 |
| Comparison groups                       | Placebo v GSK3196165 180mg                |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                             |
| Analysis type                           | other                                     |
| P-value                                 | = 0.278 <sup>[59]</sup>                   |
| Method                                  | Mixed Model Repeated Measures Analysis    |
| Parameter estimate                      | Mean difference (net)                     |
| Point estimate                          | -9  |
| Confidence interval                     |   |
| level                                   | 95 %                                      |
| sides                                   | 2-sided                                   |
| lower limit                             | -25.4                                     |
| upper limit                             | 7.5                                       |

Notes:

[59] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | For Total of all component scores, Week 10 |
| Comparison groups                 | Placebo v GSK3196165 180mg                 |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.16 <sup>[60]</sup>                 |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -12.1                                  |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -29.1                                  |
| upper limit                             | 5                                      |

Notes:

[60] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | For Total of all component scores, Week 12 |
| Comparison groups                       | Placebo v GSK3196165 180mg                 |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           | other                                      |
| P-value                                 | = 0.127 <sup>[61]</sup>                    |
| Method                                  | Mixed Model Repeated Measures Analysis     |
| Parameter estimate                      | Mean difference (net)                      |
| Point estimate                          | -13.3                                      |
| Confidence interval                     |  |
| level                                   | 95 %                                       |
| sides                                   | 2-sided                                    |
| lower limit                             | -30.5                                      |
| upper limit                             | 3.9  |

Notes:

[61] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

### **Secondary: Change from Baseline in number of soft tissue swollen hand joints at each visit**

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in number of soft tissue swollen hand joints at each visit |
|-----------------|---|

End point description:

Swollen Hand Joint Count was measured by the total number of soft tissue swollen hand joints out of a possible 30 joints: 8 distal interphalangeal, 8 proximal interphalangeal, 2 interphalangeal joints, 10 metacarpophalangeal joints, 2 carpometacarpal joint across both hands. In case of missing observations for soft tissue swollen hand joints then the remaining observations were assessed and weighted by dividing the number presented by the number of non-missing, and by multiplying by 30 for the joint count. Baseline is defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

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

End point timeframe:

Baseline (Day 1 Pre-dose), Weeks 1, 2, 4, 6, 8, 10, and 12

| <b>End point values</b>             | Placebo            | GSK3196165<br>180mg |  |  |
|-------------------------------------|--------------------|---------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed         | 22 <sup>[62]</sup> | 22 <sup>[63]</sup>  |  |  |
| Units: Swollen joints               |                    |                     |  |  |
| least squares mean (standard error) |                    |                     |  |  |
| Week 1, n = 22, 21                  | -0.3 (± 0.64)      | -0.3 (± 0.66)       |  |  |
| Week 2, n = 21, 21                  | -1.6 (± 0.85)      | -1.2 (± 0.86)       |  |  |
| Week 4, n = 22, 21                  | -1.6 (± 0.76)      | -2.1 (± 0.78)       |  |  |
| Week 6, n = 22, 21                  | -3.7 (± 0.83)      | -2.3 (± 0.85)       |  |  |
| Week 8, n = 20, 20                  | -3.0 (± 0.92)      | -2.8 (± 0.94)       |  |  |
| Week 10, n = 20, 20                 | -2.6 (± 1.08)      | -2.9 (± 1.10)       |  |  |
| Week 12, n = 21, 19                 | -2.9 (± 0.91)      | -3.1 (± 0.93)       |  |  |

Notes:

[62] - Intent-to-Treat Population.

[63] - Intent-to-Treat Population.

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 1 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.957 <sup>[64]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | 0   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.9  |
| upper limit                             | 1.8   |

Notes:

[64] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 2 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.775 <sup>[65]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | 0.3   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -2.1  |
| upper limit                             | 2.8   |

Notes:

[65] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 4 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.624 <sup>[66]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -2.7  |
| upper limit                             | 1.7   |

Notes:

[66] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 6 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.243 <sup>[67]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | 1.4   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1  |
| upper limit                             | 3.8   |

Notes:

[67] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 8 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.875 <sup>[68]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | 0.2   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -2.5    |
| upper limit         | 2.9     |

Notes:

[68] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 10 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.848 <sup>[69]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.3   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -3.4   |
| upper limit                             | 2.8  |

Notes:

[69] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 12 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.883 <sup>[70]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.2   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -2.8   |
| upper limit                             | 2.4  |

Notes:

[70] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

## Secondary: Change from Baseline in number of tender hand joints at each visit

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in number of tender hand joints at each visit |
|-----------------|--|

End point description:

Tender Hand Joint Count was measured by the total number of tender joints out of a possible 30 joints: 8 distal interphalangeal, 8 proximal interphalangeal, 2 interphalangeal joints, 10 metacarpophalangeal joints, 2 carpometacarpal joints across both hands. A joint was considered tender if it was scored >0 on

the tender joint severity scale. Joints were rated 0=no pain/tenderness, 1=mild pain, 2=moderate pain and 3=severe pain. Baseline is defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:                      |           |
| Baseline, Weeks 1, 2, 4, 6, 8, 10, and 12 |           |

| End point values                    | Placebo            | GSK3196165 180mg   |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 22 <sup>[71]</sup> | 22 <sup>[72]</sup> |  |  |
| Units: Scores on scale              |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| Week 1, n= 22, 21                   | -0.6 (± 1.10)      | -1.8 (± 1.13)      |  |  |
| Week 2, n= 21, 21                   | -1.7 (± 1.15)      | -2.1 (± 1.17)      |  |  |
| Week 4, n= 22, 21                   | -1.1 (± 1.33)      | -3.0 (± 1.36)      |  |  |
| Week 6, n= 22, 21                   | -3.7 (± 1.27)      | -4.2 (± 1.30)      |  |  |
| Week 8, n= 20, 20                   | -2.4 (± 1.36)      | -3.9 (± 1.39)      |  |  |
| Week 10, n= 20, 20                  | -3.7 (± 1.45)      | -4.4 (± 1.48)      |  |  |
| Week 12, n= 21, 19                  | -3.5 (± 1.46)      | -4.0 (± 1.51)      |  |  |

Notes:

[71] - Intent-to-Treat Population.

[72] - Intent-to-Treat Population.

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 1 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.463 <sup>[73]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -1.2  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -4.4  |
| upper limit                             | 2   |

Notes:

[73] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Difference from placebo for Week 2 is presented |
| Comparison groups                 | Placebo v GSK3196165 180mg                      |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.809 <sup>[74]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.4                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -3.7                                   |
| upper limit                             | 2.9                                    |

Notes:

[74] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 4 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           |   |
| P-value                                 | = 0.324 <sup>[75]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -1.9  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -5.8  |
| upper limit                             | 2   |

Notes:

[75] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 6 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.783 <sup>[76]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -4.2  |
| upper limit                             | 3.2   |

Notes:

[76] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 8 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.464 <sup>[77]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -1.4  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -5.4  |
| upper limit                             | 2.5   |

Notes:

[77] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 10 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.736 <sup>[78]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.7   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -4.9   |
| upper limit                             | 3.5  |

Notes:

[78] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 12 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.806 <sup>[79]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -0.5   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -4.8    |
| upper limit         | 3.7     |

Notes:

[79] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

## Secondary: Change from Baseline in physician global assessment (PhGA) of disease activity

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in physician global assessment (PhGA) of disease activity |
|-----------------|--|

End point description:

Physicians were required to complete the global assessment of disease activity using single PhGA item with a NRS ranging from 0 (none) to 10 (extremely active). Baseline was defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

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

End point timeframe:

Baseline (Day 1 Pre-dose), Weeks 2, 4, 8, and 12

| End point values                    | Placebo            | GSK3196165 180mg   |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 22 <sup>[80]</sup> | 22 <sup>[81]</sup> |  |  |
| Units: Scores on scale              |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| Week 2, n= 19, 14                   | -1.8 (± 0.39)      | -1.5 (± 0.45)      |  |  |
| Week 4, n= 20, 15                   | -2.1 (± 0.44)      | -2.6 (± 0.50)      |  |  |
| Week 8, n= 17, 15                   | -2.2 (± 0.52)      | -3.4 (± 0.57)      |  |  |
| Week 12, n= 18, 14                  | -2.7 (± 0.56)      | -3.0 (± 0.63)      |  |  |

Notes:

[80] - Intent-to-Treat Population.

[81] - Intent-to-Treat Population.

## Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Difference from placebo for Week 2 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.586 <sup>[82]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | 0.3   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -0.9    |
| upper limit         | 1.6     |

Notes:

[82] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 4 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.416 <sup>[83]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.5  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.9  |
| upper limit                             | 0.8   |

Notes:

[83] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 8 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.12 <sup>[84]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -1.2  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -2.8  |
| upper limit                             | 0.3   |

Notes:

[84] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Difference from placebo for Week 12 is presented |
| Comparison groups                 | Placebo v GSK3196165 180mg                       |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.687 <sup>[85]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.3                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -2.1                                   |
| upper limit                             | 1.4                                    |

Notes:

[85] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

## Secondary: Change from Baseline in patient global assessment (PtGA) of disease activity

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in patient global assessment (PtGA) of disease activity |
|-----------------|--|

End point description:

Participants were required to complete the global assessment of disease activity using single PtGA item with an NRS ranging from 0 (very well) to 10 (very poor). Baseline was defined as Day 1 pre-dose value. Change from Baseline is equal to post-dose visit value minus Baseline value. n=X in category titles represents the number of participants with non-missing data at the specified time-point. Only non-missing data is included in the MMRM model.

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

End point timeframe:

Baseline, Weeks 2, 4, 8, and 12

| End point values                    | Placebo            | GSK3196165 180mg   |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 22 <sup>[86]</sup> | 22 <sup>[87]</sup> |  |  |
| Units: Scores on scale              |                    |                    |  |  |
| least squares mean (standard error) |                    |                    |  |  |
| Week 2, n= 20, 21                   | -0.4 (± 0.36)      | -0.6 (± 0.35)      |  |  |
| Week 4, n= 21, 21                   | -0.6 (± 0.42)      | -1.3 (± 0.42)      |  |  |
| Week 8, n= 19, 20                   | -0.9 (± 0.47)      | -1.8 (± 0.46)      |  |  |
| Week 12, n= 20, 19                  | -0.7 (± 0.46)      | -1.8 (± 0.46)      |  |  |

Notes:

[86] - Intent-to-Treat Population.

[87] - Intent-to-Treat Population.

## Statistical analyses

|                            |   |
|----------------------------|---|
| Statistical analysis title | Difference from placebo for Week 2 is presented |
| Comparison groups          | Placebo v GSK3196165 180mg                      |

|   |  |
|---|--|
| Number of subjects included in analysis | 44                                     |
| Analysis specification                  | Pre-specified                          |
| Analysis type                           | other                                  |
| P-value                                 | = 0.651 <sup>[88]</sup>                |
| Method                                  | Mixed Model Repeated Measures Analysis |
| Parameter estimate                      | Mean difference (net)                  |
| Point estimate                          | -0.2                                   |
| Confidence interval                     |  |
| level                                   | 95 %                                   |
| sides                                   | 2-sided                                |
| lower limit                             | -1.3                                   |
| upper limit                             | 0.8                                    |

Notes:

[88] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 4 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.271 <sup>[89]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.7  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -1.9  |
| upper limit                             | 0.5   |

Notes:

[89] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 8 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                      |
| Number of subjects included in analysis | 44  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           | other   |
| P-value                                 | = 0.186 <sup>[90]</sup>                         |
| Method                                  | Mixed Model Repeated Measures Analysis          |
| Parameter estimate                      | Mean difference (net)                           |
| Point estimate                          | -0.9  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | -2.2  |
| upper limit                             | 0.4   |

Notes:

[90] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Difference from placebo for Week 12 is presented |
| Comparison groups                       | Placebo v GSK3196165 180mg                       |
| Number of subjects included in analysis | 44   |
| Analysis specification                  | Pre-specified                                    |
| Analysis type                           | other  |
| P-value                                 | = 0.109 <sup>[91]</sup>                          |
| Method                                  | Mixed Model Repeated Measures Analysis           |
| Parameter estimate                      | Mean difference (net)                            |
| Point estimate                          | -1.1   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | -2.4   |
| upper limit                             | 0.2  |

Notes:

[91] - MMRM model with fixed effects of Baseline Value, Treatment Group, Visit and Treatment Group by Visit Interaction was used. Unstructured covariance structure was used. p-value corresponds to the difference over placebo measure and confidence interval.

## Secondary: Number of participants with adverse events (AE) and serious adverse events (SAE)

|                 |  |
|-----------------|--|
| End point title | Number of participants with adverse events (AE) and serious adverse events (SAE) |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment or events associated with liver injury and impaired liver function were categorized as SAE. All participants who received at least one dose of study treatment (GSK3196165 or placebo) were included in Safety Population.

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

End point timeframe:

Up to Week 22

| End point values            | Placebo         | GSK3196165 180mg |  |  |
|-----------------------------|-----------------|------------------|--|--|
| Subject group type          | Reporting group | Reporting group  |  |  |
| Number of subjects analysed | 22              | 22               |  |  |
| Units: Participants         |                 |                  |  |  |
| Any AE                      | 11              | 13               |  |  |
| Any SAE                     | 1               | 2                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with infections

|  |  |
|--|--|
| End point title  | Number of participants with infections |
| End point description:<br>Adverse events of special interest (AESI) included serious infections like serious respiratory infections and tuberculosis and other opportunistic infections. Number of participants with infections has been reported. |  |
| End point type   | Secondary                              |
| End point timeframe:<br>Up to Week 22  |  |

| End point values            | Placebo         | GSK3196165<br>180mg |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 22              | 22                  |  |  |
| Units: Participants         |                 |                     |  |  |
| Serious Infections          | 0               | 0                   |  |  |
| Opportunistic Infections    | 0               | 0                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with pulmonary events

|  |  |
|--|--|
| End point title  | Number of participants with pulmonary events |
| End point description:<br>Pulmonary events like pulmonary alveolar proteinosis (PAP), persistent (for 3 consecutive weeks) reduction in diffusing capacity of the lungs for carbon monoxide (DLCO) > 15 percentage, persistent (for 3 consecutive weeks) cough and/or dyspnea and non- life threatening pulmonary changes related to surfactant accumulation is presented. |  |
| End point type   | Secondary                                    |
| End point timeframe:<br>Up to Week 22  |  |

| End point values            | Placebo         | GSK3196165<br>180mg |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 22              | 22                  |  |  |
| Units: Participants         |                 |                     |  |  |
| Persistent dyspnea          | 0               | 0                   |  |  |
| Persistent decrease in DLCO | 0               | 0                   |  |  |
| Persistent Cough            | 0               | 0                   |  |  |
| Abnormal Lung Auscultation  | 0               | 0                   |  |  |
| PAP                         | 0               | 0                   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with anti-GSK3196165 binding antibodies

|                 |  |
|-----------------|--|
| End point title | Number of participants with anti-GSK3196165 binding antibodies |
|-----------------|--|

End point description:

Serum samples were collected at indicated time points for anti-drug antibody (ADA) measurements. Anti-GSK3196165 binding antibody detection assay using tiered testing schema: screening, confirmation and titration steps was used for immunogenicity analysis. Samples taken after dosing with GSK3196165 that have a value at or above the cut-point were considered treatment-emergent ADA-positive. The number of participants with change from Baseline to any time post Baseline in the results of immunogenicity assessment as indicated by: negative to positive, positive to positive, positive to negative and negative to negative are presented.

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

End point timeframe:

Up to Week 22

| End point values            | Placebo         | GSK3196165<br>180mg |  |  |
|-----------------------------|-----------------|---------------------|--|--|
| Subject group type          | Reporting group | Reporting group     |  |  |
| Number of subjects analysed | 22              | 22                  |  |  |
| Units: Participants         |                 |                     |  |  |
| Negative to positive        | 0               | 1                   |  |  |
| Positive to positive        | 0               | 0                   |  |  |
| Positive to negative        | 0               | 0                   |  |  |
| Negative to negative        | 22              | 20                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Apparent clearance after subcutaneous administration (CL/F) of GSK3196165

|                 |   |
|-----------------|---|
| End point title | Apparent clearance after subcutaneous administration (CL/F) of GSK3196165 <sup>[92]</sup> |
|-----------------|---|

End point description:

Blood samples were collected at indicated time points and CL/F was estimated using population PK analysis. Participants in the 'Safety' population who have at least one valid PK assessment were included Pharmacokinetic (PK) Population.

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

End point timeframe:

Day 3 and Pre-dose on Week 1, Week 4, Week 6, Week 12 and Week 22

Notes:

[92] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

|   |                     |  |  |  |
|---|---------------------|--|--|--|
| <b>End point values</b>                             | GSK3196165<br>180mg |  |  |  |
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 21 <sup>[93]</sup>  |  |  |  |
| Units: Liters per day                               |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 4.94 (± 68.8)       |  |  |  |

Notes:

[93] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent steady state volume of distribution after subcutaneous administration (Vss/F) of GSK3196165

|                 |  |
|-----------------|--|
| End point title | Apparent steady state volume of distribution after subcutaneous administration (Vss/F) of GSK3196165 <sup>[94]</sup> |
|-----------------|--|

End point description:

Blood samples were collected at indicated time points and Vss/F was estimated using population PK analysis.

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

End point timeframe:

Day 3 and Pre-dose on Week 1, Week 4, Week 6, Week 12 and Week 22

Notes:

[94] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

|   |                     |  |  |  |
|---|---------------------|--|--|--|
| <b>End point values</b>                             | GSK3196165<br>180mg |  |  |  |
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 21 <sup>[95]</sup>  |  |  |  |
| Units: Liters                                       |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 36.5 (± 61.5)       |  |  |  |

Notes:

[95] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Absorption rate constant (Ka) of GSK3196165

|                 |   |
|-----------------|---|
| End point title | Absorption rate constant (Ka) of GSK3196165 <sup>[96]</sup> |
|-----------------|---|

End point description:

Blood samples were collected at indicated time points and Ka was estimated using population PK analysis.

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

End point timeframe:

Day 3 and Pre-dose on Week 1, Week 4, Week 6, Week 12 and Week 22

Notes:

[96] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

|   |                     |  |  |  |
|---|---------------------|--|--|--|
| <b>End point values</b>                             | GSK3196165<br>180mg |  |  |  |
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 21 <sup>[97]</sup>  |  |  |  |
| Units: Per day                                      |                     |  |  |  |
| geometric mean (geometric coefficient of variation) | 0.205 (± 72.3)      |  |  |  |

Notes:

[97] - PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum concentration of GSK3196165 by visit

|                 |  |
|-----------------|--|
| End point title | Serum concentration of GSK3196165 by visit <sup>[98]</sup> |
|-----------------|--|

End point description:

Blood samples were collected at indicated time points for pharmacokinetic analysis. Only those participants with data available at the specified time points were analyzed (represented by n= X in the category titles).

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

End point timeframe:

Pre-dose on Day 3, Weeks 1, 4, 6, 12, follow up (Week 22)

Notes:

[98] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this endpoint.

|   |                     |  |  |  |
|---|---------------------|--|--|--|
| <b>End point values</b>                             | GSK3196165<br>180mg |  |  |  |
| Subject group type                                  | Reporting group     |  |  |  |
| Number of subjects analysed                         | 22 <sup>[99]</sup>  |  |  |  |
| Units: Nanogram per milliliter                      |                     |  |  |  |
| geometric mean (geometric coefficient of variation) |                     |  |  |  |
| Day 3, n = 18                                       | 2457.05 (± 94.74)   |  |  |  |
| Week 1, n = 21                                      | 1767.55 (± 46.96)   |  |  |  |
| Week 4, n = 21                                      | 2821.12 (± 61.00)   |  |  |  |
| Week 6, n = 20                                      | 1802.09 (± 60.42)   |  |  |  |

|                             |                        |  |  |  |
|-----------------------------|------------------------|--|--|--|
| Week 12, n = 8              | 800.96 ( $\pm$ 176.33) |  |  |  |
| Follow up (Week 22), n = 12 | 56.40 ( $\pm$ 346.41)  |  |  |  |

Notes:

[99] - PK Population

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events (AEs) and serious AEs were collected up to Week 22.

Adverse event reporting additional description:

Non-serious AEs and SAE for Safety Population was reported.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

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

Reporting group description:

Participants randomized to Placebo group received total of 8 subcutaneous injections of placebo over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

|                       |                  |
|-----------------------|------------------|
| Reporting group title | GSK3196165 180mg |
|-----------------------|------------------|

Reporting group description:

Participants randomized to GSK3196165 group received total of 8 doses of GSK3196165 over a 12-week treatment period. Participants were administered loading doses on Days 1, 8, 15, 22 and 29 which was followed by 3 doses every other week (Days 43, 57, 71).

| Serious adverse events                            | Placebo        | GSK3196165 180mg |  |
|---|----------------|------------------|--|
| Total subjects affected by serious adverse events |                |                  |  |
| subjects affected / exposed                       | 1 / 22 (4.55%) | 2 / 22 (9.09%)   |  |
| number of deaths (all causes)                     | 0              | 0                |  |
| number of deaths resulting from adverse events    |                |                  |  |
| Injury, poisoning and procedural complications    |                |                  |  |
| HUMERUS FRACTURE                                  |                |                  |  |
| subjects affected / exposed                       | 0 / 22 (0.00%) | 1 / 22 (4.55%)   |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0            |  |
| Vascular disorders                                |                |                  |  |
| HYPERTENSIVE CRISIS                               |                |                  |  |
| subjects affected / exposed                       | 0 / 22 (0.00%) | 1 / 22 (4.55%)   |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0            |  |
| Cardiac disorders                                 |                |                  |  |
| ATRIAL FIBRILLATION                               |                |                  |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 22 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Placebo         | GSK3196165 180mg |  |
|---|-----------------|------------------|--|
| Total subjects affected by non-serious adverse events |                 |                  |  |
| subjects affected / exposed                           | 4 / 22 (18.18%) | 10 / 22 (45.45%) |  |
| Cardiac disorders                                     |                 |                  |  |
| PALPITATIONS  |                 |                  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)  | 0 / 22 (0.00%)   |  |
| occurrences (all)                                     | 2               | 0                |  |
| General disorders and administration site conditions  |                 |                  |  |
| INJECTION SITE ERYTHEMA                               |                 |                  |  |
| subjects affected / exposed                           | 0 / 22 (0.00%)  | 2 / 22 (9.09%)   |  |
| occurrences (all)                                     | 0               | 3                |  |
| INJECTION SITE RASH                                   |                 |                  |  |
| subjects affected / exposed                           | 0 / 22 (0.00%)  | 2 / 22 (9.09%)   |  |
| occurrences (all)                                     | 0               | 6                |  |
| Respiratory, thoracic and mediastinal disorders       |                 |                  |  |
| COUGH   |                 |                  |  |
| subjects affected / exposed                           | 2 / 22 (9.09%)  | 2 / 22 (9.09%)   |  |
| occurrences (all)                                     | 3               | 2                |  |
| Infections and infestations                           |                 |                  |  |
| CONJUNCTIVITIS  |                 |                  |  |
| subjects affected / exposed                           | 0 / 22 (0.00%)  | 2 / 22 (9.09%)   |  |
| occurrences (all)                                     | 0               | 2                |  |
| HERPES ZOSTER   |                 |                  |  |
| subjects affected / exposed                           | 0 / 22 (0.00%)  | 2 / 22 (9.09%)   |  |
| occurrences (all)                                     | 0               | 2                |  |
| NASOPHARYNGITIS                                       |                 |                  |  |
| subjects affected / exposed                           | 1 / 22 (4.55%)  | 2 / 22 (9.09%)   |  |
| occurrences (all)                                     | 1               | 3                |  |
| URINARY TRACT INFECTION                               |                 |                  |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 22 (0.00%) | 2 / 22 (9.09%) |  |
| occurrences (all)           | 0              | 2              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 16 November 2015 | Amendment No. 1: Correction of contraceptive requirements in Appendix 5, in response to regulatory review comments. Minor correction of question number in post-treatment interview guidance.  |
| 03 January 2017  | Amendment No. 2:<br>Amendment of inclusion criteria, #2, #3 and #5, clarification of exclusion criteria #9 and amendment of exclusion criteria #19(d).<br>Addition of two planned interim analyses to Section Data Analysis Considerations and associated update to study blinding details.<br>Addition of two PK sample time points (one on Day 85 and one on Day 155).<br>Further minor corrections and clarifications to wording throughout the protocol. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported