



## Clinical trial results:

### An Open-label, Sequential, Ascending, Repeated Dose-finding Study of Sarilumab, Administered with Subcutaneous (SC) Injection, in Children and Adolescents, Aged 2 to 17 Years, with Polyarticular-course Juvenile Idiopathic Arthritis (pcJIA) Followed by an Extension Phase

#### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2015-003999-79                               |
| Trial protocol           | GB IT CZ ES Outside EU/EEA EE FI NL PL DE FR |
| Global end of trial date | 28 December 2023                             |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 10 July 2024 |
| First version publication date | 10 July 2024 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | DRI13925 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT02776735     |
| WHO universal trial number (UTN)   | U1111-1177-3487 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Sanofi-Aventis Recherche & Développement   |
| Sponsor organisation address | 82 Avenue Raspail, Gentilly, France, 94250   |
| Public contact               | Trial Transparency Team, Sanofi-Aventis Recherche & Développement, Contact-US@sanofi.com |
| Scientific contact           | Trial Transparency Team, Sanofi-Aventis Recherche & Développement, Contact-US@sanofi.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001045-PIP01-10 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 02 February 2024 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 28 December 2023 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To describe the Pharmacokinetic (PK) profile of sarilumab in participants aged 2 to 17 years with polyarticular-course Juvenile Idiopathic Arthritis (pcJIA) in order to identify the dose and regimen for adequate treatment of this population.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric patients. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parents(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 03 October 2016 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 9           |
| Country: Number of subjects enrolled | Canada: 1              |
| Country: Number of subjects enrolled | Chile: 2               |
| Country: Number of subjects enrolled | Czechia: 2             |
| Country: Number of subjects enrolled | Finland: 1             |
| Country: Number of subjects enrolled | France: 4              |
| Country: Number of subjects enrolled | Germany: 12            |
| Country: Number of subjects enrolled | Italy: 1               |
| Country: Number of subjects enrolled | Mexico: 8              |
| Country: Number of subjects enrolled | Netherlands: 1         |
| Country: Number of subjects enrolled | Poland: 15             |
| Country: Number of subjects enrolled | Russian Federation: 25 |
| Country: Number of subjects enrolled | Spain: 16              |
| Country: Number of subjects enrolled | United Kingdom: 3      |
| Country: Number of subjects enrolled | United States: 2       |

|                                    |     |
|------------------------------------|-----|
| Worldwide total number of subjects | 102 |
| EEA total number of subjects       | 52  |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 63 |
| Adolescents (12-17 years)                 | 39 |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 29 centers in 15 countries. A total of 118 participants were screened from 06 September 2016 and 20 December 2021, of which 16 were screen failures. The main reasons for screen failure were based on criteria for exclusion from the study.

### Pre-assignment

Screening details:

A total of 102 participants were enrolled in the study. The dose was capped at 150 milligram (mg) and 200 mg for Cohorts 1 and 3 and Cohort 2, respectively. Cohort 2 was selected dose treatment regimen and participants enrolled directly in selected dose (portions 2 and 3) didn't have upper body weight limit.

### Period 1

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

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes                                     |
| <b>Arm title</b>             | Cohort 1: $\geq 30$ kg and $\leq 60$ kg |

Arm description:

Participants with body weight  $\geq 30$  kilograms (kg) and  $\leq 60$  kg received sarilumab 2 mg/kg subcutaneous (SC) injection once every other week (q2w) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 2 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | Cohort 1: $< 30$ kg and $\geq 10$ kg |
|------------------|--------------------------------------|

Arm description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

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

Dosage and administration details:

Sarilumab 2.5 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

|  |   |
|--|---|
| <b>Arm title</b>   | Cohort 2: $\geq 30$ kg and $\leq 60$ kg |
| Arm description:<br>Participants with body weight $\geq 30$ kg and $\leq 60$ kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks). |   |
| Arm type   | Experimental                            |
| Investigational medicinal product name   | Sarilumab                               |
| Investigational medicinal product code   |   |
| Other name   | Kevzara®                                |
| Pharmaceutical forms   | Solution for injection                  |
| Routes of administration   | Subcutaneous use                        |

**Dosage and administration details:**

Sarilumab 3 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

|   |                                      |
|---|--------------------------------------|
| <b>Arm title</b>  | Cohort 2: $< 30$ kg and $\geq 10$ kg |
| Arm description:<br>Participants with body weight $< 30$ kg and $\geq 10$ kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks). |                                      |
| Arm type  | Experimental                         |
| Investigational medicinal product name  | Sarilumab                            |
| Investigational medicinal product code  |                                      |
| Other name  | Kevzara®                             |
| Pharmaceutical forms  | Solution for injection               |
| Routes of administration  | Subcutaneous use                     |

**Dosage and administration details:**

Sarilumab 4 mg/kg q2w was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

|  |   |
|--|---|
| <b>Arm title</b>   | Cohort 3: $\geq 30$ kg and $\leq 60$ kg |
| Arm description:<br>Participants with body weight $\geq 30$ kg and $\leq 60$ kg received sarilumab 2 mg/kg SC injection once every week (qw) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks). |   |
| Arm type   | Experimental                            |
| Investigational medicinal product name   | Sarilumab                               |
| Investigational medicinal product code   |   |
| Other name   | Kevzara®                                |
| Pharmaceutical forms   | Solution for injection                  |
| Routes of administration   | Subcutaneous use                        |

**Dosage and administration details:**

Sarilumab 2 mg/kg qw was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

|   |                                      |
|---|--------------------------------------|
| <b>Arm title</b>  | Cohort 3: $< 30$ kg and $\geq 10$ kg |
| Arm description:<br>Participants with body weight $< 30$ kg and $\geq 10$ kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks). |                                      |
| Arm type  | Experimental                         |

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Sarilumab              |
| Investigational medicinal product code |                        |
| Other name                             | Kevzara®               |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Sarilumab 2.5 mg/kg qw was administered SC in 1 of the 4 quadrants of the abdomen or thigh when self injected or also in the upper arm (lateral side) if administered by a professional or a nonprofessional caregiver.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 2: $\geq 30$ kg and $\leq 60$ kg |
|---|---|--------------------------------------|---|
| Started   | 7                                       | 6                                    | 42                                      |
| Completed   | 6                                       | 6                                    | 38                                      |
| Not completed                                       | 1                                       | 0                                    | 4                                       |
| Consent withdrawn by subject                        | 1                                       | -                                    | -                                       |
| Adverse event, non-fatal                            | -                                       | -                                    | -                                       |
| Unspecified   | -                                       | -                                    | 2                                       |
| Lost to follow-up                                   | -                                       | -                                    | -                                       |
| Withdrawal by parent/guardian                       | -                                       | -                                    | 2                                       |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Cohort 2: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|---|--------------------------------------|---|--------------------------------------|
| Started   | 31                                   | 6                                       | 9                                    |
| Completed   | 27                                   | 6                                       | 7                                    |
| Not completed                                       | 4                                    | 0                                       | 2                                    |
| Consent withdrawn by subject                        | -                                    | -                                       | 1                                    |
| Adverse event, non-fatal                            | 1                                    | -                                       | 1                                    |
| Unspecified   | -                                    | -                                       | -                                    |
| Lost to follow-up                                   | 1                                    | -                                       | -                                    |
| Withdrawal by parent/guardian                       | 2                                    | -                                       | -                                    |

Notes:

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

Justification: Only treated participants included.

## Baseline characteristics

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 1: $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kilograms (kg) and  $\leq 60$  kg received sarilumab 2 mg/kg subcutaneous (SC) injection once every other week (q2w) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Cohort 1: $< 30$ kg and $\geq 10$ kg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 2: $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Cohort 2: $< 30$ kg and $\geq 10$ kg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 3: $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 2 mg/kg SC injection once every week (qw) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

| Reporting group values | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 2: $\geq 30$ kg and $\leq 60$ kg |
|------------------------|---|--------------------------------------|---|
| Number of subjects     | 7                                       | 6                                    | 42                                      |
| Age categorical        |   |                                      |   |
| Units:                 |   |                                      |   |

|                     |           |           |           |
|---------------------|-----------|-----------|-----------|
| Age Continuous      |           |           |           |
| Units: years        |           |           |           |
| arithmetic mean     | 12.3      | 6.5       | 12.6      |
| standard deviation  | $\pm 3.3$ | $\pm 3.2$ | $\pm 3.0$ |
| Sex: Female, Male   |           |           |           |
| Units: participants |           |           |           |
| Female              | 5         | 5         | 35        |
| Male                | 2         | 1         | 7         |

|   |   |   |    |
|---|---|---|----|
| Race                                      |   |   |    |
| Units: Subjects                           |   |   |    |
| American Indian or Alaska Native          | 0 | 0 | 0  |
| Asian                                     | 0 | 0 | 1  |
| Black or African American                 | 0 | 0 | 0  |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0  |
| White                                     | 6 | 3 | 39 |
| Not Reported                              | 0 | 1 | 2  |
| Unknown                                   | 1 | 2 | 0  |

|                               |                               |                               |                               |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| <b>Reporting group values</b> | Cohort 2: < 30 kg and ≥ 10 kg | Cohort 3: ≥ 30 kg and ≤ 60 kg | Cohort 3: < 30 kg and ≥ 10 kg |
| Number of subjects            | 31                            | 6                             | 9                             |
| Age categorical               |                               |                               |                               |
| Units:                        |                               |                               |                               |

|   |       |       |       |
|---|-------|-------|-------|
| Age Continuous                            |       |       |       |
| Units: years                              |       |       |       |
| arithmetic mean                           | 5.4   | 13.7  | 4.8   |
| standard deviation                        | ± 3.1 | ± 3.0 | ± 2.4 |
| Sex: Female, Male                         |       |       |       |
| Units: participants                       |       |       |       |
| Female                                    | 23    | 3     | 6     |
| Male                                      | 8     | 3     | 3     |
| Race                                      |       |       |       |
| Units: Subjects                           |       |       |       |
| American Indian or Alaska Native          | 0     | 0     | 0     |
| Asian                                     | 0     | 0     | 0     |
| Black or African American                 | 0     | 0     | 0     |
| Native Hawaiian or Other Pacific Islander | 0     | 0     | 0     |
| White                                     | 28    | 4     | 8     |
| Not Reported                              | 3     | 0     | 1     |
| Unknown                                   | 0     | 2     | 0     |

|                               |       |  |  |
|-------------------------------|-------|--|--|
| <b>Reporting group values</b> | Total |  |  |
| Number of subjects            | 101   |  |  |
| Age categorical               |       |  |  |
| Units:                        |       |  |  |

|                                  |    |  |  |
|----------------------------------|----|--|--|
| Age Continuous                   |    |  |  |
| Units: years                     |    |  |  |
| arithmetic mean                  |    |  |  |
| standard deviation               | -  |  |  |
| Sex: Female, Male                |    |  |  |
| Units: participants              |    |  |  |
| Female                           | 77 |  |  |
| Male                             | 24 |  |  |
| Race                             |    |  |  |
| Units: Subjects                  |    |  |  |
| American Indian or Alaska Native | 0  |  |  |



|  |    |  |  |
|--|----|--|--|
| Asian  | 1  |  |  |
| Black or African American                    | 0  |  |  |
| Native Hawaiian or Other Pacific<br>Islander | 0  |  |  |
| White  | 88 |  |  |
| Not Reported                                 | 7  |  |  |
| Unknown                                      | 5  |  |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Cohort 1: $\geq 30$ kg and $\leq 60$ kg |
| Reporting group description:<br>Participants with body weight $\geq 30$ kilograms (kg) and $\leq 60$ kg received sarilumab 2 mg/kg subcutaneous (SC) injection once every other week (q2w) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks). |   |
| Reporting group title  | Cohort 1: $< 30$ kg and $\geq 10$ kg    |
| Reporting group description:<br>Participants with body weight $< 30$ kg and $\geq 10$ kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).   |   |
| Reporting group title  | Cohort 2: $\geq 30$ kg and $\leq 60$ kg |
| Reporting group description:<br>Participants with body weight $\geq 30$ kg and $\leq 60$ kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).   |   |
| Reporting group title  | Cohort 2: $< 30$ kg and $\geq 10$ kg    |
| Reporting group description:<br>Participants with body weight $< 30$ kg and $\geq 10$ kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 4 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).  |   |
| Reporting group title  | Cohort 3: $\geq 30$ kg and $\leq 60$ kg |
| Reporting group description:<br>Participants with body weight $\geq 30$ kg and $\leq 60$ kg received sarilumab 2 mg/kg SC injection once every week (qw) for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).                                     |   |
| Reporting group title  | Cohort 3: $< 30$ kg and $\geq 10$ kg    |
| Reporting group description:<br>Participants with body weight $< 30$ kg and $\geq 10$ kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).  |   |

### Primary: Maximum Serum Concentration (C<sub>max</sub>) at Steady State of Sarilumab

|   |   |
|---|---|
| End point title   | Maximum Serum Concentration (C <sub>max</sub> ) at Steady State of Sarilumab <sup>[1]</sup> |
| End point description:<br>The C <sub>max</sub> was defined as maximum serum concentration. The PK analysis set included all participants in the safety population with at least 1 post-dose, non-missing serum concentration value. Only participants with data collected are reported. |   |
| End point type  | Primary   |
| End point timeframe:<br>Pre-dose on Days 1, 3, 5, 8, 12 and Weeks 2, 4, 8 and 12  |   |

#### Notes:

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

Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

| End point values                     | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |
|--------------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type                   | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed          | 5                                       | 5                                    | 39                                      | 24                                   |
| Units: milligram per liter (mg/L)    |   |                                      |   |                                      |
| arithmetic mean (standard deviation) | 11.1 ( $\pm$ 4.82)                      | 14.0 ( $\pm$ 2.97)                   | 27.1 ( $\pm$ 11.6)                      | 40.4 ( $\pm$ 7.77)                   |

| End point values                     | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |  |  |
|--------------------------------------|---|--------------------------------------|--|--|
| Subject group type                   | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed          | 5                                       | 5                                    |  |  |
| Units: milligram per liter (mg/L)    |   |                                      |  |  |
| arithmetic mean (standard deviation) | 37.6 ( $\pm$ 8.52)                      | 28.9 ( $\pm$ 5.32)                   |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Area Under the Serum Concentration Versus Time Curve Using the Trapezoidal Method During a Dose Interval (AUC<sub>0-t</sub>) at Steady State of Sarilumab

|                 |  |
|-----------------|--|
| End point title | Area Under the Serum Concentration Versus Time Curve Using the Trapezoidal Method During a Dose Interval (AUC <sub>0-t</sub> ) at Steady State of Sarilumab <sup>[2]</sup> |
|-----------------|--|

End point description:

The AUC<sub>0-t</sub> was defined as area under the concentration in serum versus time curve calculated using the trapezoidal method during a dose interval (tau). The PK analysis set included all participants in the safety population with at least 1 post-dose, non-missing serum concentration value. Only participants with data collected are reported.

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

End point timeframe:

Pre-dose on Days 1, 3, 5, 8, 12 and Weeks 2, 4, 8 and 12

Notes:

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

Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

| End point values                     | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |
|--------------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type                   | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed          | 5                                       | 5                                    | 39                                      | 24                                   |
| Units: day*mg/L                      |   |                                      |   |                                      |
| arithmetic mean (standard deviation) | 90.7 ( $\pm$ 30.8)                      | 110 ( $\pm$ 40.9)                    | 276 ( $\pm$ 121)                        | 395 ( $\pm$ 101)                     |

| End point values | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |  |  |
|------------------|---|--------------------------------------|--|--|
|------------------|---|--------------------------------------|--|--|

|                                      | 60 kg           | kg              |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 5               | 5               |  |  |
| Units: day*mg/L                      |                 |                 |  |  |
| arithmetic mean (standard deviation) | 235 (± 60.9)    | 176 (± 32.4)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Concentration Before Treatment Administration During Repeated Dosing (Ctrough) at Steady State of Sarilumab

|                 |  |
|-----------------|--|
| End point title | Concentration Before Treatment Administration During Repeated Dosing (Ctrough) at Steady State of Sarilumab <sup>[3]</sup> |
|-----------------|--|

End point description:

The Ctrough was defined as concentration observed before treatment administration during repeated dosing from baseline to Week 12. The PK analysis set included all participants in the safety population with at least 1 post-dose, non-missing serum concentration value. Only participants with data collected are reported.

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

End point timeframe:

Pre-dose on Days 1, 3, 5, 8, 12 and Weeks 2, 4, 8 and 12

Notes:

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

Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

| End point values                     | Cohort 1: >= 30 kg and <= 60 kg | Cohort 1: < 30 kg and >= 10 kg | Cohort 2: >= 30 kg and <= 60 kg | Cohort 2: < 30 kg and >= 10 kg |
|--------------------------------------|---------------------------------|--------------------------------|---------------------------------|--------------------------------|
| Subject group type                   | Reporting group                 | Reporting group                | Reporting group                 | Reporting group                |
| Number of subjects analysed          | 5                               | 5                              | 39                              | 24                             |
| Units: mg/L                          |                                 |                                |                                 |                                |
| arithmetic mean (standard deviation) | 1.36 (± 0.872)                  | 1.39 (± 1.44)                  | 9.57 (± 5.84)                   | 14.4 (± 9.81)                  |

| End point values                     | Cohort 3: >= 30 kg and <= 60 kg | Cohort 3: < 30 kg and >= 10 kg |  |  |
|--------------------------------------|---------------------------------|--------------------------------|--|--|
| Subject group type                   | Reporting group                 | Reporting group                |  |  |
| Number of subjects analysed          | 5                               | 5                              |  |  |
| Units: mg/L                          |                                 |                                |  |  |
| arithmetic mean (standard deviation) | 28.0 (± 9.06)                   | 21.6 (± 5.16)                  |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Cohorts 1 and 3: Change From Baseline in High-Sensitivity C-reactive Protein (hs-CRP) at Week 12**

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Change From Baseline in High-Sensitivity C-reactive Protein (hs-CRP) at Week 12 <sup>[4]</sup> |
|-----------------|---|

End point description:

Serum concentrations of hs-CRP was determined to assess the Pharmacodynamic (PD) effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Only participants analyzed at baseline and Week 12 are reported.

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

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[4] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                     | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|--------------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type                   | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed          | 5                                       | 6                                    | 6                                       | 9                                    |
| Units: mg/L                          |   |                                      |   |                                      |
| arithmetic mean (standard deviation) | -1.00 ( $\pm 2.53$ )                    | -0.52 ( $\pm 3.64$ )                 | -5.71 ( $\pm 8.90$ )                    | -6.83 ( $\pm 11.74$ )                |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Cohort 2: Change From Baseline in High-Sensitivity C-reactive Protein at Weeks 12, 24, 48, 96, and 156**

|                 |   |
|-----------------|---|
| End point title | Cohort 2: Change From Baseline in High-Sensitivity C-reactive Protein at Weeks 12, 24, 48, 96, and 156 <sup>[5]</sup> |
|-----------------|---|

End point description:

Serum concentrations of hs-CRP was determined to assess the PD effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Here, n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[5] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                     | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|--------------------------------------|---|--------------------------------------|--|--|
| Subject group type                   | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed          | 40                                      | 29                                   |  |  |
| Units: mg/L                          |   |                                      |  |  |
| arithmetic mean (standard deviation) |   |                                      |  |  |
| Week 12 (n= 40,29)                   | -3.54 ( $\pm 33.57$ )                   | -20.66 ( $\pm 48.35$ )               |  |  |

|                     |                 |                  |  |  |
|---------------------|-----------------|------------------|--|--|
| Week 24 (n= 37,29)  | -8.54 (± 19.17) | -11.72 (± 23.54) |  |  |
| Week 48 (n= 38,27)  | -9.93 (± 21.60) | -12.57 (± 24.23) |  |  |
| Week 96 (n= 36,23)  | -9.39 (± 21.65) | -13.88 (± 25.96) |  |  |
| Week 156 (n= 16,16) | -5.10 (± 14.68) | -12.30 (± 26.69) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Interleukin-6 (IL-6) at Week 12

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Interleukin-6 (IL-6) at Week 12 |
|-----------------|---|

End point description:

Serum concentrations of IL-6 was determined to assess the PD effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 12 are reported.

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

End point timeframe:

Baseline (Day 1) and Week 12

| End point values                     | Cohort 1: ≥ 30 kg and ≤ 60 kg | Cohort 1: < 30 kg and ≥ 10 kg | Cohort 2: ≥ 30 kg and ≤ 60 kg | Cohort 2: < 30 kg and ≥ 10 kg |
|--------------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Subject group type                   | Reporting group               | Reporting group               | Reporting group               | Reporting group               |
| Number of subjects analysed          | 4                             | 4                             | 30                            | 20                            |
| Units: nanogram (ng)/L               |                               |                               |                               |                               |
| arithmetic mean (standard deviation) | 1.27 (± 9.79)                 | 13.65 (± 18.20)               | 43.71 (± 113.42)              | 11.36 (± 35.81)               |

| End point values                     | Cohort 3: ≥ 30 kg and ≤ 60 kg | Cohort 3: < 30 kg and ≥ 10 kg |  |  |
|--------------------------------------|-------------------------------|-------------------------------|--|--|
| Subject group type                   | Reporting group               | Reporting group               |  |  |
| Number of subjects analysed          | 6                             | 5                             |  |  |
| Units: nanogram (ng)/L               |                               |                               |  |  |
| arithmetic mean (standard deviation) | 66.21 (± 86.21)               | 9.20 (± 26.50)                |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Change From Baseline in Total Soluble Interleukin-6 Receptor (sIL-6R) at Week 12**

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Total Soluble Interleukin-6 Receptor (sIL-6R) at Week 12 |
|-----------------|--|

End point description:

Serum concentrations of sIL-6R was determined to assess the PD effects of sarilumab. All treated population included participants who signed informed consent and received at least 1 dose of the study treatment. Only participants with data collected at Baseline and Week 12 are reported.

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

End point timeframe:

Baseline (Day 1) and Week 12

| End point values                     | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |
|--------------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type                   | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed          | 3                                       | 3                                    | 33                                      | 28                                   |
| Units: ng/mL                         |   |                                      |   |                                      |
| arithmetic mean (standard deviation) | 40.09 ( $\pm$ 49.75)                    | 101.50 ( $\pm$ 129.59)               | 316.77 ( $\pm$ 129.29)                  | 388.33 ( $\pm$ 185.82)               |

| End point values                     | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |  |  |
|--------------------------------------|---|--------------------------------------|--|--|
| Subject group type                   | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed          | 6                                       | 6                                    |  |  |
| Units: ng/mL                         |   |                                      |  |  |
| arithmetic mean (standard deviation) | 535.76 ( $\pm$ 98.12)                   | 582.95 ( $\pm$ 149.52)               |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology (JIA ACR) 30 Response at Week 12**

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology (JIA ACR) 30 Response at Week 12 <sup>[6]</sup> |
|-----------------|---|

End point description:

JIA ACR30 response was defined as a participant with at least 3 out of the 6 JIA core set variables with  $\geq 30\%$  improvement from baseline with no more than 1 of the remaining variables worsened by  $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

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

End point timeframe:

Week 12

Notes:

[6] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                                | Cohort 1: >= 30 kg and <= 60 kg | Cohort 1: < 30 kg and >= 10 kg | Cohort 3: >= 30 kg and <= 60 kg | Cohort 3: < 30 kg and >= 10 kg |
|---|---------------------------------|--------------------------------|---------------------------------|--------------------------------|
| Subject group type                              | Reporting group                 | Reporting group                | Reporting group                 | Reporting group                |
| Number of subjects analysed                     | 5                               | 5                              | 6                               | 5                              |
| Units: percentage of participants with response |                                 |                                |                                 |                                |
| number (not applicable)                         | 100                             | 100                            | 100                             | 100                            |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 30 Response at Weeks 12, 24, 48, 96, and 156

|                 |  |
|-----------------|--|
| End point title | Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 30 Response at Weeks 12, 24, 48, 96, and 156 <sup>[7]</sup> |
|-----------------|--|

End point description:

JIA ACR30 response was defined as a participant with at least 3 out of the 6 JIA core set variables with >= 30% improvement from baseline with no more than 1 of the remaining variables worsened by >= 30%. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[7] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                                | Cohort 2: >= 30 kg and <= 60 kg | Cohort 2: < 30 kg and >= 10 kg |  |  |
|---|---------------------------------|--------------------------------|--|--|
| Subject group type                              | Reporting group                 | Reporting group                |  |  |
| Number of subjects analysed                     | 39                              | 29                             |  |  |
| Units: percentage of participants with response |                                 |                                |  |  |
| number (not applicable)                         |                                 |                                |  |  |
| Week 12 (n= 39,29)                              | 100                             | 100                            |  |  |
| Week 24 (n= 39,27)                              | 100                             | 100                            |  |  |
| Week 48 (n= 38,26)                              | 100                             | 100                            |  |  |
| Week 96 (n= 36,24)                              | 97.2                            | 100                            |  |  |
| Week 156 (n= 17,16)                             | 94.1                            | 100                            |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 50 Response at Week 12

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 50 Response at Week 12 <sup>[8]</sup> |
|-----------------|---|

End point description:

JIA ACR50 response was defined as a participant with at least 3 out of the 6 JIA core set variables with  $\geq 50\%$  improvement from baseline with no more than 1 of the remaining variables worsened by  $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

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

End point timeframe:

Week 12

Notes:

[8] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                                | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|---|---|--------------------------------------|---|--------------------------------------|
| Subject group type                              | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed                     | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: percentage of participants with response |   |                                      |   |                                      |
| number (not applicable)                         | 80.0                                    | 100                                  | 100                                     | 100                                  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 50 Response at Weeks 12, 24, 48, 96, and 156

|                 |  |
|-----------------|--|
| End point title | Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 50 Response at Weeks 12, 24, 48, 96, and 156 <sup>[9]</sup> |
|-----------------|--|

End point description:

JIA ACR50 response was defined as a participant with at least 3 out of the 6 JIA core set variables with  $\geq 50\%$  improvement from baseline with no more than 1 of the remaining variables worsened by  $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[9] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                                | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|---|---|--------------------------------------|--|--|
| Subject group type                              | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed                     | 39                                      | 29                                   |  |  |
| Units: percentage of participants with response |   |                                      |  |  |
| number (not applicable)                         |   |                                      |  |  |
| Week 12 (n= 39,29)                              | 94.9                                    | 96.6                                 |  |  |
| Week 24 (n= 39,27)                              | 100                                     | 100                                  |  |  |
| Week 48 (n= 38,26)                              | 100                                     | 100                                  |  |  |
| Week 96 (n= 36,24)                              | 97.2                                    | 100                                  |  |  |
| Week 156 (n= 17,16)                             | 94.1                                    | 100                                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 70 Response at Week 12

|                 |  |
|-----------------|--|
| End point title | Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 70 Response at Week 12 <sup>[10]</sup> |
|-----------------|--|

End point description:

JIA ACR70 response was defined as a participant with at least 3 out of the 6 JIA core set variables with  $\geq 70\%$  improvement from baseline with no more than 1 of the remaining variables worsened by  $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

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

End point timeframe:

Week 12

Notes:

[10] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                                | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|---|---|--------------------------------------|---|--------------------------------------|
| Subject group type                              | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed                     | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: percentage of participants with response |   |                                      |   |                                      |
| number (not applicable)                         | 60.0                                    | 40.0                                 | 100                                     | 100                                  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 70 Response at Weeks 12, 24, 48, 96, and 156

|   |   |
|---|---|
| End point title   | Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 70 Response at Weeks 12, 24, 48, 96, and 156 <sup>[11]</sup> |
| End point description:<br>JIA ACR70 response was defined as a participant with at least 3 out of the 6 JIA core set variables with $\geq 70\%$ improvement from baseline with no more than 1 of the remaining variables worsened by $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Weeks 12, 24, 48, 96, and 156   |   |

Notes:

[11] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                                | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|---|---|--------------------------------------|--|--|
| Subject group type                              | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed                     | 39                                      | 29                                   |  |  |
| Units: percentage of participants with response |   |                                      |  |  |
| number (not applicable)                         |   |                                      |  |  |
| Week 12 (n= 39,29)                              | 74.4                                    | 89.7                                 |  |  |
| Week 24 (n= 39,27)                              | 87.2                                    | 96.3                                 |  |  |
| Week 48 (n= 38,26)                              | 89.5                                    | 100                                  |  |  |
| Week 96 (n= 36,24)                              | 97.2                                    | 100                                  |  |  |
| Week 156 (n= 17,16)                             | 94.1                                    | 100                                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 90 Response at Week 12

|  |  |
|--|--|
| End point title  | Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 90 Response at Week 12 <sup>[12]</sup> |
| End point description:<br>JIA ACR90 response was defined as a participant with at least 3 out of the 6 JIA core set variables with $\geq 90\%$ improvement from baseline with no more than 1 of the remaining variables worsened by $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Week 12  |  |

Notes:

[12] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                                | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|---|---|--------------------------------------|---|--------------------------------------|
| Subject group type                              | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed                     | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: percentage of participants with response |   |                                      |   |                                      |
| number (not applicable)                         | 60.0                                    | 20.0                                 | 66.7                                    | 60.0                                 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 90 Response at Weeks 12, 24, 48, 96, and 156

|                 |   |
|-----------------|---|
| End point title | Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 90 Response at Weeks 12, 24, 48, 96, and 156 <sup>[13]</sup> |
|-----------------|---|

End point description:

JIA ACR90 response was defined as a participant with at least 3 out of the 6 JIA core set variables with  $\geq 90\%$  improvement from baseline with no more than 1 of the remaining variables worsened by  $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Weeks 12, 24, 48, 96, and 156

Notes:

[13] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                                | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|---|---|--------------------------------------|--|--|
| Subject group type                              | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed                     | 39                                      | 29                                   |  |  |
| Units: percentage of participants with response |   |                                      |  |  |
| number (not applicable)                         |   |                                      |  |  |
| Week 12 (n= 39,29)                              | 43.6                                    | 48.3                                 |  |  |
| Week 24 (n= 39,27)                              | 64.1                                    | 74.1                                 |  |  |
| Week 48 (n= 38,26)                              | 68.4                                    | 88.5                                 |  |  |
| Week 96 (n= 36,24)                              | 80.6                                    | 95.8                                 |  |  |
| Week 156 (n= 17,16)                             | 76.5                                    | 100                                  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic

## Arthritis American College of Rheumatology 100 Response at Week 12

|  |   |
|--|---|
| End point title  | Cohorts 1 and 3: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 100 Response at Week 12 <sup>[14]</sup> |
| End point description:<br>JIA ACR100 response was defined as a participant with at least 3 out of the 6 JIA core set variables with $\geq 100\%$ improvement from baseline with no more than 1 of the remaining variables worsened by $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Week 12  |   |

Notes:

[14] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                                | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|---|---|--------------------------------------|---|--------------------------------------|
| Subject group type                              | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed                     | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: percentage of participants with response |   |                                      |   |                                      |
| number (not applicable)                         | 0                                       | 0                                    | 33.3                                    | 40.0                                 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 100 Response at Weeks 12, 24, 48, 96, and 156

|   |  |
|---|--|
| End point title   | Cohort 2: Percentage of Participants With Juvenile Idiopathic Arthritis American College of Rheumatology 100 Response at Weeks 12, 24, 48, 96, and 156 <sup>[15]</sup> |
| End point description:<br>JIA ACR100 response was defined as a participant with at least 3 out of the 6 JIA core set variables with $\geq 100\%$ improvement from baseline with no more than 1 of the remaining variables worsened by $\geq 30\%$ . The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Weeks 12, 24, 48, 96, and 156   |  |

Notes:

[15] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

|   |   |                                      |  |  |
|---|---|--------------------------------------|--|--|
| <b>End point values</b>                         | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
| Subject group type                              | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed                     | 39                                      | 29                                   |  |  |
| Units: percentage of participants with response |   |                                      |  |  |
| number (not applicable)                         |   |                                      |  |  |
| Week 12 (n= 39,29)                              | 12.8                                    | 24.1                                 |  |  |
| Week 24 (n= 39,27)                              | 23.1                                    | 48.1                                 |  |  |
| Week 48 (n= 38,26)                              | 42.1                                    | 53.8                                 |  |  |
| Week 96 (n= 36,24)                              | 47.2                                    | 70.8                                 |  |  |
| Week 156 (n= 17,16)                             | 52.9                                    | 87.5                                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Week 12

|                 |  |
|-----------------|--|
| End point title | Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Week 12 <sup>[16]</sup> |
|-----------------|--|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using visual analog scale (VAS), Childhood Health Questionnaire Disability Index (CHAQ-DI) and hs-CRP. Activity joint count-71 was calculated as sum (joints with active arthritis)\*(71/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

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

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[16] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

|                                  |   |                                      |   |                                      |
|----------------------------------|---|--------------------------------------|---|--------------------------------------|
| <b>End point values</b>          | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
| Subject group type               | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed      | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: joint                     |   |                                      |   |                                      |
| arithmetic mean (standard error) | -14.40 ( $\pm$ 2.159)                   | -11.20 ( $\pm$ 2.871)                | -16.50 ( $\pm$ 4.137)                   | -14.40 ( $\pm$ 5.573)                |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Weeks 12, 24, 48, 96, and 156

|                 |   |
|-----------------|---|
| End point title | Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Activity Joint Count-71, at Weeks 12, 24, 48, 96, and 156 <sup>[17]</sup> |
|-----------------|---|

### End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Activity joint count-71 was calculated as sum (joints with active arthritis)\*(71/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

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

### End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

### Notes:

[17] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                 | Cohort 2: >= 30 kg and <= 60 kg | Cohort 2: < 30 kg and >= 10 kg |  |  |
|----------------------------------|---------------------------------|--------------------------------|--|--|
| Subject group type               | Reporting group                 | Reporting group                |  |  |
| Number of subjects analysed      | 39                              | 29                             |  |  |
| Units: joint                     |                                 |                                |  |  |
| arithmetic mean (standard error) |                                 |                                |  |  |
| Week 12 (n= 39,29)               | -15.15 (± 1.511)                | -12.38 (± 1.519)               |  |  |
| Week 24 (n= 39,27)               | -16.66 (± 1.497)                | -13.26 (± 1.575)               |  |  |
| Week 48 (n= 38,26)               | -17.24 (± 1.547)                | -13.73 (± 1.618)               |  |  |
| Week 96 (n= 36,24)               | -16.47 (± 1.682)                | -13.79 (± 1.751)               |  |  |
| Week 156 (n= 17,16)              | -18.65 (± 2.334)                | -13.88 (± 2.495)               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Week 12

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Week 12 <sup>[18]</sup> |
|-----------------|---|

### End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Limited motion joint count was calculated as sum (joints with limited motion)\*(67/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline (Day 1) and Week 12   |           |
| Notes:   |           |
| [18] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.  |           |

| End point values                 | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|----------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type               | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed      | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: joint                     |   |                                      |   |                                      |
| arithmetic mean (standard error) | -7.80 ( $\pm$ 2.083)                    | -5.80 ( $\pm$ 2.267)                 | -7.83 ( $\pm$ 2.600)                    | -13.00 ( $\pm$ 4.219)                |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Weeks 12, 24, 48, 96, and 156

|                 |  |
|-----------------|--|
| End point title | Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Limited Motion Joint Count, at Weeks 12, 24, 48, 96, and 156 <sup>[19]</sup> |
|-----------------|--|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Limited motion joint count was calculated as sum (joints with limited motion)\*(67/number of joints with assessment). The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

|  |           |
|--|-----------|
| End point type                                     | Secondary |
| End point timeframe:                               |           |
| Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156 |           |

Notes:

[19] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                 | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|----------------------------------|---|--------------------------------------|--|--|
| Subject group type               | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed      | 39                                      | 29                                   |  |  |
| Units: joint                     |   |                                      |  |  |
| arithmetic mean (standard error) |   |                                      |  |  |
| Week 12 (n= 39,29)               | -9.71 ( $\pm$ 1.249)                    | -9.21 ( $\pm$ 1.540)                 |  |  |
| Week 24 (n= 39,27)               | -10.40 ( $\pm$ 1.330)                   | -10.63 ( $\pm$ 1.559)                |  |  |



|                     |                  |                  |  |  |
|---------------------|------------------|------------------|--|--|
| Week 48 (n= 38,26)  | -10.99 (± 1.498) | -10.73 (± 1.525) |  |  |
| Week 96 (n= 36,24)  | -11.14 (± 1.661) | -10.42 (± 1.493) |  |  |
| Week 156 (n= 17,16) | -11.29 (± 2.203) | -11.81 (± 2.550) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Week 12

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Week 12 <sup>[20]</sup> |
|-----------------|---|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. CHAQ questionnaire consists of 30 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain is scored on a 4-point scale ranges from 0 to 3: 0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty) and 3 (unable to do). An additional response of "not applicable" is available to indicate participant is unable to perform activities. CHAQ-DI total score is sum of domain scores divided by number of domains that have a non-missing score. This overall score ranges from 0 (best) to 3 (worst). Higher scores indicate worse outcome. Efficacy population.

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

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[20] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                 | Cohort 1: >= 30 kg and <= 60 kg | Cohort 1: < 30 kg and >= 10 kg | Cohort 3: >= 30 kg and <= 60 kg | Cohort 3: < 30 kg and >= 10 kg |
|----------------------------------|---------------------------------|--------------------------------|---------------------------------|--------------------------------|
| Subject group type               | Reporting group                 | Reporting group                | Reporting group                 | Reporting group                |
| Number of subjects analysed      | 5                               | 5                              | 6                               | 5                              |
| Units: units on a scale          |                                 |                                |                                 |                                |
| arithmetic mean (standard error) | -0.80 (± 0.242)                 | -1.08 (± 0.239)                | -0.42 (± 0.173)                 | -0.75 (± 0.213)                |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Weeks 12, 24, 48, 96, and 156

|                 |  |
|-----------------|--|
| End point title | Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Childhood Health Assessment Questionnaire Disability Index, at Weeks 12, 24, 48, 96, and 156 <sup>[21]</sup> |
|-----------------|--|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. CHAQ questionnaire consists of 30 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip and activities. Each domain is scored on a 4-point scale ranges from 0 to 3: 0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty) and 3 (unable to do). An additional response of "not applicable" is available to indicate participant is unable to perform activities. CHAQ-DI total score is sum of domain scores divided by number of domains that have a non-missing score. This overall score ranges from 0 (best) to 3 (worst). Higher scores indicate worse outcome. Efficacy population. n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[21] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                 | Cohort 2: >= 30 kg and <= 60 kg | Cohort 2: < 30 kg and >= 10 kg |  |  |
|----------------------------------|---------------------------------|--------------------------------|--|--|
| Subject group type               | Reporting group                 | Reporting group                |  |  |
| Number of subjects analysed      | 39                              | 29                             |  |  |
| Units: units on a scale          |                                 |                                |  |  |
| arithmetic mean (standard error) |                                 |                                |  |  |
| Week 12 (n= 39,29)               | -0.77 (± 0.092)                 | -0.74 (± 0.113)                |  |  |
| Week 24 (n= 39,27)               | -0.90 (± 0.096)                 | -0.95 (± 0.132)                |  |  |
| Week 48 (n= 38,27)               | -0.88 (± 0.084)                 | -1.08 (± 0.119)                |  |  |
| Week 96 (n= 36,24)               | -0.92 (± 0.109)                 | -1.13 (± 0.136)                |  |  |
| Week 156 (n= 17,16)              | -1.07 (± 0.163)                 | -1.20 (± 0.169)                |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Week 12

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Week 12 <sup>[22]</sup> |
|-----------------|---|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Serum concentrations of hs-CRP was determined to assess the PD effects of sarilumab. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline (Day 1) and Week 12   |           |
| Notes:   |           |
| [22] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.  |           |

| End point values                 | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|----------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type               | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed      | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: mg/L                      |   |                                      |   |                                      |
| arithmetic mean (standard error) | -1.00 ( $\pm$ 1.130)                    | -1.67 ( $\pm$ 1.139)                 | -5.71 ( $\pm$ 3.633)                    | -2.54 ( $\pm$ 1.845)                 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Weeks 12, 24, 48, 96, and 156

|                 |  |
|-----------------|--|
| End point title | Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, C-Reactive Protein, at Weeks 12, 24, 48, 96, and 156 <sup>[23]</sup> |
|-----------------|--|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Serum concentrations of hs-CRP was determined to assess the PD effects of sarilumab. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156   |           |
| Notes:   |           |
| [23] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.   |           |

| End point values                 | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|----------------------------------|---|--------------------------------------|--|--|
| Subject group type               | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed      | 39                                      | 29                                   |  |  |
| Units: mg/L                      |   |                                      |  |  |
| arithmetic mean (standard error) |   |                                      |  |  |
| Week 12 (n= 39,27)               | -3.84 ( $\pm$ 5.437)                    | -20.66 ( $\pm$ 9.304)                |  |  |
| Week 24 (n= 37,29)               | -8.54 ( $\pm$ 3.151)                    | -11.72 ( $\pm$ 4.371)                |  |  |

|                     |                 |                  |  |  |
|---------------------|-----------------|------------------|--|--|
| Week 48 (n= 38,27)  | -9.93 (± 3.505) | -12.57 (± 4.664) |  |  |
| Week 96 (n= 36,23)  | -9.39 (± 3.608) | -13.88 (± 5.414) |  |  |
| Week 156 (n= 16,16) | -5.10 (± 3.671) | -12.30 (± 6.672) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Week 12

|                 |  |
|-----------------|--|
| End point title | Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Week 12 <sup>[24]</sup> |
|-----------------|--|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Physician global assessment of disease activity was assessed on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

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

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[24] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                 | Cohort 1: >= 30 kg and <= 60 kg | Cohort 1: < 30 kg and >= 10 kg | Cohort 3: >= 30 kg and <= 60 kg | Cohort 3: < 30 kg and >= 10 kg |
|----------------------------------|---------------------------------|--------------------------------|---------------------------------|--------------------------------|
| Subject group type               | Reporting group                 | Reporting group                | Reporting group                 | Reporting group                |
| Number of subjects analysed      | 5                               | 5                              | 6                               | 5                              |
| Units: units on a scale          |                                 |                                |                                 |                                |
| arithmetic mean (standard error) | -3.56 (± 0.969)                 | -6.30 (± 0.397)                | -4.55 (± 0.509)                 | -5.68 (± 1.163)                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Weeks 12, 24, 48, 96, and 156

|                 |   |
|-----------------|---|
| End point title | Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Physician Global Assessment of Disease Activity, at Weeks 12, 24, 48, |
|-----------------|---|

## End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Physician global assessment of disease activity was assessed on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

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

## End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

## Notes:

[25] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                 | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|----------------------------------|---|--------------------------------------|--|--|
| Subject group type               | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed      | 39                                      | 29                                   |  |  |
| Units: units on a scale          |   |                                      |  |  |
| arithmetic mean (standard error) |   |                                      |  |  |
| Week 12 (n= 39,29)               | -4.50 ( $\pm$ 0.248)                    | -4.09 ( $\pm$ 0.367)                 |  |  |
| Week 24 (n= 39,27)               | -4.99 ( $\pm$ 0.237)                    | -5.01 ( $\pm$ 0.341)                 |  |  |
| Week 48 (n= 38,26)               | -5.27 ( $\pm$ 0.263)                    | -5.25 ( $\pm$ 0.321)                 |  |  |
| Week 96 (n= 36,24)               | -5.30 ( $\pm$ 0.306)                    | -5.35 ( $\pm$ 0.347)                 |  |  |
| Week 156 (n= 17,16)              | -5.66 ( $\pm$ 0.396)                    | -5.73 ( $\pm$ 0.437)                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Week 12

|                 |  |
|-----------------|--|
| End point title | Cohorts 1 and 3: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Week 12 <sup>[26]</sup> |
|-----------------|--|

## End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Participant/parent assessment of overall well-being was rated on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab.

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

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[26] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                 | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|----------------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type               | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed      | 5                                       | 5                                    | 6                                       | 5                                    |
| Units: units on a scale          |   |                                      |   |                                      |
| arithmetic mean (standard error) | -3.30 ( $\pm 1.014$ )                   | -3.16 ( $\pm 1.364$ )                | -3.05 ( $\pm 0.992$ )                   | -5.00 ( $\pm 0.969$ )                |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Weeks 12, 24, 48, 96, and 156

|                 |   |
|-----------------|---|
| End point title | Cohort 2: Change From Baseline in Juvenile Idiopathic Arthritis American College of Rheumatology Component, Participant/Parent Assessment of Overall Well-Being, at Weeks 12, 24, 48, 96, and 156 <sup>[27]</sup> |
|-----------------|---|

End point description:

The JIA ACR components included joints with active arthritis (0 to 71 joints), joints with limited motion (0 to 67 joints), physician global assessment of disease activity and participant/parent assessment of overall well-being using VAS, CHAQ-DI and hs-CRP. Participant/parent assessment of overall well-being was rated on an anchored 100 mm horizontal VAS score ranging from 0 to 100 where 0 is considered the best disease activity (no disease activity) and 100 the worst (most disease activity). Higher scores indicate worse outcome. The efficacy analysis set included all participants who received at least 1 dose of sarilumab. Here, n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[27] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                 | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |  |  |
|----------------------------------|---|--------------------------------------|--|--|
| Subject group type               | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed      | 39                                      | 29                                   |  |  |
| Units: units on a scale          |   |                                      |  |  |
| arithmetic mean (standard error) |   |                                      |  |  |
| Week 12 (n= 39,29)               | -3.73 ( $\pm 0.335$ )                   | -4.01 ( $\pm 0.435$ )                |  |  |

|                     |                 |                 |  |  |
|---------------------|-----------------|-----------------|--|--|
| Week 24 (n= 39,27)  | -4.38 (± 0.313) | -4.39 (± 0.475) |  |  |
| Week 48 (n= 38,27)  | -4.21 (± 0.356) | -4.64 (± 0.510) |  |  |
| Week 96 (n= 36,23)  | -4.36 (± 0.387) | -5.09 (± 0.521) |  |  |
| Week 156 (n= 17,16) | -4.19 (± 0.738) | -5.01 (± 0.636) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohorts 1 and 3: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score (JADAS-27) at Week 12

|                 |   |
|-----------------|---|
| End point title | Cohorts 1 and 3: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score (JADAS-27) at Week 12 <sup>[28]</sup> |
|-----------------|---|

End point description:

The JADAS is used for assessment of disease activity and it includes 4 measures (physician global assessment of disease activity, parent/participant global assessment of well-being, count of joints with active disease and index of inflammation). JADAS total score is calculated as sum of scores of its 4 components. Total score ranges from 0 to 10 where 0= no activity and 10= maximum activity. Higher scores indicate better outcome. JADAS-27 count includes a count of 27 joints (cervical spine, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, hips, knees and ankles). Index of inflammation is determined by ESR or hs-CRP level. ESR normalized to 0-10 scale according to following formula: (ESR [mm/hour]20)/10. hs-CRP normalized to 0-10 scale according to following formula: (CRP [mg/L]10)/10. Clinical JADAS-27 is without CRP or ESR component. Efficacy population. Here, n= number of participants analyzed at baseline and Week 12 are reported.

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

End point timeframe:

Baseline (Day 1) and Week 12

Notes:

[28] - 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: Only participants treated in Cohorts 1 and 3 are analyzed for this endpoint.

| End point values                       | Cohort 1: >= 30 kg and <= 60 kg | Cohort 1: < 30 kg and >= 10 kg | Cohort 3: >= 30 kg and <= 60 kg | Cohort 3: < 30 kg and >= 10 kg |
|--|---------------------------------|--------------------------------|---------------------------------|--------------------------------|
| Subject group type                     | Reporting group                 | Reporting group                | Reporting group                 | Reporting group                |
| Number of subjects analysed            | 7                               | 6                              | 6                               | 9                              |
| Units: units on a scale                |                                 |                                |                                 |                                |
| number (not applicable)                |                                 |                                |                                 |                                |
| JADAS-27-ESR: Week 12 (n=5,5,6,4)      | -15.4                           | -19.1                          | -20.0                           | -19.4                          |
| JADAS-27-CRP: Week 12 (n=7,6,6,9)      | -16.04                          | -18.06                         | -18.48                          | -21.08                         |
| Clinical JADAS-27: Week 12 (n=7,6,6,9) | -16.06                          | -18.06                         | -18.27                          | -21.08                         |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cohort 2: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score at Weeks 12, 24, 48, 96, and 156

|                 |   |
|-----------------|---|
| End point title | Cohort 2: Mean Change From Baseline in Juvenile Arthritis Disease Activity Score at Weeks 12, 24, 48, 96, and 156 <sup>[29]</sup> |
|-----------------|---|

End point description:

The JADAS is used for assessment of disease activity and it includes 4 measures (physician global assessment of disease activity, parent/participant global assessment of well-being, count of joints with active disease and index of inflammation). JADAS total score is calculated as sum of scores of its 4 components. Total score ranges from 0 to 10 where 0= no activity and 10= maximum activity. Higher scores indicate better outcome. JADAS-27 count includes a count of 27 joints (cervical spine, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints, hips, knees and ankles). Index of inflammation is determined by ESR or hs-CRP level. ESR normalized to 0-10 scale according to following formula: (ESR [mm/hour]20)/10. hs-CRP normalized to 0-10 scale according to following formula: (CRP [mg/L]10)/10. Clinical JADAS-27 is without CRP or ESR component. Efficacy population. Here, n= number of participants analyzed at specific timepoints.

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

End point timeframe:

Baseline (Day 1) and Weeks 12, 24, 48, 96, and 156

Notes:

[29] - 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: Only participants treated in Cohort 2 are analyzed for this endpoint.

| End point values                       | Cohort 2: >= 30 kg and <= 60 kg | Cohort 2: < 30 kg and >= 10 kg |  |  |
|--|---------------------------------|--------------------------------|--|--|
| Subject group type                     | Reporting group                 | Reporting group                |  |  |
| Number of subjects analysed            | 42                              | 31                             |  |  |
| Units: units on a scale                |                                 |                                |  |  |
| number (not applicable)                |                                 |                                |  |  |
| JADAS-27-ESR: Week 12 (n= 37,29)       | -18.9                           | -16.9                          |  |  |
| JADAS-27-ESR: Week 24 (n= 39,24)       | -21.9                           | -18.3                          |  |  |
| JADAS-27-ESR: Week 48 (n= 38,26)       | -22.3                           | -19.4                          |  |  |
| JADAS-27-ESR: Week 96 (n= 36,22)       | -22.4                           | -20.4                          |  |  |
| JADAS-27-ESR: Week 156 (n= 16,14)      | -23.2                           | -20.6                          |  |  |
| JADAS-27-CRP: Week 12 (n= 42,31)       | -18.23                          | -16.31                         |  |  |
| JADAS-27-CRP: Week 24 (n= 42,31)       | -20.92                          | -18.84                         |  |  |
| JADAS-27-CRP: Week 48 (n= 42,31)       | -21.65                          | -19.44                         |  |  |
| JADAS-27-CRP: Week 96 (n= 42,31)       | -21.90                          | -20.06                         |  |  |
| JADAS-27-CRP: Week 156 (n= 42,31)      | -21.79                          | -20.21                         |  |  |
| Clinical JADAS-27: Week 12 (n= 42,31)  | -17.93                          | -15.99                         |  |  |
| Clinical JADAS-27: Week 24 (n= 42,31)  | -20.47                          | -17.96                         |  |  |
| Clinical JADAS-27: Week 48 (n= 42,31)  | -20.98                          | -18.77                         |  |  |
| Clinical JADAS-27: Week 96 (n= 42,31)  | -21.21                          | -19.46                         |  |  |
| Clinical JADAS-27: Week 156 (n= 42,31) | -21.21                          | -19.31                         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment Emergent Adverse Events



## (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)

|   |  |
|---|--|
| End point title   | Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs) |
| End point description:<br>An adverse events (AEs) is any untoward medical occurrence in a participant or in a clinical investigation participant administered a medicinal product and which does not necessarily have a causal relationship with the study treatment. An SAE is any untoward medical occurrence that at any dose results in death or is life-threatening or requires inpatient hospitalization or prolongation of existing hospitalization or results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect or is an important medical event. TEAEs are defined as AEs that develop or worsen during the on-treatment period [that is, from the time of first dose of study treatment up to 6 weeks after the last administration of the study treatment]. The Safety analysis set included all participants who received at least 1 dose or part of a dose of the study treatment, analyzed according to the treatment actually received. |  |
| End point type  | Secondary  |
| End point timeframe:<br>From the first administration of study treatment (Day 1) up to end of treatment period, maximum of 156 weeks for portions 1 and 2 and 96 weeks for portion 3  |  |

| End point values            | Cohort 1: >= 30 kg and <= 60 kg | Cohort 1: < 30 kg and >= 10 kg | Cohort 2: >= 30 kg and <= 60 kg | Cohort 2: < 30 kg and >= 10 kg |
|-----------------------------|---------------------------------|--------------------------------|---------------------------------|--------------------------------|
| Subject group type          | Reporting group                 | Reporting group                | Reporting group                 | Reporting group                |
| Number of subjects analysed | 7                               | 6                              | 42                              | 31                             |
| Units: participants         |                                 |                                |                                 |                                |
| Any TEAE                    | 7                               | 6                              | 40                              | 30                             |
| Any treatment emergent SAE  | 2                               | 0                              | 3                               | 3                              |

| End point values            | Cohort 3: >= 30 kg and <= 60 kg | Cohort 3: < 30 kg and >= 10 kg |  |  |
|-----------------------------|---------------------------------|--------------------------------|--|--|
| Subject group type          | Reporting group                 | Reporting group                |  |  |
| Number of subjects analysed | 6                               | 9                              |  |  |
| Units: participants         |                                 |                                |  |  |
| Any TEAE                    | 5                               | 9                              |  |  |
| Any treatment emergent SAE  | 0                               | 0                              |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Local Site Reactions

|  |  |
|--|--|
| End point title  | Number of Participants With Local Site Reactions |
| End point description:<br>Participants were observed for at least 30 minutes after each study treatment administration either on site or at home and any local reactions were noted in the diary regardless of being clinically significant. The Safety analysis set included all participants who received at least 1 dose or part of a dose of the study treatment, analyzed according to the treatment actually received. |  |

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| From the first administration of study treatment (Day 1) up to end of treatment period, maximum of 156 weeks for portions 1 and 2 and 96 weeks for portion 3 |           |

| End point values            | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 1: $< 30$ kg and $\geq 10$ kg | Cohort 2: $\geq 30$ kg and $\leq 60$ kg | Cohort 2: $< 30$ kg and $\geq 10$ kg |
|-----------------------------|---|--------------------------------------|---|--------------------------------------|
| Subject group type          | Reporting group                         | Reporting group                      | Reporting group                         | Reporting group                      |
| Number of subjects analysed | 7                                       | 6                                    | 42                                      | 31                                   |
| Units: participants         | 1                                       | 0                                    | 21                                      | 19                                   |

| End point values            | Cohort 3: $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |  |  |
|-----------------------------|---|--------------------------------------|--|--|
| Subject group type          | Reporting group                         | Reporting group                      |  |  |
| Number of subjects analysed | 6                                       | 9                                    |  |  |
| Units: participants         | 3                                       | 1                                    |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first administration of study treatment (Day 1) up to end of treatment period, maximum of 156 weeks for portions 1 and 2 and 96 weeks for portion 3.

Adverse event reporting additional description:

Analysis was performed on the safety analysis set.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 1: $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 2 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection q2w until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection q2w in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 2 (from Baseline): $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 3 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1).

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 2.5 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Cohort 1: $< 30$ kg and $\geq 10$ kg |
|-----------------------|--------------------------------------|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 2.5 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2.5 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 4 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

|                       |  |
|-----------------------|--|
| Reporting group title | Cohort 2 (from Baseline): $< 30$ kg and $\geq 10$ kg |
|-----------------------|--|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 4 mg/kg SC injection q2w for 12 weeks in core treatment phase (portion 1).

|                       |  |
|-----------------------|--|
| Reporting group title | Cohort 2(Post dose-adjustment from Dose 1): $< 30$ kg and $\geq 10$ kg |
|-----------------------|--|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 4 mg/kg SC injection q2w for 144 weeks in portion 2.

|                       |  |
|-----------------------|--|
| Reporting group title | Cohort 2(Post dose-adjustment from Dose 3): $< 30$ kg and $\geq 10$ kg |
|-----------------------|--|

Reporting group description:

Participants with body weight  $< 30$  kg and  $\geq 10$  kg received sarilumab 4 mg/kg SC injection q2w for 84 weeks in portion 3.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 2(Post dose-adjustment from Dose 3): $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 3 mg/kg SC injection q2w for 84 weeks in portion 3.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 2(Post dose-adjustment from Dose 1): $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 3 mg/kg SC injection q2w for 144 weeks in portion 2.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort 3: $\geq 30$ kg and $\leq 60$ kg |
|-----------------------|---|

Reporting group description:

Participants with body weight  $\geq 30$  kg and  $\leq 60$  kg received sarilumab 2 mg/kg SC injection qw for 12 weeks in core treatment phase (portion 1). Eligible participants continued to receive 2 mg/kg SC injection qw until the selected dose was found and then switched to selected dose of 3 mg/kg SC injection qw in extension phase (portion 2: up to 144 weeks and portion 3: up to 84 weeks).

| <b>Serious adverse events</b>                     | Cohort 1: $\geq 30$ kg and $\leq 60$ kg | Cohort 2 (from Baseline): $\geq 30$ kg and $\leq 60$ kg | Cohort 3: $< 30$ kg and $\geq 10$ kg |
|---|---|---|--------------------------------------|
| Total subjects affected by serious adverse events |   |   |                                      |
| subjects affected / exposed                       | 2 / 7 (28.57%)                          | 3 / 42 (7.14%)  | 0 / 9 (0.00%)                        |
| number of deaths (all causes)                     | 0                                       | 0   | 0                                    |
| number of deaths resulting from adverse events    | 0                                       | 0   | 0                                    |
| Injury, poisoning and procedural complications    |   |   |                                      |
| Ligament Rupture                                  |   |   |                                      |
| subjects affected / exposed                       | 0 / 7 (0.00%)                           | 1 / 42 (2.38%)  | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0                                   | 0 / 1   | 0 / 0                                |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0   | 0 / 0                                |
| Meniscus Injury                                   |   |   |                                      |
| subjects affected / exposed                       | 0 / 7 (0.00%)                           | 1 / 42 (2.38%)  | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0                                   | 0 / 1   | 0 / 0                                |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0   | 0 / 0                                |
| Nervous system disorders                          |   |   |                                      |
| Syncope   |   |   |                                      |
| subjects affected / exposed                       | 1 / 7 (14.29%)                          | 0 / 42 (0.00%)  | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 1                                   | 0 / 0   | 0 / 0                                |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0   | 0 / 0                                |
| Gastrointestinal disorders                        |   |   |                                      |
| Inguinal Hernia                                   |   |   |                                      |
| subjects affected / exposed                       | 0 / 7 (0.00%)                           | 0 / 42 (0.00%)  | 0 / 9 (0.00%)                        |
| occurrences causally related to treatment / all   | 0 / 0                                   | 0 / 0   | 0 / 0                                |
| deaths causally related to treatment / all        | 0 / 0                                   | 0 / 0   | 0 / 0                                |
| Pancreatic Pseudocyst                             |   |   |                                      |

|   |                               |   |   |
|---|-------------------------------|---|---|
| subjects affected / exposed                     | 0 / 7 (0.00%)                 | 0 / 42 (0.00%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0                         | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| Pancreatitis Acute                              |                               |   |   |
| subjects affected / exposed                     | 0 / 7 (0.00%)                 | 0 / 42 (0.00%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0                         | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| Respiratory, thoracic and mediastinal disorders |                               |   |   |
| Tonsillar Hypertrophy                           |                               |   |   |
| subjects affected / exposed                     | 0 / 7 (0.00%)                 | 0 / 42 (0.00%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0                         | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| Musculoskeletal and connective tissue disorders |                               |   |   |
| Juvenile Idiopathic Arthritis                   |                               |   |   |
| subjects affected / exposed                     | 0 / 7 (0.00%)                 | 1 / 42 (2.38%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0                         | 0 / 1   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| Infections and infestations                     |                               |   |   |
| Acute Sinusitis                                 |                               |   |   |
| subjects affected / exposed                     | 0 / 7 (0.00%)                 | 1 / 42 (2.38%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0                         | 0 / 1   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| Infectious Mononucleosis                        |                               |   |   |
| subjects affected / exposed                     | 1 / 7 (14.29%)                | 0 / 42 (0.00%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 1                         | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| Bone Tuberculosis                               |                               |   |   |
| subjects affected / exposed                     | 0 / 7 (0.00%)                 | 0 / 42 (0.00%)                                | 0 / 9 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0                         | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all      | 0 / 0                         | 0 / 0   | 0 / 0   |
| <b>Serious adverse events</b>                   | Cohort 1: < 30 kg and ≥ 10 kg | Cohort 2 (from Baseline): < 30 kg and ≥ 10 kg | Cohort 2(Post dose-adjustment from Dose 1): <30 kg and ≥10 kg |
| Total subjects affected by serious              |                               |   |   |

|   |               |                |               |
|---|---------------|----------------|---------------|
| adverse events                                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 3 / 31 (9.68%) | 0 / 5 (0.00%) |
| number of deaths (all causes)                   | 0             | 0              | 0             |
| number of deaths resulting from adverse events  | 0             | 0              | 0             |
| Injury, poisoning and procedural complications  |               |                |               |
| Ligament Rupture                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 31 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Meniscus Injury                                 |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 31 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Nervous system disorders                        |               |                |               |
| Syncope   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 31 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |               |                |               |
| Inguinal Hernia                                 |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 31 (3.23%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pancreatic Pseudocyst                           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 31 (3.23%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pancreatitis Acute                              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 31 (3.23%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |                |               |
| Tonsillar Hypertrophy                           |               |                |               |

|  |               |                |               |
|--|---------------|----------------|---------------|
| subjects affected / exposed                            | 0 / 6 (0.00%) | 1 / 31 (3.23%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0         |
| <b>Musculoskeletal and connective tissue disorders</b> |               |                |               |
| Juvenile Idiopathic Arthritis                          |               |                |               |
| subjects affected / exposed                            | 0 / 6 (0.00%) | 0 / 31 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0         |
| <b>Infections and infestations</b>                     |               |                |               |
| Acute Sinusitis  |               |                |               |
| subjects affected / exposed                            | 0 / 6 (0.00%) | 0 / 31 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0         |
| Infectious Mononucleosis                               |               |                |               |
| subjects affected / exposed                            | 0 / 6 (0.00%) | 0 / 31 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0         |
| Bone Tuberculosis                                      |               |                |               |
| subjects affected / exposed                            | 0 / 6 (0.00%) | 1 / 31 (3.23%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all             | 0 / 0         | 0 / 0          | 0 / 0         |

| <b>Serious adverse events</b>                     | Cohort 2(Post dose-adjustment from Dose 3): <30 kg and >=10 kg | Cohort 2(Post dose-adjustment from Dose 3):>=30 kg and <=60 kg | Cohort 2(Post dose-adjustment from Dose 1):>=30 kg and <=60 kg |
|---|--|--|--|
| Total subjects affected by serious adverse events |  |  |  |
| subjects affected / exposed                       | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| number of deaths (all causes)                     | 0  | 0  | 0  |
| number of deaths resulting from adverse events    | 0  | 0  | 0  |
| Injury, poisoning and procedural complications    |  |  |  |
| Ligament Rupture                                  |  |  |  |
| subjects affected / exposed                       | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all        | 0 / 0  | 0 / 0  | 0 / 0  |
| Meniscus Injury                                   |  |  |  |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nervous system disorders                        |               |               |               |
| Syncope   |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |               |               |               |
| Inguinal Hernia                                 |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pancreatic Pseudocyst                           |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pancreatitis Acute                              |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |               |               |
| Tonsillar Hypertrophy                           |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |               |               |
| Juvenile Idiopathic Arthritis                   |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Infections and infestations                     |               |               |               |
| Acute Sinusitis                                 |               |               |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Infectious Mononucleosis                        |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bone Tuberculosis                               |               |               |               |
| subjects affected / exposed                     | 0 / 5 (0.00%) | 0 / 6 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |                                    |  |  |
|---|------------------------------------|--|--|
| <b>Serious adverse events</b>                     | Cohort 3: >= 30 kg<br>and <= 60 kg |  |  |
| Total subjects affected by serious adverse events |                                    |  |  |
| subjects affected / exposed                       | 0 / 6 (0.00%)                      |  |  |
| number of deaths (all causes)                     | 0                                  |  |  |
| number of deaths resulting from adverse events    | 0                                  |  |  |
| Injury, poisoning and procedural complications    |                                    |  |  |
| Ligament Rupture                                  |                                    |  |  |
| subjects affected / exposed                       | 0 / 6 (0.00%)                      |  |  |
| occurrences causally related to treatment / all   | 0 / 0                              |  |  |
| deaths causally related to treatment / all        | 0 / 0                              |  |  |
| Meniscus Injury                                   |                                    |  |  |
| subjects affected / exposed                       | 0 / 6 (0.00%)                      |  |  |
| occurrences causally related to treatment / all   | 0 / 0                              |  |  |
| deaths causally related to treatment / all        | 0 / 0                              |  |  |
| Nervous system disorders                          |                                    |  |  |
| Syncope   |                                    |  |  |
| subjects affected / exposed                       | 0 / 6 (0.00%)                      |  |  |
| occurrences causally related to treatment / all   | 0 / 0                              |  |  |
| deaths causally related to treatment / all        | 0 / 0                              |  |  |
| Gastrointestinal disorders                        |                                    |  |  |
| Inguinal Hernia                                   |                                    |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pancreatic Pseudocyst                           |               |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pancreatitis Acute                              |               |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Respiratory, thoracic and mediastinal disorders |               |  |  |
| Tonsillar Hypertrophy                           |               |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Musculoskeletal and connective tissue disorders |               |  |  |
| Juvenile Idiopathic Arthritis                   |               |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Infections and infestations                     |               |  |  |
| Acute Sinusitis                                 |               |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Infectious Mononucleosis                        |               |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Bone Tuberculosis                               |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 6 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |

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

| <b>Non-serious adverse events</b>                                   | Cohort 1: $\geq 30$ kg<br>and $\leq 60$ kg | Cohort 2 (from<br>Baseline): $\geq 30$ kg<br>and $\leq 60$ kg | Cohort 3: $< 30$ kg<br>and $\geq 10$ kg |
|---|--|---|---|
| Total subjects affected by non-serious adverse events               |  |   |   |
| subjects affected / exposed   | 7 / 7 (100.00%)                            | 39 / 42 (92.86%)  | 9 / 9 (100.00%)                         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |   |
| Skin Papilloma  |  |   |   |
| subjects affected / exposed   | 1 / 7 (14.29%)                             | 1 / 42 (2.38%)  | 0 / 9 (0.00%)                           |
| occurrences (all)   | 1  | 1   | 0                                       |
| Vascular disorders  |  |   |   |
| Essential Hypertension  |  |   |   |
| subjects affected / exposed   | 1 / 7 (14.29%)                             | 0 / 42 (0.00%)  | 0 / 9 (0.00%)                           |
| occurrences (all)   | 1  | 0   | 0                                       |
| General disorders and administration site conditions                |  |   |   |
| Administration Site Erythema  |  |   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                              | 0 / 42 (0.00%)  | 0 / 9 (0.00%)                           |
| occurrences (all)   | 0  | 0   | 0                                       |
| Fatigue   |  |   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                              | 0 / 42 (0.00%)  | 0 / 9 (0.00%)                           |
| occurrences (all)   | 0  | 0   | 0                                       |
| Gait Disturbance  |  |   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                              | 0 / 42 (0.00%)  | 1 / 9 (11.11%)                          |
| occurrences (all)   | 0  | 0   | 1                                       |
| Injection Site Haemorrhage  |  |   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                              | 0 / 42 (0.00%)  | 0 / 9 (0.00%)                           |
| occurrences (all)   | 0  | 0   | 0                                       |
| Injection Site Erythema   |  |   |   |
| subjects affected / exposed   | 1 / 7 (14.29%)                             | 4 / 42 (9.52%)  | 0 / 9 (0.00%)                           |
| occurrences (all)   | 1  | 20  | 0                                       |
| Injection Site Pruritus   |  |   |   |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0 | 3 / 42 (7.14%)<br>3 | 0 / 9 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Injection Site Urticaria<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Injection Site Reaction<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 7 (0.00%)<br>0 | 2 / 42 (4.76%)<br>3 | 0 / 9 (0.00%)<br>0  |
| Immune system disorders<br>Allergy To Arthropod Bite<br>subjects affected / exposed<br>occurrences (all)     | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 2 / 42 (4.76%)<br>4 | 0 / 9 (0.00%)<br>0  |
| Increased Bronchial Secretion<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Rhinitis Allergic<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0 | 1 / 42 (2.38%)<br>1 | 2 / 9 (22.22%)<br>3 |
| Psychiatric disorders<br>Affective Disorder<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Major Depression   |                    |                     |                     |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Investigations   |                     |                      |                     |
| Blood Pressure Systolic Decreased<br>subjects affected / exposed<br>occurrences (all)    | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Blood Bilirubin Increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Blood Alkaline Phosphatase Increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Aspartate Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 2 / 42 (4.76%)<br>2  | 0 / 9 (0.00%)<br>0  |
| Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 5 / 42 (11.90%)<br>6 | 1 / 9 (11.11%)<br>1 |
| Eosinophil Count Increased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Lymphocyte Count Increased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Monocyte Count Decreased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 7 (0.00%)<br>0  | 2 / 42 (4.76%)<br>2  | 0 / 9 (0.00%)<br>0  |
| Mean Cell Volume Decreased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Transaminases Increased<br>subjects affected / exposed<br>occurrences (all)              | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0  | 0 / 9 (0.00%)<br>0  |
| Neutrophil Count Decreased   |                     |                      |                     |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 2 / 42 (4.76%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0              |
| Monocyte Count Increased                       |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 42 (2.38%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Accidental Overdose                            |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 4 / 42 (9.52%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 5              | 0              |
| Arthropod Bite                                 |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 42 (2.38%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Ligament Sprain                                |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 2 / 42 (4.76%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 4              | 0              |
| Hand Fracture                                  |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Fall   |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 3 / 42 (7.14%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 3              | 0              |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 3 / 42 (7.14%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 4              | 0              |
| Thermal Burn                                   |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Traumatic Haematoma                            |                |                |                |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0              |
| Cardiac disorders                              |                |                |                |
| Cardiovascular Disorder                        |                |                |                |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Nervous system disorders                       |                |                |                |

|   |                     |                        |                     |
|---|---------------------|------------------------|---------------------|
| Dizziness<br>subjects affected / exposed<br>occurrences (all)       | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 2 / 42 (4.76%)<br>4    | 1 / 9 (11.11%)<br>2 |
| Blood and lymphatic system disorders                                |                     |                        |                     |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)     | 3 / 7 (42.86%)<br>3 | 10 / 42 (23.81%)<br>23 | 6 / 9 (66.67%)<br>9 |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)     | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 1 / 42 (2.38%)<br>1    | 0 / 9 (0.00%)<br>0  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)      | 1 / 7 (14.29%)<br>1 | 0 / 42 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Ear and labyrinth disorders   |                     |                        |                     |
| Ear Pain<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 3 / 42 (7.14%)<br>3    | 0 / 9 (0.00%)<br>0  |
| Eye disorders   |                     |                        |                     |
| Keratitis<br>subjects affected / exposed<br>occurrences (all)       | 1 / 7 (14.29%)<br>1 | 0 / 42 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Uveitis<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 1 / 42 (2.38%)<br>2    | 0 / 9 (0.00%)<br>0  |
| Gastrointestinal disorders  |                     |                        |                     |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 4 / 42 (9.52%)<br>4    | 0 / 9 (0.00%)<br>0  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)       | 0 / 7 (0.00%)<br>0  | 3 / 42 (7.14%)<br>3    | 2 / 9 (22.22%)<br>2 |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Dental Discomfort                      |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 2              | 0              | 0              |
| Constipation                           |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Aphthous Ulcer                         |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 1 / 42 (2.38%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0              |
| Abdominal Pain Upper                   |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 3 / 42 (7.14%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 5              | 0              |
| Pulpless Tooth                         |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Nausea                                 |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 3 / 42 (7.14%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 4              | 0              |
| Mouth Ulceration                       |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 2 / 42 (4.76%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 1              | 4              | 0              |
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 2 / 42 (4.76%) | 1 / 9 (11.11%) |
| occurrences (all)                      | 0              | 3              | 1              |
| Hepatobiliary disorders                |                |                |                |
| Hyperbilirubinaemia                    |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Pityriasis Alba                        |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Allergic                    |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Ingrowing Nail                                  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 42 (2.38%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Acne  |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Rash Pruritic                                   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Rash Papular                                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Rash  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 42 (2.38%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Skin Reaction                                   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Urticaria Chronic                               |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Juvenile Idiopathic Arthritis                   |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 3 / 42 (7.14%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 1              | 3              | 0              |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 42 (4.76%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 3              | 0              |
| Pain In Extremity                               |                |                |                |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 7 (14.29%)<br>1 | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 |
| Infections and infestations                      |                     |                     |                    |
| Conjunctivitis                                   |                     |                     |                    |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 0 / 42 (0.00%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 1                   | 0                   | 1                  |
| Acute Sinusitis                                  |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 2 / 42 (4.76%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 2                   | 0                  |
| Bronchitis                                       |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 4 / 42 (9.52%)      | 2 / 9 (22.22%)     |
| occurrences (all)                                | 0                   | 4                   | 5                  |
| Covid-19   |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 4 / 42 (9.52%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 4                   | 0                  |
| Cellulitis                                       |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 0 / 42 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Conjunctivitis Bacterial                         |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 0 / 42 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Cystitis   |                     |                     |                    |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 0 / 42 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 4                   | 0                   | 0                  |
| Dengue Fever                                     |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 0 / 42 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Ear Infection                                    |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 1 / 42 (2.38%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Eczema Impetiginous                              |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 0 / 42 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Escherichia Urinary Tract Infection              |                     |                     |                    |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 0 / 42 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| Gastritis Viral                      |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Gastroenteritis                      |                |                |                |
| subjects affected / exposed          | 1 / 7 (14.29%) | 4 / 42 (9.52%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 1              | 5              | 0              |
| Gastrointestinal Bacterial Infection |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Infected Bite                        |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Impetigo                             |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Gastrointestinal Infection           |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 42 (2.38%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 1              | 0              |
| Groin Abscess                        |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Infectious Mononucleosis             |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Influenza                            |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Laryngitis                           |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Molluscum Contagiosum                |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Otitis Externa                       |                |                |                |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 42 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |

|                             |                |                  |                |
|-----------------------------|----------------|------------------|----------------|
| Oral Herpes                 |                |                  |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 42 (2.38%)   | 1 / 9 (11.11%) |
| occurrences (all)           | 1              | 4                | 2              |
| Oral Candidiasis            |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Nasopharyngitis             |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 11 / 42 (26.19%) | 3 / 9 (33.33%) |
| occurrences (all)           | 0              | 21               | 6              |
| Otitis Media                |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Pharyngitis Bacterial       |                |                  |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0              |
| Pharyngitis                 |                |                  |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 6 / 42 (14.29%)  | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 6                | 0              |
| Paronychia                  |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 42 (9.52%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 5                | 0              |
| Otitis Media Acute          |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 42 (4.76%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0              |
| Pharyngitis Streptococcal   |                |                  |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0              |
| Pharyngotonsillitis         |                |                  |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0              |
| Pneumonia                   |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Scarlet Fever               |                |                  |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 42 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Rhinitis                                    |                |                 |                |
| subjects affected / exposed                 | 2 / 7 (28.57%) | 4 / 42 (9.52%)  | 3 / 9 (33.33%) |
| occurrences (all)                           | 2              | 7               | 3              |
| Respiratory Syncytial Virus Infection       |                |                 |                |
| subjects affected / exposed                 | 1 / 7 (14.29%) | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 1              | 0               | 0              |
| Pyelonephritis Acute                        |                |                 |                |
| subjects affected / exposed                 | 0 / 7 (0.00%)  | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0              |
| Sinobronchitis                              |                |                 |                |
| subjects affected / exposed                 | 0 / 7 (0.00%)  | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0              |
| Tinea Pedis                                 |                |                 |                |
| subjects affected / exposed                 | 1 / 7 (14.29%) | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 1              | 0               | 0              |
| Sinusitis                                   |                |                 |                |
| subjects affected / exposed                 | 0 / 7 (0.00%)  | 2 / 42 (4.76%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 0              | 2               | 0              |
| Tonsillitis                                 |                |                 |                |
| subjects affected / exposed                 | 1 / 7 (14.29%) | 2 / 42 (4.76%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 1              | 2               | 0              |
| Varicella                                   |                |                 |                |
| subjects affected / exposed                 | 0 / 7 (0.00%)  | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0              |
| Urinary Tract Infection                     |                |                 |                |
| subjects affected / exposed                 | 1 / 7 (14.29%) | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 1              | 0               | 0              |
| Upper Respiratory Tract Infection Bacterial |                |                 |                |
| subjects affected / exposed                 | 0 / 7 (0.00%)  | 0 / 42 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0              |
| Upper Respiratory Tract Infection           |                |                 |                |
| subjects affected / exposed                 | 4 / 7 (57.14%) | 6 / 42 (14.29%) | 2 / 9 (22.22%) |
| occurrences (all)                           | 10             | 10              | 3              |
| Tracheitis                                  |                |                 |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 1 / 42 (2.38%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Viral Upper Respiratory Tract Infection          |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 1 / 7 (14.29%)<br>2 | 1 / 42 (2.38%)<br>1 | 1 / 9 (11.11%)<br>2 |
| Viral Pharyngitis                                |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Metabolism and nutrition disorders               |                     |                     |                     |
| Vitamin D Deficiency                             |                     |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 42 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |

| <b>Non-serious adverse events</b>                                      | Cohort 1: < 30 kg<br>and >= 10 kg | Cohort 2 (from<br>Baseline): < 30 kg<br>and >= 10 kg | Cohort 2(Post dose-<br>adjustment from<br>Dose 1): <30 kg<br>and >=10 kg |
|--|-----------------------------------|--|--|
| Total subjects affected by non-serious<br>adverse events               |                                   |  |  |
| subjects affected / exposed  | 6 / 6 (100.00%)                   | 29 / 31 (93.55%)                                     | 5 / 5 (100.00%)  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |                                   |  |  |
| Skin Papilloma   |                                   |  |  |
| subjects affected / exposed<br>occurrences (all)                       | 0 / 6 (0.00%)<br>0                | 0 / 31 (0.00%)<br>0                                  | 0 / 5 (0.00%)<br>0   |
| Vascular disorders   |                                   |  |  |
| Essential Hypertension   |                                   |  |  |
| subjects affected / exposed<br>occurrences (all)                       | 0 / 6 (0.00%)<br>0                | 0 / 31 (0.00%)<br>0                                  | 0 / 5 (0.00%)<br>0   |
| General disorders and administration<br>site conditions                |                                   |  |  |
| Administration Site Erythema   |                                   |  |  |
| subjects affected / exposed<br>occurrences (all)                       | 0 / 6 (0.00%)<br>0                | 0 / 31 (0.00%)<br>0                                  | 1 / 5 (20.00%)<br>1  |
| Fatigue  |                                   |  |  |
| subjects affected / exposed<br>occurrences (all)                       | 0 / 6 (0.00%)<br>0                | 2 / 31 (6.45%)<br>2                                  | 0 / 5 (0.00%)<br>0   |
| Gait Disturbance   |                                   |  |  |
| subjects affected / exposed<br>occurrences (all)                       | 0 / 6 (0.00%)<br>0                | 0 / 31 (0.00%)<br>0                                  | 0 / 5 (0.00%)<br>0   |
| Injection Site Haemorrhage   |                                   |  |  |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Injection Site Erythema                         |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 5 / 31 (16.13%) | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 7               | 0             |
| Injection Site Pruritus                         |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 31 (3.23%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 1               | 0             |
| Pyrexia   |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 31 (6.45%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 6               | 0             |
| Malaise   |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Injection Site Urticaria                        |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 31 (3.23%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 1               | 0             |
| Injection Site Reaction                         |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 3 / 31 (9.68%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 8               | 0             |
| Immune system disorders                         |                |                 |               |
| Allergy To Arthropod Bite                       |                |                 |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 1              | 0               | 0             |
| Respiratory, thoracic and mediastinal disorders |                |                 |               |
| Cough   |                |                 |               |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 5 / 31 (16.13%) | 0 / 5 (0.00%) |
| occurrences (all)                               | 2              | 9               | 0             |
| Epistaxis                                       |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 31 (6.45%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 2               | 0             |
| Increased Bronchial Secretion                   |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Rhinitis Allergic                               |                |                 |               |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 2 / 6 (33.33%)<br>2 | 1 / 31 (3.23%)<br>1 | 0 / 5 (0.00%)<br>0 |
| Psychiatric disorders                            |                     |                     |                    |
| Affective Disorder                               |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 31 (0.00%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Major Depression                                 |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 31 (0.00%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Investigations                                   |                     |                     |                    |
| Blood Pressure Systolic Decreased                |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 2 / 31 (6.45%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 2                   | 0                  |
| Blood Bilirubin Increased                        |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 31 (0.00%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Blood Alkaline Phosphatase Increased             |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 3 / 31 (9.68%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 3                   | 0                  |
| Aspartate Aminotransferase Increased             |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 0 / 31 (0.00%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Alanine Aminotransferase Increased               |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 2 / 31 (6.45%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 2                   | 0                  |
| Eosinophil Count Increased                       |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 6 / 31 (19.35%)     | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 9                   | 0                  |
| Lymphocyte Count Increased                       |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 3 / 31 (9.68%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 5                   | 0                  |
| Monocyte Count Decreased                         |                     |                     |                    |
| subjects affected / exposed                      | 0 / 6 (0.00%)       | 2 / 31 (6.45%)      | 0 / 5 (0.00%)      |
| occurrences (all)                                | 0                   | 2                   | 0                  |
| Mean Cell Volume Decreased                       |                     |                     |                    |



|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0              |
| Transaminases Increased                        |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Neutrophil Count Decreased                     |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 3 / 31 (9.68%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 6              | 0              |
| Monocyte Count Increased                       |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Accidental Overdose                            |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 3 / 31 (9.68%) | 1 / 5 (20.00%) |
| occurrences (all)                              | 0              | 6              | 1              |
| Arthropod Bite                                 |                |                |                |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 1              | 2              | 0              |
| Ligament Sprain                                |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Hand Fracture                                  |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Fall   |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 3 / 31 (9.68%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 3              | 0              |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Thermal Burn                                   |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Traumatic Haematoma                            |                |                |                |

|   |   |   |  |
|---|---|---|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0   | 0 / 5 (0.00%)<br>0   |
| Cardiac disorders<br>Cardiovascular Disorder<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0   | 0 / 5 (0.00%)<br>0   |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0<br><br>3 / 31 (9.68%)<br>4  | 0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0   |
| Blood and lymphatic system disorders<br>Neutropenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Lymphopenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)<br><br>Leukopenia<br>subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1<br><br>0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0 | 15 / 31 (48.39%)<br>78<br><br>0 / 31 (0.00%)<br>0<br><br>0 / 31 (0.00%)<br>0<br><br>3 / 31 (9.68%)<br>4 | 2 / 5 (40.00%)<br>2<br><br>0 / 5 (0.00%)<br>0<br><br>1 / 5 (20.00%)<br>1<br><br>0 / 5 (0.00%)<br>0 |
| Ear and labyrinth disorders<br>Ear Pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1   | 0 / 5 (0.00%)<br>0   |
| Eye disorders<br>Keratitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Uveitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>1   | 0 / 31 (0.00%)<br>0<br><br>0 / 31 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0<br><br>0 / 5 (0.00%)<br>0   |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| Gastrointestinal disorders             |                |                 |                |
| Abdominal Pain                         |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 31 (3.23%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Diarrhoea                              |                |                 |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 4 / 31 (12.90%) | 0 / 5 (0.00%)  |
| occurrences (all)                      | 2              | 6               | 0              |
| Dental Discomfort                      |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Constipation                           |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Aphthous Ulcer                         |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 2               | 0              |
| Abdominal Pain Upper                   |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 2               | 0              |
| Pulpless Tooth                         |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Nausea                                 |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 2               | 0              |
| Mouth Ulceration                       |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 31 (3.23%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Vomiting                               |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 3 / 31 (9.68%)  | 2 / 5 (40.00%) |
| occurrences (all)                      | 0              | 4               | 2              |
| Hepatobiliary disorders                |                |                 |                |
| Hyperbilirubinaemia                    |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Skin and subcutaneous tissue disorders |                |                 |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Pityriasis Alba                                 |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Alopecia  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Dermatitis Allergic                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 31 (3.23%) | 2 / 5 (40.00%) |
| occurrences (all)                               | 0              | 1              | 2              |
| Ingrowing Nail                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Acne  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Rash Pruritic                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Rash Papular                                    |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 31 (3.23%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Rash  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 8              | 0              |
| Skin Reaction                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Urticaria Chronic                               |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Urticaria                                       |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 2              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |

|   |                     |                      |                     |
|---|---------------------|----------------------|---------------------|
| Juvenile Idiopathic Arthritis<br>subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>2 | 0 / 31 (0.00%)<br>0  | 1 / 5 (20.00%)<br>2 |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 6 (33.33%)<br>2 | 3 / 31 (9.68%)<br>3  | 0 / 5 (0.00%)<br>0  |
| Pain In Extremity<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 3 / 31 (9.68%)<br>3  | 0 / 5 (0.00%)<br>0  |
| Infections and infestations   |                     |                      |                     |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 6 / 31 (19.35%)<br>8 | 0 / 5 (0.00%)<br>0  |
| Acute Sinusitis<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1  | 0 / 5 (0.00%)<br>0  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 6 (16.67%)<br>1 | 3 / 31 (9.68%)<br>5  | 0 / 5 (0.00%)<br>0  |
| Covid-19<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 6 (0.00%)<br>0  | 5 / 31 (16.13%)<br>5 | 0 / 5 (0.00%)<br>0  |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 6 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Conjunctivitis Bacterial<br>subjects affected / exposed<br>occurrences (all)      | 1 / 6 (16.67%)<br>1 | 0 / 31 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Cystitis<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 6 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Dengue Fever<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Ear Infection   |                     |                      |                     |

|                                      |               |                 |                |
|--------------------------------------|---------------|-----------------|----------------|
| subjects affected / exposed          | 0 / 6 (0.00%) | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 2               | 0              |
| Eczema Impetiginous                  |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 0               | 0              |
| Escherichia Urinary Tract Infection  |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 0               | 0              |
| Gastritis Viral                      |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 0               | 0              |
| Gastroenteritis                      |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 9 / 31 (29.03%) | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 11              | 0              |
| Gastrointestinal Bacterial Infection |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 0               | 0              |
| Infected Bite                        |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 0               | 0              |
| Impetigo                             |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 2               | 0              |
| Gastrointestinal Infection           |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 2               | 0              |
| Groin Abscess                        |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                    | 0             | 0               | 1              |
| Infectious Mononucleosis             |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 0 / 31 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 0               | 0              |
| Influenza                            |               |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%) | 2 / 31 (6.45%)  | 0 / 5 (0.00%)  |
| occurrences (all)                    | 0             | 2               | 0              |
| Laryngitis                           |               |                 |                |

|                             |                |                  |                |
|-----------------------------|----------------|------------------|----------------|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 31 (0.00%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0              |
| Molluscum Contagiosum       |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 31 (0.00%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Otitis Externa              |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 31 (0.00%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0              |
| Oral Herpes                 |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 31 (3.23%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0              |
| Oral Candidiasis            |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 31 (3.23%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0              |
| Nasopharyngitis             |                |                  |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 17 / 31 (54.84%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 1              | 38               | 0              |
| Otitis Media                |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 4 / 31 (12.90%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 5                | 0              |
| Pharyngitis Bacterial       |                |                  |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 31 (0.00%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0              |
| Pharyngitis                 |                |                  |                |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 31 (3.23%)   | 2 / 5 (40.00%) |
| occurrences (all)           | 3              | 1                | 4              |
| Paronychia                  |                |                  |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 31 (3.23%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 1              | 1                | 0              |
| Otitis Media Acute          |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 31 (9.68%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 7                | 0              |
| Pharyngitis Streptococcal   |                |                  |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 31 (3.23%)   | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0              |
| Pharyngotonsillitis         |                |                  |                |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed           | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 6              | 0              |
| Pneumonia                             |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 2              | 0              |
| Scarlet Fever                         |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Rhinitis                              |                |                |                |
| subjects affected / exposed           | 1 / 6 (16.67%) | 3 / 31 (9.68%) | 1 / 5 (20.00%) |
| occurrences (all)                     | 3              | 3              | 1              |
| Respiratory Syncytial Virus Infection |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Pyelonephritis Acute                  |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Sinobronchitis                        |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Tinea Pedis                           |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Sinusitis                             |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Tonsillitis                           |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 2 / 31 (6.45%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 0              | 2              | 0              |
| Varicella                             |                |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 3 / 31 (9.68%) | 1 / 5 (20.00%) |
| occurrences (all)                     | 0              | 3              | 1              |
| Urinary Tract Infection               |                |                |                |
| subjects affected / exposed           | 1 / 6 (16.67%) | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                     | 1              | 0              | 0              |
| Upper Respiratory Tract Infection     |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Bacterial                               |                |                |                |
| subjects affected / exposed             | 1 / 6 (16.67%) | 0 / 31 (0.00%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 1              | 0              | 0              |
| Upper Respiratory Tract Infection       |                |                |                |
| subjects affected / exposed             | 2 / 6 (33.33%) | 3 / 31 (9.68%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 2              | 6              | 0              |
| Tracheitis                              |                |                |                |
| subjects affected / exposed             | 1 / 6 (16.67%) | 0 / 31 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all)                       | 1              | 0              | 1              |
| Viral Upper Respiratory Tract Infection |                |                |                |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 3 / 31 (9.68%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 4              | 0              |
| Viral Pharyngitis                       |                |                |                |
| subjects affected / exposed             | 1 / 6 (16.67%) | 1 / 31 (3.23%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 1              | 1              | 0              |
| Metabolism and nutrition disorders      |                |                |                |
| Vitamin D Deficiency                    |                |                |                |
| subjects affected / exposed             | 0 / 6 (0.00%)  | 3 / 31 (9.68%) | 0 / 5 (0.00%)  |
| occurrences (all)                       | 0              | 3              | 0              |

| <b>Non-serious adverse events</b>                                   | Cohort 2(Post dose-adjustment from Dose 3): <30 kg and >=10 kg | Cohort 2(Post dose-adjustment from Dose 3):>=30 kg and <=60 kg | Cohort 2(Post dose-adjustment from Dose 1):>=30 kg and <=60 kg |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 5 / 5 (100.00%)  | 5 / 6 (83.33%)   | 4 / 4 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Skin Papilloma  |  |  |  |
| subjects affected / exposed   | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |
| Vascular disorders  |  |  |  |
| Essential Hypertension  |  |  |  |
| subjects affected / exposed   | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |
| General disorders and administration site conditions                |  |  |  |
| Administration Site Erythema  |  |  |  |
| subjects affected / exposed   | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Fatigue   |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Gait Disturbance                                |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Injection Site Haemorrhage                      |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Injection Site Erythema                         |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Injection Site Pruritus                         |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Pyrexia   |                |                |               |
| subjects affected / exposed                     | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0             |
| Malaise   |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Injection Site Urticaria                        |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Injection Site Reaction                         |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Immune system disorders                         |                |                |               |
| Allergy To Arthropod Bite                       |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Respiratory, thoracic and mediastinal disorders |                |                |               |
| Cough   |                |                |               |
| subjects affected / exposed                     | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Epistaxis                                       |                |                |               |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Increased Bronchial Secretion<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 |
| Rhinitis Allergic<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Psychiatric disorders<br>Affective Disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Major Depression<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Investigations<br>Blood Pressure Systolic Decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Blood Bilirubin Increased<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Blood Alkaline Phosphatase Increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Aspartate Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 5 (20.00%)<br>1 | 1 / 6 (16.67%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Eosinophil Count Increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Lymphocyte Count Increased  |                     |                     |                     |

|  |               |                |                |
|--|---------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Monocyte Count Decreased                       |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Mean Cell Volume Decreased                     |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Transaminases Increased                        |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Neutrophil Count Decreased                     |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Monocyte Count Increased                       |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Injury, poisoning and procedural complications |               |                |                |
| Accidental Overdose                            |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 1              | 0              |
| Arthropod Bite                                 |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 1              | 0              |
| Ligament Sprain                                |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 2 / 4 (50.00%) |
| occurrences (all)                              | 0             | 0              | 2              |
| Hand Fracture                                  |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Fall   |               |                |                |
| subjects affected / exposed                    | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0             | 0              | 0              |
| Contusion                                      |               |                |                |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Thermal Burn                         |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Traumatic Haematoma                  |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Cardiac disorders                    |                |                |                |
| Cardiovascular Disorder              |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Nervous system disorders             |                |                |                |
| Dizziness                            |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Headache                             |                |                |                |
| subjects affected / exposed          | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |
| Blood and lymphatic system disorders |                |                |                |
| Neutropenia                          |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0              | 0              | 1              |
| Lymphopenia                          |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Lymphadenopathy                      |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Leukopenia                           |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 2              | 0              |
| Ear and labyrinth disorders          |                |                |                |
| Ear Pain                             |                |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Eye disorders                        |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Keratitis                   |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Uveitis                     |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Gastrointestinal disorders  |                |                |                |
| Abdominal Pain              |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Diarrhoea                   |                |                |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Dental Discomfort           |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Constipation                |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Aphthous Ulcer              |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Abdominal Pain Upper        |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pulpless Tooth              |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Nausea                      |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Mouth Ulceration            |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Vomiting                    |                |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 2 / 5 (40.00%)<br>2 | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Hepatobiliary disorders<br>Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Pityriasis Alba<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Dermatitis Allergic<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Ingrowing Nail<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Acne<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Rash Pruritic<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 |
| Rash Papular<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Skin Reaction<br>subjects affected / exposed<br>occurrences (all)   | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Urticaria Chronic   |                     |                     |                     |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Juvenile Idiopathic Arthritis<br>subjects affected / exposed<br>occurrences (all) | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Pain In Extremity<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Infections and infestations<br>Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Acute Sinusitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Covid-19<br>subjects affected / exposed<br>occurrences (all)   | 1 / 5 (20.00%)<br>1 | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 | 0 / 4 (0.00%)<br>0 |
| Conjunctivitis Bacterial<br>subjects affected / exposed<br>occurrences (all)   | 0 / 5 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Cystitis   |                     |                     |                    |



|                                      |               |                |                |
|--------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Dengue Fever                         |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 1              | 0              |
| Ear Infection                        |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Eczema Impetiginous                  |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Escherichia Urinary Tract Infection  |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 2              |
| Gastritis Viral                      |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Gastroenteritis                      |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Gastrointestinal Bacterial Infection |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 1              | 0              |
| Infected Bite                        |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                    | 0             | 0              | 1              |
| Impetigo                             |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Gastrointestinal Infection           |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Groin Abscess                        |               |                |                |
| subjects affected / exposed          | 0 / 5 (0.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                    | 0             | 0              | 0              |
| Infectious Mononucleosis             |               |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Influenza                   |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Laryngitis                  |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Molluscum Contagiosum       |                |                |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Otitis Externa              |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 1              | 1              |
| Oral Herpes                 |                |                |                |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 11             | 1              | 0              |
| Oral Candidiasis            |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Nasopharyngitis             |                |                |                |
| subjects affected / exposed | 3 / 5 (60.00%) | 4 / 6 (66.67%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 5              | 6              | 0              |
| Otitis Media                |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pharyngitis Bacterial       |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pharyngitis                 |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Paronychia                  |                |                |                |
| subjects affected / exposed | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Otitis Media Acute          |                |                |                |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed           | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 1              | 0              |
| Pharyngitis Streptococcal             |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Pharyngotonsillitis                   |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Pneumonia                             |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Scarlet Fever                         |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Rhinitis                              |                |                |                |
| subjects affected / exposed           | 2 / 5 (40.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 5              | 0              | 0              |
| Respiratory Syncytial Virus Infection |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Pyelonephritis Acute                  |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 1 / 6 (16.67%) | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 1              | 0              |
| Sinobronchitis                        |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Tinea Pedis                           |                |                |                |
| subjects affected / exposed           | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Sinusitis                             |                |                |                |
| subjects affected / exposed           | 1 / 5 (20.00%) | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 1              | 0              | 0              |
| Tonsillitis                           |                |                |                |
| subjects affected / exposed           | 1 / 5 (20.00%) | 1 / 6 (16.67%) | 1 / 4 (25.00%) |
| occurrences (all)                     | 1              | 1              | 1              |
| Varicella                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Urinary Tract Infection                     |                |                |                |
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Upper Respiratory Tract Infection Bacterial |                |                |                |
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Upper Respiratory Tract Infection           |                |                |                |
| subjects affected / exposed                 | 1 / 5 (20.00%) | 1 / 6 (16.67%) | 3 / 4 (75.00%) |
| occurrences (all)                           | 1              | 2              | 5              |
| Tracheitis                                  |                |                |                |
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Viral Upper Respiratory Tract Infection     |                |                |                |
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Viral Pharyngitis                           |                |                |                |
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |
| Metabolism and nutrition disorders          |                |                |                |
| Vitamin D Deficiency                        |                |                |                |
| subjects affected / exposed                 | 0 / 5 (0.00%)  | 0 / 6 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              | 0              |

|   |                                    |  |  |
|---|------------------------------------|--|--|
| <b>Non-serious adverse events</b>                                   | Cohort 3: >= 30 kg<br>and <= 60 kg |  |  |
| Total subjects affected by non-serious adverse events               |                                    |  |  |
| subjects affected / exposed   | 5 / 6 (83.33%)                     |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                    |  |  |
| Skin Papilloma  |                                    |  |  |
| subjects affected / exposed   | 1 / 6 (16.67%)                     |  |  |
| occurrences (all)   | 1                                  |  |  |
| Vascular disorders  |                                    |  |  |
| Essential Hypertension  |                                    |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                                    | 0              |  |  |
| General disorders and administration site conditions |                |  |  |
| Administration Site Erythema                         |                |  |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                                    | 0              |  |  |
| Fatigue  |                |  |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                                    | 0              |  |  |
| Gait Disturbance                                     |                |  |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                                    | 0              |  |  |
| Injection Site Haemorrhage                           |                |  |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Injection Site Erythema                              |                |  |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                                    | 0              |  |  |
| Injection Site Pruritus                              |                |  |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                                    | 0              |  |  |
| Pyrexia  |                |  |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Malaise  |                |  |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Injection Site Urticaria                             |                |  |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Injection Site Reaction                              |                |  |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                                    | 1              |  |  |
| Immune system disorders                              |                |  |  |

|   |  |  |  |
|---|--|--|--|
| Allergy To Arthropod Bite<br>subjects affected / exposed<br>occurrences (all)   | 1 / 6 (16.67%)<br>1  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)<br><br>Increased Bronchial Secretion<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinitis Allergic<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0 |  |  |
| Psychiatric disorders<br>Affective Disorder<br>subjects affected / exposed<br>occurrences (all)<br><br>Major Depression<br>subjects affected / exposed<br>occurrences (all)   | 1 / 6 (16.67%)<br>1<br><br>1 / 6 (16.67%)<br>1   |  |  |
| Investigations<br>Blood Pressure Systolic Decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood Bilirubin Increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Blood Alkaline Phosphatase Increased<br>subjects affected / exposed<br>occurrences (all)<br><br>Aspartate Aminotransferase Increased                | 0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>1<br><br>0 / 6 (0.00%)<br>0                          |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                    | 1 / 6 (16.67%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Alanine Aminotransferase Increased             |                |  |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) |  |  |
| occurrences (all)                              | 1              |  |  |
| Eosinophil Count Increased                     |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Lymphocyte Count Increased                     |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Monocyte Count Decreased                       |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Mean Cell Volume Decreased                     |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Transaminases Increased                        |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Neutrophil Count Decreased                     |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Monocyte Count Increased                       |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Injury, poisoning and procedural complications |                |  |  |
| Accidental Overdose                            |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Arthropod Bite                                 |                |  |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) |  |  |
| occurrences (all)                              | 2              |  |  |
| Ligament Sprain                                |                |  |  |

|                                      |                |  |  |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Hand Fracture                        |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Fall                                 |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Contusion                            |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Thermal Burn                         |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Traumatic Haematoma                  |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Cardiac disorders                    |                |  |  |
| Cardiovascular Disorder              |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Nervous system disorders             |                |  |  |
| Dizziness                            |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Headache                             |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Blood and lymphatic system disorders |                |  |  |
| Neutropenia                          |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 2              |  |  |
| Lymphopenia                          |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Lymphadenopathy                      |                |  |  |



|  |   |  |  |
|--|---|--|--|
| subjects affected / exposed<br>occurrences (all)<br><br>Leukopenia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>1   |  |  |
| Ear and labyrinth disorders<br>Ear Pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  |  |  |
| Eye disorders<br>Keratitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Uveitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0  |  |  |
| Gastrointestinal disorders<br>Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Dental Discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Aphthous Ulcer<br>subjects affected / exposed<br>occurrences (all)<br><br>Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)<br><br>Pulpless Tooth | 1 / 6 (16.67%)<br>1<br><br>1 / 6 (16.67%)<br>1<br><br>0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>1<br><br>0 / 6 (0.00%)<br>0 |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed            | 1 / 6 (16.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Nausea                                 |                |  |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Mouth Ulceration                       |                |  |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Vomiting                               |                |  |  |
| subjects affected / exposed            | 1 / 6 (16.67%) |  |  |
| occurrences (all)                      | 3              |  |  |
| Hepatobiliary disorders                |                |  |  |
| Hyperbilirubinaemia                    |                |  |  |
| subjects affected / exposed            | 1 / 6 (16.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |
| Pityriasis Alba                        |                |  |  |
| subjects affected / exposed            | 1 / 6 (16.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Alopecia                               |                |  |  |
| subjects affected / exposed            | 1 / 6 (16.67%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Dermatitis Allergic                    |                |  |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Ingrowing Nail                         |                |  |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Acne                                   |                |  |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Rash Pruritic                          |                |  |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                      | 0              |  |  |
| Rash Papular                           |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 6 (16.67%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Rash  |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Skin Reaction                                   |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Urticaria Chronic                               |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Urticaria                                       |                |  |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Juvenile Idiopathic Arthritis                   |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Arthralgia                                      |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Pain In Extremity                               |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Infections and infestations                     |                |  |  |
| Conjunctivitis                                  |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Acute Sinusitis                                 |                |  |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) |  |  |
| occurrences (all)                               | 1              |  |  |
| Bronchitis                                      |                |  |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                               | 0              |  |  |
| Covid-19  |                |  |  |

|                                      |                |  |  |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Cellulitis                           |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Conjunctivitis Bacterial             |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Cystitis                             |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Dengue Fever                         |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Ear Infection                        |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Eczema Impetiginous                  |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Escherichia Urinary Tract Infection  |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Gastritis Viral                      |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Gastroenteritis                      |                |  |  |
| subjects affected / exposed          | 1 / 6 (16.67%) |  |  |
| occurrences (all)                    | 2              |  |  |
| Gastrointestinal Bacterial Infection |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Infected Bite                        |                |  |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                    | 0              |  |  |
| Impetigo                             |                |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Gastrointestinal Infection  |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Groin Abscess               |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Infectious Mononucleosis    |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Influenza                   |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Laryngitis                  |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Molluscum Contagiosum       |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Otitis Externa              |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Oral Herpes                 |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Oral Candidiasis            |                |  |  |
| subjects affected / exposed | 1 / 6 (16.67%) |  |  |
| occurrences (all)           | 1              |  |  |
| Nasopharyngitis             |                |  |  |
| subjects affected / exposed | 3 / 6 (50.00%) |  |  |
| occurrences (all)           | 5              |  |  |
| Otitis Media                |                |  |  |
| subjects affected / exposed | 0 / 6 (0.00%)  |  |  |
| occurrences (all)           | 0              |  |  |
| Pharyngitis Bacterial       |                |  |  |

|                                       |                |  |  |
|---------------------------------------|----------------|--|--|
| subjects affected / exposed           | 1 / 6 (16.67%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Pharyngitis                           |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Paronychia                            |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Otitis Media Acute                    |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Pharyngitis Streptococcal             |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Pharyngotonsillitis                   |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Pneumonia                             |                |  |  |
| subjects affected / exposed           | 2 / 6 (33.33%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Scarlet Fever                         |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Rhinitis                              |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Respiratory Syncytial Virus Infection |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Pyelonephritis Acute                  |                |  |  |
| subjects affected / exposed           | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                     | 0              |  |  |
| Sinobronchitis                        |                |  |  |
| subjects affected / exposed           | 1 / 6 (16.67%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Tinea Pedis                           |                |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Sinusitis                                      |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Tonsillitis                                    |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Varicella                                      |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Urinary Tract Infection                        |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Upper Respiratory Tract Infection<br>Bacterial |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Upper Respiratory Tract Infection              |                |  |  |
| subjects affected / exposed                    | 2 / 6 (33.33%) |  |  |
| occurrences (all)                              | 2              |  |  |
| Tracheitis                                     |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Viral Upper Respiratory Tract<br>Infection     |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Viral Pharyngitis                              |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |
| Metabolism and nutrition disorders             |                |  |  |
| Vitamin D Deficiency                           |                |  |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  |  |  |
| occurrences (all)                              | 0              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 06 April 2018     | <ul style="list-style-type: none"><li>• To modify the study design to implement the amended Pediatric Investigations Plan approved by the European Medicines Agency.</li><li>• To split the 12-week core treatment phase of the study into 2 portions: a dose-finding portion corresponding to the 12-week core treatment phase of the initial protocol where 3 ascending dose regimens will be tested in 36 participants; and a second portion where additional participants will receive the dose regimen selected from data of the first portion of the study in order to provide sufficient precision for PK parameters and PK-PD relationship assessments at that selected dose regimen.</li><li>• To prolong the extension phase of the study from 92 weeks to 144 weeks for a total study duration of 166 weeks (per participant).</li><li>• To increase the number of enrolled participants from 36 to 60 evaluable participants by 24 additional participants enrolled in the second portion of the study.</li><li>• To revise the secondary efficacy endpoints.</li><li>• To update the exclusion criteria section to better define the study population.</li><li>• To incorporate several local protocol amendments that have already been approved, which address local health authorities and/or IRB requests related to the initial protocol.</li></ul> |
| 13 December 2018  | To update the stopping rules for Grade 4 neutropenia: The stopping rules for Grade 4 neutropenia was updated during the study after analysis of the 12-week core phase of the Portion 1 in order to provide the best chance for participants to benefit from treatment while continuously monitoring for safety events. Prior to the amendment, sarilumab had to be discontinued in case of Grade 4 neutropenia (absolute neutrophil count <0.5 Giga/liter) whether or not associated with signs of infection. Per the amendment, any Grade 4 neutropenia without infection led to temporary hold of treatment and the decision to resume sarilumab could be considered by the Investigator when absolute neutrophil count returned to >1.0 Giga/liter and based upon medical benefit-to-risk assessment. The rule stayed unchanged for any Grade 3 and 4 neutropenia associated with signs of infection (discontinuation) and Grade 3 neutropenia without infection (absolute neutrophil count ≥0.5 Giga/liter and <1.0 Giga/liter) (temporary hold).  |
| 12 September 2019 | To increase the planned total number of enrolled participants (28 additional participants) to achieve a total of approximately 100 treated participants (based on health authority recommendations).  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported