



## Clinical trial results:

### A Phase 3, Multicenter, Randomized, Double-blind, Active Comparator-controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Adults 50 Years of Age or Older (PNEU-AGE)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-004316-22 |
| Trial protocol           | ES             |
| Global end of trial date | 02 July 2020   |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 10 March 2021 |
| First version publication date | 10 March 2021 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | V114-019 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |  |
|------------------------------------|--|
| ISRCTN number                      | -  |
| ClinicalTrials.gov id (NCT number) | NCT03950622                                |
| WHO universal trial number (UTN)   | -  |
| Other trial identifiers            | JAPIC-CTI: 194845, Study Acronym: PNEU-AGE |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Merck Sharp & Dohme Corp.  |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, United States, 07033                                   |
| Public contact               | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |
| Scientific contact           | Clinical Trials Disclosure, Merck Sharp & Dohme Corp.,<br>ClinicalTrialsDisclosure@merck.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 30 March 2020 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 30 March 2020 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 02 July 2020  |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is 1) to evaluate the safety and tolerability of V114 and 2) to compare the immune responses of the 15 serotypes contained in V114 with V114 versus Prevnar 13™. The primary hypotheses are that 1) V114 is noninferior to Prevnar 13™ as measured by the serotype specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) for 13 shared serotypes at 30 days postvaccination and that 2) V114 is superior to Prevnar 13™ as measured by serotype-specific OPA GMTs for 2 unique serotypes in V114 at 30 days postvaccination.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 13 June 2019 |
| 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 | Canada: 188        |
| Country: Number of subjects enrolled | Japan: 245         |
| Country: Number of subjects enrolled | Spain: 100         |
| Country: Number of subjects enrolled | Taiwan: 40         |
| Country: Number of subjects enrolled | United States: 632 |
| Worldwide total number of subjects   | 1205               |
| EEA total number of subjects         | 100                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23 months)  | 0 |

|                           |     |
|---------------------------|-----|
| Children (2-11 years)     | 0   |
| Adolescents (12-17 years) | 0   |
| Adults (18-64 years)      | 374 |
| From 65 to 84 years       | 826 |
| 85 years and over         | 5   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 1200 participants were planned to be enrolled/randomized.

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |      |
|------------------|------|
| <b>Arm title</b> | V114 |
|------------------|------|

Arm description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1.

|  |                   |
|--|-------------------|
| Arm type                               | Experimental      |
| Investigational medicinal product name | V114              |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

15-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F in each 0.5 mL dose.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | Pprevnar 13™ |
|------------------|--------------|

Arm description:

Participants received a single 0.5 mL IM injection of Pprevnar 13™ on Day 1.

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Pprevnar 13™      |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intramuscular use |

Dosage and administration details:

13-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F in each 0.5 mL dose.

| <b>Number of subjects in period 1</b> | V114 | Prevnar 13™ |
|---------------------------------------|------|-------------|
| Started                               | 604  | 601         |
| Vaccinated                            | 602  | 600         |
| Completed                             | 596  | 594         |
| Not completed                         | 8    | 7           |
| Adverse event, serious fatal          | 1    | 1           |
| Physician decision                    | 1    | -           |
| Consent withdrawn by subject          | 1    | -           |
| Protocol Deviation                    | -    | 1           |
| Lost to follow-up                     | 5    | 5           |

## Baseline characteristics

### Reporting groups

|  |             |
|--|-------------|
| Reporting group title  | V114        |
| Reporting group description:   |             |
| Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1. |             |
| Reporting group title  | Prevnar 13™ |
| Reporting group description:   |             |
| Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1.          |             |

| Reporting group values                             | V114  | Prevnar 13™ | Total |
|--|-------|-------------|-------|
| Number of subjects                                 | 604   | 601         | 1205  |
| Age categorical                                    |       |             |       |
| Units: Participants                                |       |             |       |
| In utero   | 0     | 0           | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0     | 0           | 0     |
| Newborns (0-27 days)                               | 0     | 0           | 0     |
| Infants and toddlers (28 days-23 months)           | 0     | 0           | 0     |
| Children (2-11 years)                              | 0     | 0           | 0     |
| Adolescents (12-17 years)                          | 0     | 0           | 0     |
| Adults (18-64 years)                               | 187   | 187         | 374   |
| From 65-84 years                                   | 412   | 414         | 826   |
| 85 years and over                                  | 5     | 0           | 5     |
| Age Continuous                                     |       |             |       |
| Units: years                                       |       |             |       |
| arithmetic mean                                    | 66.2  | 65.7        |       |
| standard deviation                                 | ± 7.7 | ± 7.4       | -     |
| Sex: Female, Male                                  |       |             |       |
| Units: Participants                                |       |             |       |
| Female   | 359   | 332         | 691   |
| Male   | 245   | 269         | 514   |
| Race (NIH/OMB)                                     |       |             |       |
| Units: Subjects                                    |       |             |       |
| American Indian or Alaska Native                   | 0     | 1           | 1     |
| Asian  | 150   | 152         | 302   |
| Native Hawaiian or Other Pacific Islander          | 1     | 0           | 1     |
| Black or African American                          | 36    | 37          | 73    |
| White  | 410   | 407         | 817   |
| More than one race                                 | 7     | 4           | 11    |
| Unknown or Not Reported                            | 0     | 0           | 0     |
| Ethnicity (NIH/OMB)                                |       |             |       |
| Units: Subjects                                    |       |             |       |
| Hispanic or Latino                                 | 135   | 129         | 264   |
| Not Hispanic or Latino                             | 469   | 471         | 940   |
| Unknown or Not Reported                            | 0     | 1           | 1     |

## End points

### End points reporting groups

|  |             |
|--|-------------|
| Reporting group title  | V114        |
| Reporting group description:   |             |
| Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1. |             |
| Reporting group title  | Prevnam 13™ |
| Reporting group description:   |             |
| Participants received a single 0.5 mL IM injection of Prevnam 13™ on Day 1.          |             |

### Primary: Percentage of Participants with a Solicited Injection-site Adverse Event

|   |  |
|---|--|
| End point title   | Percentage of Participants with a Solicited Injection-site Adverse Event |
| End point description:  |  |
| An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited injection-site AEs consist of redness/erythema, swelling, and tenderness/pain. The analysis population included all randomized participants who received study vaccination and were included in the intervention group according to the intervention they received. |  |
| End point type  | Primary  |
| End point timeframe:  |  |
| Up to Day 5 postvaccination   |  |

| End point values                  | V114            | Prevnam 13™     |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 602             | 600             |  |  |
| Units: Percentage of Participants |                 |                 |  |  |
| number (not applicable)           |                 |                 |  |  |
| Injection site erythema           | 9.0             | 11.3            |  |  |
| Injection site pain               | 54.0            | 42.3            |  |  |
| Injection site swelling           | 12.5            | 11.2            |  |  |

### Statistical analyses

|   |                                 |
|---|---------------------------------|
| Statistical analysis title              | Injection site redness/erythema |
| Comparison groups                       | V114 v Prevnam 13™              |
| Number of subjects included in analysis | 1202                            |
| Analysis specification                  | Pre-specified                   |
| Analysis type                           |                                 |
| P-value                                 | = 0.175                         |
| Method                                  | Miettinen & Nurminen            |
| Parameter estimate                      | Difference in Percent           |
| Point estimate                          | -2.4                            |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -5.8    |
| upper limit         | 1.1     |

|   |                                |
|---|--------------------------------|
| <b>Statistical analysis title</b>       | Injection site tenderness/pain |
| Comparison groups                       | V114 v Prevnar 13™             |
| Number of subjects included in analysis | 1202                           |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           |                                |
| P-value                                 | < 0.001                        |
| Method                                  | Miettinen & Nurminen           |
| Parameter estimate                      | Difference in Percent          |
| Point estimate                          | 11.7                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 6                              |
| upper limit                             | 17.2                           |

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>       | Injection site swelling |
| Comparison groups                       | V114 v Prevnar 13™      |
| Number of subjects included in analysis | 1202                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.488                 |
| Method                                  | Miettinen & Nurminen    |
| Parameter estimate                      | Difference in Percent   |
| Point estimate                          | 1.3                     |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | -2.4                    |
| upper limit                             | 5                       |

### Primary: Percentage of Participants with Solicited Systemic Adverse Events

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with Solicited Systemic Adverse Events |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following vaccination with V114 or Prevnar 13™, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were muscle pain/myalgia, joint pain/arthritis, headache, and tiredness/fatigue. The analysis population included all randomized participants who



received study vaccination and were included in the intervention group according to the intervention they received.

|                              |         |
|------------------------------|---------|
| End point type               | Primary |
| End point timeframe:         |         |
| Up to Day 14 postvaccination |         |

| End point values                  | V114            | Pprevnar 13™    |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 602             | 600             |  |  |
| Units: Percentage of Participants |                 |                 |  |  |
| number (not applicable)           |                 |                 |  |  |
| Joint pain/arthritis              | 5.3             | 5.5             |  |  |
| Tiredness/fatigue                 | 17.4            | 17.3            |  |  |
| Headache                          | 11.6            | 13.0            |  |  |
| Muscle pain/myalgia               | 15.4            | 12.0            |  |  |

## Statistical analyses

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Joint pain/arthritis  |
| Comparison groups                       | V114 v Pprevnar 13™   |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | = 0.888               |
| Method                                  | Miettinen & Nurminen  |
| Parameter estimate                      | Difference in Percent |
| Point estimate                          | -0.2                  |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | -2.8                  |
| upper limit                             | 2.4                   |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Tiredness/fatigue     |
| Comparison groups                       | V114 v Pprevnar 13™   |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | = 0.96                |
| Method                                  | Miettinen & Nurminen  |
| Parameter estimate                      | Difference in Percent |
| Point estimate                          | 0.1                   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -4.2    |
| upper limit         | 4.4     |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Headache              |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | = 0.469               |
| Method                                  | Miettinen & Nurminen  |
| Parameter estimate                      | Difference in Percent |
| Point estimate                          | -1.4                  |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | -5.1                  |
| upper limit                             | 2.4                   |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Muscle pain/myalgia   |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | = 0.082               |
| Method                                  | Miettinen & Nurminen  |
| Parameter estimate                      | Difference in Percent |
| Point estimate                          | 3.4                   |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | -0.4                  |
| upper limit                             | 7.4                   |

### **Primary: Percentage of Participants with a Vaccine-related Serious Adverse Event**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with a Vaccine-related Serious Adverse Event |
|-----------------|---|

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that, at any dose, results in death, is life threatening, requires inpatient hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is another important medical event. SAEs that are reported to be at least possibly related by the investigator to study vaccination will be summarized. The analysis population included all randomized participants who

received study vaccination and were included in the intervention group according to the intervention they received.

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Up to Month 6        |         |

| End point values                  | V114            | Prevnar 13™     |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 602             | 600             |  |  |
| Units: Percentage of Participants |                 |                 |  |  |
| number (not applicable)           | 0.0             | 0.0             |  |  |

## Statistical analyses

|   |                       |
|---|-----------------------|
| Statistical analysis title              | Vaccine-related SAEs  |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| Method                                  | Miettinen & Nurminen  |
| Parameter estimate                      | Difference in Percent |
| Point estimate                          | 0                     |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | -0.6                  |
| upper limit                             | 0.6                   |

## Primary: Geometric Mean Titer of Serotype-specific Opsonophagocytic Activity at Day 30

|                        |   |
|------------------------|---|
| End point title        | Geometric Mean Titer of Serotype-specific Opsonophagocytic Activity at Day 30   |
| End point description: | Serotype-specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) (estimated) and GMT ratios with 95% CIs were calculated using a constrained longitudinal data analysis (cLDA) model utilizing data from both vaccination groups. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the GMT ratios); within-group CIs were not calculated. OPA for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) were determined using a multiplexed opsonophagocytic assay (MOPA). The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination. |
| End point type         | Primary   |
| End point timeframe:   |   |
| Day 30                 |   |

| <b>End point values</b>                    | V114            | Prevnar 13™     |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                         | Reporting group | Reporting group |  |  |
| Number of subjects analysed                | 602             | 600             |  |  |
| Units: Titers                              |                 |                 |  |  |
| number (not applicable)                    |                 |                 |  |  |
| Serotype 1 (Shared) (n=598, 598)           | 256.3           | 322.6           |  |  |
| Serotype 3 (Shared) (n=598, 598)           | 216.2           | 135.1           |  |  |
| Serotype 4 (Shared) (n=598, 598)           | 1125.6          | 1661.6          |  |  |
| Serotype 5 (Shared) (n=598, 598)           | 447.3           | 563.5           |  |  |
| Serotype 6A (Shared) (n=596, 598)          | 5407.2          | 5424.5          |  |  |
| Serotype 6B (Shared) (n=598, 598)          | 4011.7          | 3258.2          |  |  |
| Serotype 7F (Shared) (n=597, 598)          | 4617.3          | 5880.6          |  |  |
| Serotype 9V (Shared) (n=598, 597)          | 1817.3          | 2232.9          |  |  |
| Serotype 14 (Shared) (n=598, 598)          | 1999.3          | 2656.7          |  |  |
| Serotype 18C (Shared) (n=598, 598)         | 2757.7          | 2583.7          |  |  |
| Serotype 19A (Shared) (n=598, 598)         | 3194.3          | 3979.8          |  |  |
| Serotype 19F (Shared) (n=598, 598)         | 1695.1          | 1917.8          |  |  |
| Serotype 23F (Shared) (n=598, 598)         | 2045.4          | 1740.4          |  |  |
| Serotype 22F (Unique to V114) (n=598, 598) | 2375.2          | 74.6            |  |  |
| Serotype 33F (Unique to V114) (n=598, 598) | 7994.7          | 1124.9          |  |  |

## Statistical analyses

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 1 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| P-value                                 | < 0.001             |
| Method                                  | cLDA                |
| Parameter estimate                      | GMT Ratio           |
| Point estimate                          | 0.79                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 0.66                |
| upper limit                             | 0.96                |

|                                   |                     |
|-----------------------------------|---------------------|
| <b>Statistical analysis title</b> | Serotype 3 (Shared) |
| Comparison groups                 | V114 v Prevnar 13™  |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 1202          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| P-value                                 | < 0.001       |
| Method                                  | cLDA          |
| Parameter estimate                      | GMT Ratio     |
| Point estimate                          | 1.6           |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | 1.38          |
| upper limit                             | 1.85          |

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 4 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| P-value                                 | < 0.001             |
| Method                                  | cLDA                |
| Parameter estimate                      | GMT Ratio           |
| Point estimate                          | 0.68                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 0.57                |
| upper limit                             | 0.8                 |

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 5 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| P-value                                 | < 0.001             |
| Method                                  | cLDA                |
| Parameter estimate                      | GMT Ratio           |
| Point estimate                          | 0.79                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 0.64                |
| upper limit                             | 0.98                |

|                                   |                      |
|-----------------------------------|----------------------|
| <b>Statistical analysis title</b> | Serotype 6A (Shared) |
|-----------------------------------|----------------------|

|   |                    |
|---|--------------------|
| Comparison groups                       | V114 v Prevnar 13™ |
| Number of subjects included in analysis | 1202               |
| Analysis specification                  | Pre-specified      |
| Analysis type                           |                    |
| P-value                                 | < 0.001            |
| Method                                  | cLDA               |
| Parameter estimate                      | GMT Ratio          |
| Point estimate                          | 1                  |
| Confidence interval                     |                    |
| level                                   | 95 %               |
| sides                                   | 2-sided            |
| lower limit                             | 0.84               |
| upper limit                             | 1.19               |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 6B (Shared) |
| Comparison groups                       | V114 v Prevnar 13™   |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| P-value                                 | < 0.001              |
| Method                                  | cLDA                 |
| Parameter estimate                      | GMT Ratio            |
| Point estimate                          | 1.23                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 1.02                 |
| upper limit                             | 1.48                 |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 7F (Shared) |
| Comparison groups                       | V114 v Prevnar 13™   |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| P-value                                 | < 0.001              |
| Method                                  | cLDA                 |
| Parameter estimate                      | GMT Ratio            |
| Point estimate                          | 0.79                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.68                 |
| upper limit                             | 0.9                  |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 9V (Shared) |
| Comparison groups                       | V114 v Pevnar 13™    |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| P-value                                 | < 0.001              |
| Method                                  | cLDA                 |
| Parameter estimate                      | GMT Ratio            |
| Point estimate                          | 0.81                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.7                  |
| upper limit                             | 0.94                 |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 14 (Shared) |
| Comparison groups                       | V114 v Pevnar 13™    |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| P-value                                 | < 0.001              |
| Method                                  | cLDA                 |
| Parameter estimate                      | GMT Ratio            |
| Point estimate                          | 0.75                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.64                 |
| upper limit                             | 0.89                 |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 18C (Shared) |
| Comparison groups                       | V114 v Pevnar 13™     |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | < 0.001               |
| Method                                  | cLDA                  |
| Parameter estimate                      | GMT Ratio             |
| Point estimate                          | 1.07                  |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.91                  |
| upper limit                             | 1.26                  |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 19A (Shared) |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | < 0.001               |
| Method                                  | cLDA                  |
| Parameter estimate                      | GMT Ratio             |
| Point estimate                          | 0.8                   |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.7                   |
| upper limit                             | 0.93                  |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 19F (Shared) |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | < 0.001               |
| Method                                  | cLDA                  |
| Parameter estimate                      | GMT Ratio             |
| Point estimate                          | 0.88                  |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.76                  |
| upper limit                             | 1.02                  |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 23F (Shared) |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| P-value                                 | < 0.001               |
| Method                                  | cLDA                  |
| Parameter estimate                      | GMT Ratio             |
| Point estimate                          | 1.18                  |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.96    |
| upper limit         | 1.44    |

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Serotype 22F (Unique to V114) |
| Comparison groups                       | V114 v Prevnar 13™            |
| Number of subjects included in analysis | 1202                          |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| P-value                                 | < 0.001                       |
| Method                                  | cLDA                          |
| Parameter estimate                      | GMT Ratio                     |
| Point estimate                          | 31.83                         |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 25.35                         |
| upper limit                             | 39.97                         |

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Serotype 33F (Unique to V114) |
| Comparison groups                       | V114 v Prevnar 13™            |
| Number of subjects included in analysis | 1202                          |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| P-value                                 | < 0.001                       |
| Method                                  | cLDA                          |
| Parameter estimate                      | GMT Ratio                     |
| Point estimate                          | 7.11                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 6.07                          |
| upper limit                             | 8.32                          |

### **Primary: Percentage of Participants with ≥4-Fold Rise in Serotype-specific OPA for 2 Unique V114 Serotypes**

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with ≥4-Fold Rise in Serotype-specific OPA for 2 Unique V114 Serotypes |
|-----------------|---|

#### **End point description:**

Activity for the serotypes contained in Prevnar 13™ and V114 was determined using a multiplexed opsonophagocytic assay (MOPA). The percentage of participants who had ≥4-fold rise in OPA titers were calculated from baseline (Day 1) to 30 days postvaccination (Day 30) for OPA responses for the 2 unique serotypes in V114. The observed response percentage (m/n) included: m=the number of

participants with the indicated response divided by n=the number of participants contributing to the analysis. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the percentage point difference); within-group CIs were not calculated.

|                             |         |
|-----------------------------|---------|
| End point type              | Primary |
| End point timeframe:        |         |
| Day 1 (Baseline) and Day 30 |         |

| End point values                           | V114            | Prevnar 13™     |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                         | Reporting group | Reporting group |  |  |
| Number of subjects analysed                | 602             | 600             |  |  |
| Units: Percentage of Participants          |                 |                 |  |  |
| number (not applicable)                    |                 |                 |  |  |
| Serotype 22F (Unique to V114) (n=524, 498) | 71.4            | 14.3            |  |  |
| Serotype 33F (Unique to V114)(n=578, 560)  | 56.7            | 6.3             |  |  |

## Statistical analyses

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Serotype 22F (Unique to V114) |
| Comparison groups                       | V114 v Prevnar 13™            |
| Number of subjects included in analysis | 1202                          |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| P-value                                 | < 0.001                       |
| Method                                  | Miettinen & Nurminen          |
| Parameter estimate                      | Percentage Point Difference   |
| Point estimate                          | 57.1                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 52                            |
| upper limit                             | 61.8                          |

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Serotype 33F (Unique to V114) |
| Comparison groups                       | V114 v Prevnar 13™            |
| Number of subjects included in analysis | 1202                          |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| P-value                                 | < 0.001                       |
| Method                                  | Miettinen & Nurminen          |
| Parameter estimate                      | Percentage Point Difference   |
| Point estimate                          | 50.5                          |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 45.9    |
| upper limit         | 54.9    |

### Secondary: GMT of Serotype-specific OPA for Serotype 3 at Day 30

|   |   |
|---|---|
| End point title   | GMT of Serotype-specific OPA for Serotype 3 at Day 30 |
| End point description:  |   |
| Serotype-specific OPA GMTs (estimated) and GMT ratios with 95% CIs were calculated using a cLDA model utilizing data from both vaccination groups. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the GMT ratios); within-group CIs were not calculated. OPA for serotype 3 contained in Prevnar 13™ and V114 was determined using a MOPA. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Day 30  |   |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | V114            | Prevnar 13™     |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 598             | 598             |  |  |
| Units: Titers               |                 |                 |  |  |
| number (not applicable)     | 216.2           | 135.1           |  |  |

### Statistical analyses

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 3 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1196                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| P-value                                 | < 0.001             |
| Method                                  | cLDA                |
| Parameter estimate                      | GMT Ratio           |
| Point estimate                          | 1.6                 |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 1.38                |
| upper limit                             | 1.85                |

## Secondary: Percentage of Participants with $\geq 4$ -Fold Rise in Serotype-specific OPA for Serotype 3 OPA Responses

|   |   |
|---|---|
| End point title   | Percentage of Participants with $\geq 4$ -Fold Rise in Serotype-specific OPA for Serotype 3 OPA Responses |
| End point description:<br>Activity for serotype 3 contained in Prevnar 13™ and V114 was determined using a MOPA. The observed response percentage of participants (m/n) who had $\geq 4$ -fold rise in OPA titers were calculated from baseline to postvaccination. n=Number of participants contributing to the analysis; m=Number of participants with the indicated response. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the percentage point difference); within-group CIs were not calculated. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Day 1 (Baseline) and Day 30   |   |

| End point values                  | V114            | Prevnar 13™     |  |  |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type                | Reporting group | Reporting group |  |  |
| Number of subjects analysed       | 580             | 576             |  |  |
| Units: Percentage of Participants |                 |                 |  |  |
| number (not applicable)           | 70.2            | 58.7            |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Serotype 3 (Shared) $\geq 4$ -Fold Rise in OPA |
| Comparison groups                       | V114 v Prevnar 13™                             |
| Number of subjects included in analysis | 1156   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           |  |
| P-value                                 | < 0.001  |
| Method                                  | Miettinen & Nurminen                           |
| Parameter estimate                      | Percentage Point Difference                    |
| Point estimate                          | 11.5   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 6  |
| upper limit                             | 16.9   |

## Secondary: Geometric Mean Concentration of Serotype-specific IgG at Day 30

|  |   |
|--|---|
| End point title  | Geometric Mean Concentration of Serotype-specific IgG at Day 30 |
| End point description:<br>Serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) (estimated) and GMC ratios with 95% confidence intervals (CIs) were calculated using a cLDA model utilizing data from both vaccination groups. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the GMC ratios); within-group CIs were not calculated. IgG for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) will be |   |

determined using an electrochemiluminescence assay. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 30               |           |

| End point values                           | V114            | Prevnar 13™     |  |  |
|--|-----------------|-----------------|--|--|
| Subject group type                         | Reporting group | Reporting group |  |  |
| Number of subjects analysed                | 602             | 600             |  |  |
| Units: µg/mL                               |                 |                 |  |  |
| number (not applicable)                    |                 |                 |  |  |
| Serotype 1 (Shared) (n=598, 598)           | 5.30            | 7.34            |  |  |
| Serotype 3 (Shared) (n=598, 598)           | 0.96            | 0.64            |  |  |
| Serotype 4 (Shared) (n=598, 598)           | 1.88            | 2.62            |  |  |
| Serotype 5 (Shared) (n=598, 598)           | 4.57            | 5.56            |  |  |
| Serotype 6A (Shared) (n=598, 598)          | 7.21            | 7.01            |  |  |
| Serotype 6B (Shared) (n=598, 598)          | 8.60            | 6.19            |  |  |
| Serotype 7F (Shared) (n=598, 598)          | 6.18            | 8.09            |  |  |
| Serotype 9V (Shared) (n=598, 598)          | 4.77            | 5.52            |  |  |
| Serotype 14 (Shared) (n=598, 598)          | 9.39            | 12.30           |  |  |
| Serotype 18C (Shared) (n=598, 598)         | 8.99            | 10.00           |  |  |
| Serotype 19A (Shared) (n=598, 598)         | 14.60           | 17.38           |  |  |
| Serotype 19F (Shared) (n=598, 598)         | 8.77            | 9.70            |  |  |
| Serotype 23F (Shared) (n=598, 598)         | 6.67            | 6.13            |  |  |
| Serotype 22F (Unique to V114) (n=598, 598) | 3.44            | 0.32            |  |  |
| Serotype 33F (Unique to V114) (n=598, 598) | 11.05           | 1.23            |  |  |

## Statistical analyses

|   |                     |
|---|---------------------|
| Statistical analysis title              | Serotype 1 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| Parameter estimate                      | GMC Ratio           |
| Point estimate                          | 0.72                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 0.62                |
| upper limit                             | 0.83                |

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 3 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| Parameter estimate                      | GMC Ratio           |
| Point estimate                          | 1.51                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 1.33                |
| upper limit                             | 1.71                |

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 4 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| Parameter estimate                      | GMC Ratio           |
| Point estimate                          | 0.72                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 0.62                |
| upper limit                             | 0.83                |

|   |                     |
|---|---------------------|
| <b>Statistical analysis title</b>       | Serotype 5 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™  |
| Number of subjects included in analysis | 1202                |
| Analysis specification                  | Pre-specified       |
| Analysis type                           |                     |
| Parameter estimate                      | GMC Ratio           |
| Point estimate                          | 0.82                |
| Confidence interval                     |                     |
| level                                   | 95 %                |
| sides                                   | 2-sided             |
| lower limit                             | 0.7                 |
| upper limit                             | 0.96                |

|                                   |                      |
|-----------------------------------|----------------------|
| <b>Statistical analysis title</b> | Serotype 6A (Shared) |
| Comparison groups                 | V114 v Prevnar 13™   |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 1202          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| Parameter estimate                      | GMC Ratio     |
| Point estimate                          | 1.03          |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | 0.87          |
| upper limit                             | 1.21          |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 6B (Shared) |
| Comparison groups                       | V114 v Prevnar 13™   |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| Parameter estimate                      | GMC Ratio            |
| Point estimate                          | 1.39                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 1.17                 |
| upper limit                             | 1.64                 |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 7F (Shared) |
| Comparison groups                       | V114 v Prevnar 13™   |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| Parameter estimate                      | GMC Ratio            |
| Point estimate                          | 0.76                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.66                 |
| upper limit                             | 0.89                 |

|                                   |                      |
|-----------------------------------|----------------------|
| <b>Statistical analysis title</b> | Serotype 9V (Shared) |
| Comparison groups                 | V114 v Prevnar 13™   |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 1202          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| Parameter estimate                      | GMC Ratio     |
| Point estimate                          | 0.86          |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | 0.75          |
| upper limit                             | 1             |

|   |                      |
|---|----------------------|
| <b>Statistical analysis title</b>       | Serotype 14 (Shared) |
| Comparison groups                       | V114 v Prevnar 13™   |
| Number of subjects included in analysis | 1202                 |
| Analysis specification                  | Pre-specified        |
| Analysis type                           |                      |
| Parameter estimate                      | GMC Ratio            |
| Point estimate                          | 0.76                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.65                 |
| upper limit                             | 0.89                 |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 18C (Shared) |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| Parameter estimate                      | GMC Ratio             |
| Point estimate                          | 0.9                   |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.77                  |
| upper limit                             | 1.05                  |

|                                   |                       |
|-----------------------------------|-----------------------|
| <b>Statistical analysis title</b> | Serotype 19A (Shared) |
| Comparison groups                 | V114 v Prevnar 13™    |



|   |               |
|---|---------------|
| Number of subjects included in analysis | 1202          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| Parameter estimate                      | GMC Ratio     |
| Point estimate                          | 0.84          |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | 0.73          |
| upper limit                             | 0.97          |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 19F (Shared) |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| Parameter estimate                      | GMC Ratio             |
| Point estimate                          | 0.9                   |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.78                  |
| upper limit                             | 1.05                  |

|   |                       |
|---|-----------------------|
| <b>Statistical analysis title</b>       | Serotype 23F (Shared) |
| Comparison groups                       | V114 v Prevnar 13™    |
| Number of subjects included in analysis | 1202                  |
| Analysis specification                  | Pre-specified         |
| Analysis type                           |                       |
| Parameter estimate                      | GMC Ratio             |
| Point estimate                          | 1.09                  |
| Confidence interval                     |                       |
| level                                   | 95 %                  |
| sides                                   | 2-sided               |
| lower limit                             | 0.92                  |
| upper limit                             | 1.28                  |

|                                   |                               |
|-----------------------------------|-------------------------------|
| <b>Statistical analysis title</b> | Serotype 22F (Unique to V114) |
| Comparison groups                 | V114 v Prevnar 13™            |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 1202          |
| Analysis specification                  | Pre-specified |
| Analysis type                           |               |
| Parameter estimate                      | GMC Ratio     |
| Point estimate                          | 10.62         |
| Confidence interval                     |               |
| level                                   | 95 %          |
| sides                                   | 2-sided       |
| lower limit                             | 9.37          |
| upper limit                             | 12.03         |

|   |                               |
|---|-------------------------------|
| <b>Statistical analysis title</b>       | Serotype 33F (Unique to V114) |
| Comparison groups                       | V114 v Prevnar 13™            |
| Number of subjects included in analysis | 1202                          |
| Analysis specification                  | Pre-specified                 |
| Analysis type                           |                               |
| Parameter estimate                      | GMC Ratio                     |
| Point estimate                          | 8.98                          |
| Confidence interval                     |                               |
| level                                   | 95 %                          |
| sides                                   | 2-sided                       |
| lower limit                             | 8                             |
| upper limit                             | 10.07                         |

## Secondary: Geometric Mean Fold Rise in Serotype-specific OPA

|                        |   |
|------------------------|---|
| End point title        | Geometric Mean Fold Rise in Serotype-specific OPA   |
| End point description: | Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using a Multiplexed Opsonophagocytic Assay. Geometric mean fold rise (GMFR) is defined as the geometric mean of the ratio of concentration at Day 30 after vaccination divided by concentration at baseline. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination. |
| End point type         | Secondary   |
| End point timeframe:   | Day 1 (Baseline) and Day 30   |

|  |                     |                     |  |  |
|--|---------------------|---------------------|--|--|
| <b>End point values</b>                  | V114                | Prevnar 13™         |  |  |
| Subject group type                       | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed              | 602                 | 600                 |  |  |
| Units: Ratio                             |                     |                     |  |  |
| geometric mean (confidence interval 95%) |                     |                     |  |  |
| Serotype 1 (Shared) (n=583, 573)         | 14.3 (12.5 to 16.4) | 18.7 (16.2 to 21.5) |  |  |

|   |                     |                     |  |  |
|---|---------------------|---------------------|--|--|
| Serotype 3 (Shared) (n=580, 576)          | 7.7 (7.0 to 8.6)    | 5.2 (4.7 to 5.7)    |  |  |
| Serotype 4 (Shared) (n=586, 578)          | 17.8 (15.7 to 20.3) | 24.4 (21.3 to 27.8) |  |  |
| Serotype 5 (Shared) (n=588, 584)          | 12.3 (10.7 to 14.2) | 15.3 (13.2 to 17.6) |  |  |
| Serotype 6A (Shared) (n=545, 550)         | 13.0 (11.4 to 14.9) | 13.3 (11.6 to 15.2) |  |  |
| Serotype 6B (Shared) (n=579, 576)         | 26.3 (22.4 to 30.8) | 21.6 (18.5 to 25.2) |  |  |
| Serotype 7F (Shared) (n=566, 555)         | 12.0 (10.3 to 13.9) | 14.1 (12.1 to 16.5) |  |  |
| Serotype 9V (Shared) (n=578, 573)         | 5.3 (4.8 to 6.0)    | 6.3 (5.6 to 7.1)    |  |  |
| Serotype 14 (Shared) (n=579,576)          | 6.2 (5.4 to 7.2)    | 8.7 (7.5 to 10.0)   |  |  |
| Serotype 18C (Shared) (n=578,579)         | 11.3 (10.0 to 12.9) | 10.4 (9.1 to 11.8)  |  |  |
| Serotype 19A (Shared) (n=581,575)         | 10.9 (9.5 to 12.5)  | 13.1 (11.4 to 15.1) |  |  |
| Serotype 19F (Shared) (n=579,576)         | 6.6 (5.9 to 7.5)    | 7.4 (6.6 to 8.3)    |  |  |
| Serotype 23F (Shared) (n=555,555)         | 16.2 (14.0 to 18.9) | 13.5 (11.5 to 15.9) |  |  |
| Serotype 22F (Unique to V114) (n=524,498) | 28.3 (22.8 to 35.1) | 1.2 (1.0 to 1.4)    |  |  |
| Serotype 33F (Unique to V114)(n=578,560)  | 7.4 (6.4 to 8.6)    | 1.0 (1.0 to 1.2)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Fold Rise in Serotype-specific IgG

|  |   |
|--|---|
| End point title  | Geometric Mean Fold Rise in Serotype-specific IgG |
| End point description:   |   |
| Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using an electrochemiluminescence assay. Geometric mean fold rise (GMFR) is defined as the geometric mean of the ratio of concentration at Day 30 after vaccination divided by concentration at baseline. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Day 1 (Baseline) and Day 30  |   |

| End point values                         | V114               | Prevnar 13™         |  |  |
|--|--------------------|---------------------|--|--|
| Subject group type                       | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed              | 602                | 600                 |  |  |
| Units: Ratio                             |                    |                     |  |  |
| geometric mean (confidence interval 95%) |                    |                     |  |  |
| Serotype 1 (Shared) (n=588,584)          | 10.6 (9.4 to 12.0) | 14.7 (13.1 to 16.6) |  |  |
| Serotype 3 (Shared) (n=588,582)          | 6.8 (6.2 to 7.6)   | 4.7 (4.2 to 5.1)    |  |  |

|   |                     |                     |  |  |
|---|---------------------|---------------------|--|--|
| Serotype 4 (Shared) (n=586,583)           | 8.0 (7.2 to 9.0)    | 11.2 (10.0 to 12.5) |  |  |
| Serotype 5 (Shared) (n=588,584)           | 4.7 (4.2 to 5.2)    | 5.8 (5.2 to 6.5)    |  |  |
| Serotype 6A (Shared) (n=588,584)          | 19.9 (17.6 to 22.6) | 19.7 (17.4 to 22.3) |  |  |
| Serotype 6B (Shared) (n=588,582)          | 19.1 (16.8 to 21.7) | 13.8 (12.3 to 15.6) |  |  |
| Serotype 7F (Shared) (n=588,584)          | 12.3 (10.9 to 13.9) | 15.8 (13.9 to 18.0) |  |  |
| Serotype 9V (Shared) (n=588,584)          | 9.9 (8.9 to 11.1)   | 11.1 (9.9 to 12.4)  |  |  |
| Serotype 14 (Shared) (n=587,583)          | 5.1 (4.5 to 5.7)    | 7.2 (6.3 to 8.2)    |  |  |
| Serotype 18C (Shared) (n=588,583)         | 12.8 (11.3 to 14.5) | 14.3 (12.6 to 16.2) |  |  |
| Serotype 19A (Shared) (n=588,584)         | 8.7 (7.8 to 9.8)    | 10.6 (9.5 to 11.9)  |  |  |
| Serotype 19F (Shared) (n=583,580)         | 10.9 (9.7 to 12.3)  | 12.5 (11.1 to 14.0) |  |  |
| Serotype 23F (Shared) (n=586,584)         | 13.5 (11.9 to 15.3) | 12.2 (10.8 to 13.7) |  |  |
| Serotype 22F (Unique to V114) (n=588,583) | 11.7 (10.3 to 13.3) | 1.1 (1.1 to 1.1)    |  |  |
| Serotype 33F (Unique to V114) (n=588,584) | 9.1 (8.0 to 10.2)   | 1.0 (1.0 to 1.0)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With $\geq 4$ -Fold Rise in Serotype-specific OPA Titer

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants With $\geq 4$ -Fold Rise in Serotype-specific OPA Titer |
|-----------------|--|

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using a multiplexed opsonophagocytic assay. The percentage of participants who had  $\geq 4$ -fold rise in OPA titers were calculated from baseline to postvaccination. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

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

End point timeframe:

Day 1 (Baseline) and Day 30

| End point values                  | V114                | Prevnar 13™         |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 602                 | 600                 |  |  |
| Units: Percentage of Participants |                     |                     |  |  |
| number (confidence interval 95%)  |                     |                     |  |  |
| Serotype 1 (Shared) (n=583,573)   | 75.1 (71.4 to 78.6) | 77.7 (74.0 to 81.0) |  |  |

|   |                     |                     |  |  |
|---|---------------------|---------------------|--|--|
| Serotype 3 (Shared) (n=580,576)           | 70.2 (66.3 to 73.9) | 58.7 (54.5 to 62.7) |  |  |
| Serotype 4 (Shared) (n=586,578)           | 79.5 (76.0 to 82.7) | 84.8 (81.6 to 87.6) |  |  |
| Serotype 5 (Shared) (n=588,584)           | 71.6 (67.8 to 75.2) | 75.3 (71.6 to 78.8) |  |  |
| Serotype 6A (Shared) (n=545,550)          | 76.5 (72.7 to 80.0) | 74.9 (71.1 to 78.5) |  |  |
| Serotype 6B (Shared) (n=579,576)          | 81.2 (77.7 to 84.3) | 79.2 (75.6 to 82.4) |  |  |
| Serotype 7F (Shared) (n=566,555)          | 66.4 (62.4 to 70.3) | 72.4 (68.5 to 76.1) |  |  |
| Serotype 9V (Shared) (n=578,573)          | 54.0 (49.8 to 58.1) | 60.0 (55.9 to 64.1) |  |  |
| Serotype 14 (Shared) (n=579,576)          | 52.2 (48.0 to 56.3) | 60.8 (56.6 to 64.8) |  |  |
| Serotype 18C (Shared) (n=578,579)         | 71.3 (67.4 to 74.9) | 69.1 (65.1 to 72.8) |  |  |
| Serotype 19A (Shared) (n=581,575)         | 70.6 (66.7 to 74.2) | 71.1 (67.2 to 74.8) |  |  |
| Serotype 19F (Shared) (n=579,576)         | 62.0 (57.9 to 66.0) | 65.1 (61.1 to 69.0) |  |  |
| Serotype 23F (Shared) (n=555,555)         | 75.0 (71.1 to 78.5) | 71.4 (67.4 to 75.1) |  |  |
| Serotype 22F (Unique to V114) (n=524,498) | 71.4 (67.3 to 75.2) | 14.3 (11.3 to 17.6) |  |  |
| Serotype 33F (Unique to V114) (n=578,560) | 56.7 (52.6 to 60.8) | 6.3 (4.4 to 8.6)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with $\geq 4$ -Fold Rise in Serotype-specific IgG Concentration

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with $\geq 4$ -Fold Rise in Serotype-specific IgG Concentration |
|-----------------|--|

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) will be determined using an electrochemiluminescence assay. The percentage of participants who had  $\geq 4$ -fold rise in IgG concentration are calculated from baseline to postvaccination. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

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

End point timeframe:

Day 1 (Baseline) and Day 30

| End point values                          | V114                | Prevnar 13™         |  |  |
|---|---------------------|---------------------|--|--|
| Subject group type                        | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed               | 602                 | 600                 |  |  |
| Units: Percentage of Participants         |                     |                     |  |  |
| number (confidence interval 95%)          |                     |                     |  |  |
| Serotype 1 (Shared) (n=588,584)           | 73.1 (69.4 to 76.7) | 78.4 (74.9 to 81.7) |  |  |
| Serotype 3 (Shared) (n=588,582)           | 61.6 (57.5 to 65.5) | 51.4 (47.2 to 55.5) |  |  |
| Serotype 4 (Shared) (n=586,583)           | 65.0 (61.0 to 68.9) | 76.0 (72.3 to 79.4) |  |  |
| Serotype 5 (Shared) (n=588,584)           | 45.1 (41.0 to 49.2) | 53.4 (49.3 to 57.5) |  |  |
| Serotype 6A (Shared) (n=588,584)          | 83.5 (80.3 to 86.4) | 83.4 (80.1 to 86.3) |  |  |
| Serotype 6B (Shared) (n=588,582)          | 82.8 (79.5 to 85.8) | 77.5 (73.9 to 80.8) |  |  |
| Serotype 7F (Shared) (n=588,584)          | 73.5 (69.7 to 77.0) | 78.6 (75.0 to 81.9) |  |  |
| Serotype 9V (Shared) (n=588,584)          | 69.6 (65.7 to 73.3) | 75.5 (71.8 to 79.0) |  |  |
| Serotype 14 (Shared) (n=587,583)          | 49.4 (45.3 to 53.5) | 59.5 (55.4 to 63.5) |  |  |
| Serotype 18C (Shared) (n=588,583)         | 73.1 (69.4 to 76.7) | 76.3 (72.7 to 79.7) |  |  |
| Serotype 19A (Shared) (n=588,584)         | 67.2 (63.2 to 71.0) | 71.2 (67.4 to 74.9) |  |  |
| Serotype 19F (Shared) (n=583,580)         | 69.5 (65.6 to 73.2) | 75.5 (71.8 to 79.0) |  |  |
| Serotype 23F (Shared) (n=586,584)         | 74.9 (71.2 to 78.4) | 74.3 (70.6 to 77.8) |  |  |
| Serotype 22F (Unique to V114) (n=588,583) | 71.4 (67.6 to 75.0) | 1.7 (0.8 to 3.1)    |  |  |
| Serotype 33F (Unique to V114) (n=588,584) | 66.5 (62.5 to 70.3) | 1.7 (0.8 to 3.1)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events: Up to 14 days after vaccination; Serious adverse events and all-cause mortality: Up to ~Month 6 (Up to 194 days after vaccination).

Adverse event reporting additional description:

The analysis population for adverse events and serious adverse events: all randomized participants who received study vaccination and were included in the intervention group according to the intervention they received. All randomized participants were included in the number of deaths (all causes).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |      |
|-----------------------|------|
| Reporting group title | V114 |
|-----------------------|------|

Reporting group description: -

|                       |       |
|-----------------------|-------|
| Reporting group title | PCV13 |
|-----------------------|-------|

Reporting group description: -

| Serious adverse events  | V114            | PCV13            |  |
|---|-----------------|------------------|--|
| Total subjects affected by serious adverse events                   |                 |                  |  |
| subjects affected / exposed   | 9 / 602 (1.50%) | 13 / 600 (2.17%) |  |
| number of deaths (all causes)                                       | 1               | 1                |  |
| number of deaths resulting from adverse events                      | 0               | 0                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                  |  |
| Basal cell carcinoma  |                 |                  |  |
| subjects affected / exposed   | 0 / 602 (0.00%) | 1 / 600 (0.17%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Gastrointestinal carcinoma  |                 |                  |  |
| subjects affected / exposed   | 0 / 602 (0.00%) | 1 / 600 (0.17%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Lung neoplasm malignant   |                 |                  |  |
| subjects affected / exposed   | 0 / 602 (0.00%) | 1 / 600 (0.17%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0            |  |
| Non-small cell lung cancer  |                 |                  |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostate cancer                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostate cancer stage II                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Meniscus injury                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Acute myocardial infarction                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Angina unstable                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Arrhythmia                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |



|  |                 |                 |  |
|--|-----------------|-----------------|--|
| Myocardial infarction                                |                 |                 |  |
| subjects affected / exposed                          | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders                 |                 |                 |  |
| Anaemia  |                 |                 |  |
| subjects affected / exposed                          | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Death  |                 |                 |  |
| subjects affected / exposed                          | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Gastrointestinal disorders                           |                 |                 |  |
| Incarcerated umbilical hernia                        |                 |                 |  |
| subjects affected / exposed                          | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Oesophagitis ulcerative                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders             |                 |                 |  |
| Pelvic pain  |                 |                 |  |
| subjects affected / exposed                          | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |  |
| Acute respiratory failure                            |                 |                 |  |
| subjects affected / exposed                          | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                          |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Ureterolithiasis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteoarthritis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 602 (0.17%) | 0 / 600 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Viral infection                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 602 (0.00%) | 1 / 600 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | V114               | PCV13              |  |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                    |                    |  |
| subjects affected / exposed                           | 395 / 602 (65.61%) | 336 / 600 (56.00%) |  |
| Nervous system disorders                              |                    |                    |  |
| Headache  |                    |                    |  |
| subjects affected / exposed                           | 70 / 602 (11.63%)  | 78 / 600 (13.00%)  |  |
| occurrences (all)                                     | 93                 | 105                |  |
| General disorders and administration site conditions  |                    |                    |  |

|   |                    |                    |  |
|---|--------------------|--------------------|--|
| Fatigue   |                    |                    |  |
| subjects affected / exposed                     | 105 / 602 (17.44%) | 104 / 600 (17.33%) |  |
| occurrences (all)                               | 144                | 140                |  |
| Injection site erythema                         |                    |                    |  |
| subjects affected / exposed                     | 60 / 602 (9.97%)   | 73 / 600 (12.17%)  |  |
| occurrences (all)                               | 62                 | 77                 |  |
| Injection site pain                             |                    |                    |  |
| subjects affected / exposed                     | 327 / 602 (54.32%) | 257 / 600 (42.83%) |  |
| occurrences (all)                               | 367                | 294                |  |
| Injection site swelling                         |                    |                    |  |
| subjects affected / exposed                     | 76 / 602 (12.62%)  | 73 / 600 (12.17%)  |  |
| occurrences (all)                               | 79                 | 78                 |  |
| Musculoskeletal and connective tissue disorders |                    |                    |  |
| Arthralgia                                      |                    |                    |  |
| subjects affected / exposed                     | 32 / 602 (5.32%)   | 33 / 600 (5.50%)   |  |
| occurrences (all)                               | 38                 | 39                 |  |
| Myalgia   |                    |                    |  |
| subjects affected / exposed                     | 93 / 602 (15.45%)  | 72 / 600 (12.00%)  |  |
| occurrences (all)                               | 111                | 85                 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 06 April 2020 | Amendment 01- Revisions were made to include assessment of superiority for Serotype 3 and to include a revised statistical criterion for assessment of superiority for serotypes 22F and 33F. to make it a more stringent test. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported