



## Clinical trial results:

**A phase II, randomized, controlled, observer-blind study to assess the safety, reactogenicity and immunogenicity of GlaxoSmithKline (GSK) Biologicals' Streptococcus pneumoniae protein containing vaccine formulations when administered according to a 0-2-6 month schedule, in healthy children aged 12-23 months at the time of first vaccination.**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2009-012701-19 |
| Trial protocol           | CZ             |
| Global end of trial date | 02 March 2011  |

## Results information

|                                |                                                                                                                                          |
|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Result version number          | v2                                                                                                                                       |
| This version publication date  | 28 April 2016                                                                                                                            |
| First version publication date | 01 August 2015                                                                                                                           |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Data correction due to a system error in EudraCT – Results |

## Trial information

### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 113171 |
|-----------------------|--------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00985751 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |                                                                                                         |
|------------------------------|---------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline Biologicals                                                                             |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330                                                        |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.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? | Yes |

Notes:

## Results analysis stage

|                                                      |                 |
|------------------------------------------------------|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 25 July 2011    |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 12 October 2010 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 02 March 2011   |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To compare the two formulations of GSK Biologicals' S. pneumoniae protein containing vaccine combined with GSK Biologicals' 10-valent pneumococcal conjugate vaccine (pooled groups) versus GSK Biologicals' 10-valent pneumococcal conjugate vaccine with respect to the percentage of subjects reporting fever >40.0°C (rectal temperature) within 7 days after at least one dose of primary vaccination.

To compare the two formulations of GSK Biologicals' S. pneumoniae protein containing vaccine (pooled groups) versus GSK Biologicals' 10-valent pneumococcal conjugate vaccine with respect to the percentage of subjects reporting fever >40.0°C (rectal temperature) within 7 days after at least one dose of primary vaccination.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 24 November 2009 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Czech Republic: 257 |
| Worldwide total number of subjects   | 257                 |
| EEA total number of subjects         | 257                 |

Notes:

### Subjects enrolled per age group

|                                        |   |
|----------------------------------------|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|                                          |     |
|------------------------------------------|-----|
| wk                                       |     |
| Newborns (0-27 days)                     | 0   |
| Infants and toddlers (28 days-23 months) | 257 |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 0   |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

### Period 1

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

Blinding implementation details:

Serological data was not available to any investigator or any person involved in the conduct of the study (including data cleaning).

Data were collected in an observer-blind manner: vaccine recipient and those responsible for evaluation of any endpoint (safety, reactogenicity, and immunogenicity) was unaware of which vaccine was administered. To do so, vaccine preparation and administration was done by authorised medical personnel who did not participate in any of the clinical evaluation assays

### Arms

|                              |                    |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes                |
| <b>Arm title</b>             | dPly-PhtD-LD Group |

Arm description:

Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.

|                                        |                                                               |
|----------------------------------------|---------------------------------------------------------------|
| Arm type                               | Experimental                                                  |
| Investigational medicinal product name | Pneumococcal protein vaccine (low dose formulation), adsorbed |
| Investigational medicinal product code |                                                               |
| Other name                             | GSK 2189242A , dPly/PhtD-LD                                   |
| Pharmaceutical forms                   | Suspension for injection                                      |
| Routes of administration               | Intramuscular use                                             |

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | dPly-PhtD-HD Group |
|------------------|--------------------|

Arm description:

Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.

|                                        |                                                                |
|----------------------------------------|----------------------------------------------------------------|
| Arm type                               | Experimental                                                   |
| Investigational medicinal product name | Pneumococcal protein vaccine (high dose formulation), adsorbed |
| Investigational medicinal product code |                                                                |
| Other name                             | GSK 2189242A , dPly/PhtD-LD                                    |
| Pharmaceutical forms                   | Suspension for injection                                       |
| Routes of administration               | Intramuscular use                                              |

Dosage and administration details:

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was

not adequate).

|                                                                                                                                                                                                                                                                                      |                                                                                             |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                                                                                                     | 10Pn-dPly-PhtD-LD Group                                                                     |
| Arm description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6. |                                                                                             |
| Arm type                                                                                                                                                                                                                                                                             | Experimental                                                                                |
| Investigational medicinal product name                                                                                                                                                                                                                                               | 10 valent pneumococcal conjugate vaccine combined with free pneumococcal proteins, adsorbed |
| Investigational medicinal product code                                                                                                                                                                                                                                               |                                                                                             |
| Other name                                                                                                                                                                                                                                                                           | 10Pn/dPly/PhtD-LD                                                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                 | Suspension for injection                                                                    |
| Routes of administration                                                                                                                                                                                                                                                             | Intramuscular use                                                                           |

**Dosage and administration details:**

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

|                                                                                                                                                                                                                                                                                       |                                                                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                                                                                                      | 10Pn-dPly-PhtD-HD Group                                                                     |
| Arm description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6. |                                                                                             |
| Arm type                                                                                                                                                                                                                                                                              | Experimental                                                                                |
| Investigational medicinal product name                                                                                                                                                                                                                                                | 10 valent pneumococcal conjugate vaccine combined with free pneumococcal proteins, adsorbed |
| Investigational medicinal product code                                                                                                                                                                                                                                                |                                                                                             |
| Other name                                                                                                                                                                                                                                                                            | 10Pn/dPly/PhtD-HD                                                                           |
| Pharmaceutical forms                                                                                                                                                                                                                                                                  | Suspension for injection                                                                    |
| Routes of administration                                                                                                                                                                                                                                                              | Intramuscular use                                                                           |

**Dosage and administration details:**

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

|                                                                                                                                                |                          |
|------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| <b>Arm title</b>                                                                                                                               | 10Pn Group               |
| Arm description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine at Month 0 and Month 2 and a booster dose at Month 6. |                          |
| Arm type                                                                                                                                       | Active comparator        |
| Investigational medicinal product name                                                                                                         | Synflorix™               |
| Investigational medicinal product code                                                                                                         |                          |
| Other name                                                                                                                                     | 10Pn-PD-DiT              |
| Pharmaceutical forms                                                                                                                           | Suspension for injection |
| Routes of administration                                                                                                                       | Intramuscular use        |

**Dosage and administration details:**

The vaccine was administered, according to a 2 dose schedule at Month 0 and Month 2 and a booster dose at Month 6, into the deltoid muscle or into the anterolateral thigh (if the deltoid muscle size was not adequate).

| <b>Number of subjects in period 1</b> | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group |
|---------------------------------------|--------------------|--------------------|-------------------------|
| Started                               | 51                 | 52                 | 52                      |
| Completed                             | 51                 | 52                 | 52                      |
| Not completed                         | 0                  | 0                  | 0                       |
| Adverse event, non-fatal              | -                  | -                  | -                       |

| <b>Number of subjects in period 1</b> | 10Pn-dPly-PhtD-HD Group | 10Pn Group |
|---------------------------------------|-------------------------|------------|
| Started                               | 51                      | 51         |
| Completed                             | 51                      | 50         |
| Not completed                         | 0                       | 1          |
| Adverse event, non-fatal              | -                       | 1          |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                   |                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Reporting group title                                                                                                                                                                                                                                                                             | dPly-PhtD-LD Group      |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.             |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | dPly-PhtD-HD Group      |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.            |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | 10Pn-dPly-PhtD-LD Group |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.  |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | 10Pn-dPly-PhtD-HD Group |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6. |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | 10Pn Group              |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine at Month 0 and Month 2 and a booster dose at Month 6.                                                                                                                                        |                         |

| Reporting group values                                                                                                                                                                                                                                    | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--------------------|-------------------------|
| Number of subjects                                                                                                                                                                                                                                        | 51                 | 52                 | 52                      |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |                    |                    |                         |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                    |                    |                         |
| Age continuous<br>Units: months                                                                                                                                                                                                                           |                    |                    |                         |
| arithmetic mean                                                                                                                                                                                                                                           | 17                 | 16.7               | 17.1                    |
| standard deviation                                                                                                                                                                                                                                        | ± 3.6              | ± 3.81             | ± 4.03                  |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |                    |                    |                         |
| Female                                                                                                                                                                                                                                                    | 25                 | 22                 | 23                      |
| Male                                                                                                                                                                                                                                                      | 26                 | 30                 | 29                      |

| <b>Reporting group values</b>                         | 10Pn-dPly-PhtD-HD Group | 10Pn Group | Total |
|-------------------------------------------------------|-------------------------|------------|-------|
| Number of subjects                                    | 51                      | 51         | 257   |
| Age categorical<br>Units: Subjects                    |                         |            |       |
| In utero                                              |                         |            | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |                         |            | 0     |
| Newborns (0-27 days)                                  |                         |            | 0     |
| Infants and toddlers (28 days-23 months)              |                         |            | 0     |
| Children (2-11 years)                                 |                         |            | 0     |
| Adolescents (12-17 years)                             |                         |            | 0     |
| Adults (18-64 years)                                  |                         |            | 0     |
| From 65-84 years                                      |                         |            | 0     |
| 85 years and over                                     |                         |            | 0     |
| Age continuous<br>Units: months                       |                         |            |       |
| arithmetic mean                                       | 16.8                    | 16.3       |       |
| standard deviation                                    | ± 3.96                  | ± 4.18     | -     |
| Gender categorical<br>Units: Subjects                 |                         |            |       |
| Female                                                | 29                      | 28         | 127   |
| Male                                                  | 22                      | 23         | 130   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                   |                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Reporting group title                                                                                                                                                                                                                                                                             | dPly-PhtD-LD Group      |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.             |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | dPly-PhtD-HD Group      |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of GSK Biologicals' candidate pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.            |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | 10Pn-dPly-PhtD-LD Group |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, Low Dose (LD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6.  |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | 10Pn-dPly-PhtD-HD Group |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine combined with the pneumococcal protein vaccine containing the pneumococcal proteins dPly and PhtD, High Dose (HD) vaccine formulation, at Month 0 and Month 2 and a booster dose at Month 6. |                         |
| Reporting group title                                                                                                                                                                                                                                                                             | 10Pn Group              |
| Reporting group description:<br>Subjects received 2 primary vaccination doses of 10Pn-PD-DiT vaccine at Month 0 and Month 2 and a booster dose at Month 6.                                                                                                                                        |                         |
| Subject analysis set title                                                                                                                                                                                                                                                                        | dPly-PhtD Group         |
| Subject analysis set type                                                                                                                                                                                                                                                                         | Sub-group analysis      |
| Subject analysis set description:<br>Pooled dPly-PhtD-LD and dPly-PhtD-HD groups                                                                                                                                                                                                                  |                         |
| Subject analysis set title                                                                                                                                                                                                                                                                        | 10Pn-dPly-PhtD Group    |
| Subject analysis set type                                                                                                                                                                                                                                                                         | Sub-group analysis      |
| Subject analysis set description:<br>Pooled 10Pn-dPly-PhtD-LD and 10Pn-dPly-PhtD-HD groups                                                                                                                                                                                                        |                         |

### Primary: Number of subjects with fever > 40.0°C (rectal temperature)

|                                                                                                             |                                                                            |
|-------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| End point title                                                                                             | Number of subjects with fever > 40.0°C (rectal temperature) <sup>[1]</sup> |
| End point description:                                                                                      |                                                                            |
| End point type                                                                                              | Primary                                                                    |
| End point timeframe:<br>Within 7 days (day 0-day 6) following at least one dose of the primary vaccination. |                                                                            |

#### Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is reporting the parameter for pooled groups containing the baseline groups.

| End point values            | 10Pn Group      | 10Pn-dPly-PhtD Group |  |  |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type          | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed | 51              | 103                  |  |  |
| Units: Subjects             |                 |                      |  |  |
| Fever >40°C                 | 0               | 1                    |  |  |

## Statistical analyses

| Statistical analysis title | Fever >40°C -non-inferiority |
|----------------------------|------------------------------|
|----------------------------|------------------------------|

Statistical analysis description:

To compare the 2 formulations of GSK Biologicals' S. pneumoniae protein containing vaccine combined with 10Pn-PD-DiT vaccine (pooled groups) versus 10Pn-PD-DiT vaccine (10Pn-dPly-PhtD Group minus 10Pn Group) with respect to the percentage of subjects reporting fever > 40.0°C (rectal temperature) within 7 days after at least 1 dose of primary vaccination.

|                                         |                                   |
|-----------------------------------------|-----------------------------------|
| Comparison groups                       | 10Pn Group v 10Pn-dPly-PhtD Group |
| Number of subjects included in analysis | 154                               |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | non-inferiority <sup>[2]</sup>    |
| Parameter estimate                      | Difference in percentage          |
| Point estimate                          | 0.97                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | -6.1                              |
| upper limit                             | 5.32                              |

Notes:

[2] - The 95% CI for the difference between groups in the percentage of subjects with rectal temperature > 40.0°C within the 7-day follow-up period following primary vaccination was computed for the 10Pn-dPly-PhtD minus the 10Pn group. No statistically significant difference between groups in rectal temperature >40.0°C would be detected if the 95% CIs included 0 and non-inferiority would be expressed if the upper limit of the 2-sided 95% CI on the group difference < 10%.

### Primary: Number of subjects with fever > 40.0°C (rectal temperature)

|                 |                                                                            |
|-----------------|----------------------------------------------------------------------------|
| End point title | Number of subjects with fever > 40.0°C (rectal temperature) <sup>[3]</sup> |
|-----------------|----------------------------------------------------------------------------|

End point description:

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

End point timeframe:

Within 7 days (day 0-day 6) following at least one dose of the primary vaccination.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is reporting the parameter for pooled groups containing the baseline groups.

| End point values            | 10Pn Group      | dPly-PhtD Group      |  |  |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type          | Reporting group | Subject analysis set |  |  |
| Number of subjects analysed | 51              | 103                  |  |  |
| Units: Subjects             |                 |                      |  |  |
| Fever >40°C                 | 0               | 1                    |  |  |

## Statistical analyses

|                                                                                                                                                                                                                                                                                                                               |                                |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                                             | Fever >40°C -non-inferiority   |
| Statistical analysis description:                                                                                                                                                                                                                                                                                             |                                |
| To compare the 2 formulations of GSK Biologicals' S. pneumoniae protein containing vaccine (pooled groups) versus 10Pn-PD-DiT vaccine (dPly-PhtD Group minus 10Pn Group) with respect to the percentage of subjects reporting fever > 40.0°C (rectal temperature) within 7 days after at least 1 dose of primary vaccination. |                                |
| Comparison groups                                                                                                                                                                                                                                                                                                             | 10Pn Group v dPly-PhtD Group   |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                                       | 154                            |
| Analysis specification                                                                                                                                                                                                                                                                                                        | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                                                                                                 | non-inferiority <sup>[4]</sup> |
| Parameter estimate                                                                                                                                                                                                                                                                                                            | Difference in percentage       |
| Point estimate                                                                                                                                                                                                                                                                                                                | 0.97                           |
| Confidence interval                                                                                                                                                                                                                                                                                                           |                                |
| level                                                                                                                                                                                                                                                                                                                         | 95 %                           |
| sides                                                                                                                                                                                                                                                                                                                         | 2-sided                        |
| lower limit                                                                                                                                                                                                                                                                                                                   | -6.1                           |
| upper limit                                                                                                                                                                                                                                                                                                                   | 5.32                           |

Notes:

[4] - The 95% CI for the difference between groups in the percentage of subjects with rectal temperature > 40.0°C within the 7-day follow-up period following primary vaccination was computed for the dPly-PhtD minus the 10Pn group. No statistically significant difference between groups in rectal temperature >40.0°C would be detected if the 95% CIs included 0 and non-inferiority would be expressed if the upper limit of the 2-sided 95% CI on the group difference < 10%.

## Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

|                                                                                                                                                                                                                                                                                                                                   |                                                                       |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| <b>End point title</b>                                                                                                                                                                                                                                                                                                            | Number of subjects reporting any and grade 3 solicited local symptoms |
| End point description:                                                                                                                                                                                                                                                                                                            |                                                                       |
| Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity. |                                                                       |
| End point type                                                                                                                                                                                                                                                                                                                    | Secondary                                                             |
| End point timeframe:                                                                                                                                                                                                                                                                                                              |                                                                       |
| During the 7-day (Days 0-6) post-vaccination period following each dose (Dose 1, Dose 2 and Booster dose)                                                                                                                                                                                                                         |                                                                       |

| <b>End point values</b>                | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|----------------------------------------|--------------------|--------------------|-------------------------|-------------------------|
| Subject group type                     | Reporting group    | Reporting group    | Reporting group         | Reporting group         |
| Number of subjects analysed            | 51                 | 52                 | 52                      | 51                      |
| Units: Subjects                        |                    |                    |                         |                         |
| Any Pain Dose 1 [N=51;52;52;51;51]     | 18                 | 15                 | 31                      | 23                      |
| Grade 3 Pain Dose 1 [N=51;52;52;51;51] | 0                  | 0                  | 1                       | 2                       |

|                                                |    |    |    |    |
|------------------------------------------------|----|----|----|----|
| Any Redness Dose 1<br>[N=51;52;52;51;51]       | 17 | 20 | 32 | 28 |
| Grade 3 Redness Dose 1<br>[N=51;52;52;51;51]   | 1  | 0  | 5  | 4  |
| Any Swelling Dose 1<br>[N=51;52;52;51;51]      | 8  | 5  | 19 | 17 |
| Grade 3 Swelling Dose 1<br>[N=51;52;52;51;51]  | 0  | 0  | 2  | 2  |
| Any Pain Dose 2 [N=51;52;52;51;50]             | 15 | 22 | 24 | 27 |
| Grade 3 Pain Dose 2<br>[N=51;52;52;51;50]      | 0  | 0  | 2  | 2  |
| Any Redness Dose 2<br>[N=51;52;52;51;50]       | 21 | 25 | 23 | 22 |
| Grade 3 Redness Dose 2<br>[N=51;52;52;51;50]   | 1  | 1  | 4  | 1  |
| Any Swelling Dose 2<br>[N=51;52;52;51;50]      | 11 | 9  | 18 | 11 |
| Grade 3 Swelling Dose 2<br>[N=51;52;52;51;50]  | 0  | 0  | 5  | 1  |
| Any Pain Booster [N=51;51;52;51;50]            | 18 | 22 | 32 | 26 |
| Grade 3 Pain Booster<br>[N=51;51;52;51;50]     | 0  | 0  | 3  | 2  |
| Any Redness Booster<br>[N=51;51;52;51;50]      | 19 | 20 | 28 | 22 |
| Grade 3 Redness Booster<br>[N=51;51;52;51;50]  | 2  | 2  | 5  | 4  |
| Any Swelling Booster<br>[N=51;51;52;51;50]     | 11 | 8  | 18 | 15 |
| Grade 3 Swelling Booster<br>[N=51;51;52;51;50] | 0  | 3  | 3  | 1  |

| End point values                              | 10Pn Group      |  |  |  |
|-----------------------------------------------|-----------------|--|--|--|
| Subject group type                            | Reporting group |  |  |  |
| Number of subjects analysed                   | 51              |  |  |  |
| Units: Subjects                               |                 |  |  |  |
| Any Pain Dose 1 [N=51;52;52;51;51]            | 26              |  |  |  |
| Grade 3 Pain Dose 1<br>[N=51;52;52;51;51]     | 4               |  |  |  |
| Any Redness Dose 1<br>[N=51;52;52;51;51]      | 25              |  |  |  |
| Grade 3 Redness Dose 1<br>[N=51;52;52;51;51]  | 2               |  |  |  |
| Any Swelling Dose 1<br>[N=51;52;52;51;51]     | 19              |  |  |  |
| Grade 3 Swelling Dose 1<br>[N=51;52;52;51;51] | 1               |  |  |  |
| Any Pain Dose 2 [N=51;52;52;51;50]            | 27              |  |  |  |
| Grade 3 Pain Dose 2<br>[N=51;52;52;51;50]     | 3               |  |  |  |
| Any Redness Dose 2<br>[N=51;52;52;51;50]      | 24              |  |  |  |
| Grade 3 Redness Dose 2<br>[N=51;52;52;51;50]  | 3               |  |  |  |
| Any Swelling Dose 2<br>[N=51;52;52;51;50]     | 16              |  |  |  |
| Grade 3 Swelling Dose 2<br>[N=51;52;52;51;50] | 2               |  |  |  |

|                                                |    |  |  |  |
|------------------------------------------------|----|--|--|--|
| Any Pain Booster [N=51;51;52;51;50]            | 25 |  |  |  |
| Grade 3 Pain Booster<br>[N=51;51;52;51;50]     | 1  |  |  |  |
| Any Redness Booster<br>[N=51;51;52;51;50]      | 21 |  |  |  |
| Grade 3 Redness Booster<br>[N=51;51;52;51;50]  | 3  |  |  |  |
| Any Swelling Booster<br>[N=51;51;52;51;50]     | 13 |  |  |  |
| Grade 3 Swelling Booster<br>[N=51;51;52;51;50] | 3  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms

|                 |                                                                                  |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms |
|-----------------|----------------------------------------------------------------------------------|

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectally temperature  $\geq 38.0^{\circ}\text{C}$ ), irritability, and loss of appetite. Grade 3 drowsiness = drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectally temperature) above ( $>$ )  $40.0^{\circ}\text{C}$ . Grade 3 irritability = crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite = not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination.

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

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose ( Dose 1, Dose 2, Booster dose)

| End point values                                      | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|-------------------------------------------------------|--------------------|--------------------|-------------------------|-------------------------|
| Subject group type                                    | Reporting group    | Reporting group    | Reporting group         | Reporting group         |
| Number of subjects analysed                           | 51                 | 52                 | 52                      | 51                      |
| Units: Subjects                                       |                    |                    |                         |                         |
| Any Drowsiness Dose 1<br>[N=51;52;52;51;51]           | 16                 | 13                 | 24                      | 20                      |
| Grade 3 Drowsiness Dose 1<br>[N=51;52;52;51;51]       | 0                  | 0                  | 0                       | 0                       |
| Related Drowsiness Dose 1<br>[N=51;52;52;51;51]       | 6                  | 6                  | 13                      | 10                      |
| Any Irritability Dose 1<br>[N=51;52;52;51;51]         | 21                 | 16                 | 31                      | 27                      |
| Grade 3 Irritability Dose 1<br>[N=51;52;52;51;51]     | 0                  | 0                  | 0                       | 0                       |
| Related Irritability Dose 1<br>[N=51;52;52;51;51]     | 6                  | 9                  | 17                      | 16                      |
| Any Loss of appetite Dose 1<br>[N=51;52;52;51;51]     | 15                 | 7                  | 14                      | 12                      |
| Grade 3 Loss of appetite Dose 1<br>[N=51;52;52;51;51] | 2                  | 0                  | 1                       | 0                       |

|                                                        |    |    |    |    |
|--------------------------------------------------------|----|----|----|----|
| Related Loss of appetite Dose 1<br>[N=51;52;52;51;51]  | 4  | 5  | 9  | 3  |
| Any Fever Dose 1 [N=51;52;52;51;51]                    | 7  | 8  | 14 | 12 |
| Grade 3 Fever Dose 1<br>[N=51;52;52;51;51]             | 0  | 1  | 1  | 0  |
| Related Fever Dose 1<br>[N=51;52;52;51;51]             | 3  | 2  | 7  | 8  |
| Any Drowsiness Dose 2<br>[N=51;52;52;51;50]            | 12 | 16 | 17 | 15 |
| Grade 3 Drowsiness Dose 2<br>[N=51;52;52;51;50]        | 0  | 0  | 0  | 0  |
| Related Drowsiness Dose 2<br>[N=51;52;52;51;50]        | 6  | 11 | 11 | 10 |
| Any Irritability Dose 2<br>[N=51;52;52;51;50]          | 12 | 18 | 22 | 24 |
| Grade 3 Irritability Dose 2<br>[N=51;52;52;51;50]      | 0  | 0  | 0  | 0  |
| Related Irritability Dose 2<br>[N=51;52;52;51;50]      | 3  | 11 | 17 | 18 |
| Any Loss of appetite Dose 2<br>[N=51;52;52;51;50]      | 8  | 10 | 12 | 9  |
| Grade 3 Loss of appetite Dose 2<br>[N=51;52;52;51;50]  | 1  | 0  | 0  | 0  |
| Related Loss of appetite Dose 2<br>[N=51;52;52;51;50]  | 4  | 5  | 9  | 5  |
| Any Fever Dose 2 [N=51;52;52;51;50]                    | 9  | 12 | 8  | 9  |
| Grade 3 Fever Dose 2<br>[N=51;52;52;51;50]             | 0  | 0  | 0  | 0  |
| Related Fever Dose 2<br>[N=51;52;52;51;50]             | 2  | 6  | 5  | 7  |
| Any Drowsiness Booster<br>[N=51;51;52;51;50]           | 13 | 13 | 18 | 12 |
| Grade 3 Drowsiness Booster<br>[N=51;51;52;51;50]       | 0  | 0  | 0  | 0  |
| Related Drowsiness Booster<br>[N=51;51;52;51;50]       | 7  | 9  | 11 | 10 |
| Any Irritability Booster<br>[N=51;51;52;51;50]         | 15 | 17 | 26 | 17 |
| Grade 3 Irritability Booster<br>[N=51;51;52;51;50]     | 0  | 0  | 0  | 1  |
| Related Irritability Booster<br>[N=51;51;52;51;50]     | 9  | 11 | 15 | 13 |
| Any Loss of appetite Booster<br>[N=51;51;52;51;50]     | 6  | 10 | 13 | 15 |
| Grade 3 Loss of appetite Booster<br>[N=51;51;52;51;50] | 2  | 0  | 1  | 1  |
| Related Loss of appetite Booster<br>[N=51;51;52;51;50] | 4  | 4  | 7  | 7  |
| Any Fever Booster [N=51;51;52;51;50]                   | 8  | 10 | 10 | 5  |
| Grade 3 Fever Booster<br>[N=51;51;52;51;50]            | 0  | 0  | 0  | 0  |
| Related Fever Dose 3 Booster<br>[N=51;51;52;51;50]     | 5  | 3  | 7  | 2  |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | 10Pn Group      |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 51              |  |  |  |

| Units: Subjects                                       |    |  |  |  |
|-------------------------------------------------------|----|--|--|--|
| Any Drowsiness Dose 1<br>[N=51;52;52;51;51]           | 26 |  |  |  |
| Grade 3 Drowsiness Dose 1<br>[N=51;52;52;51;51]       | 0  |  |  |  |
| Related Drowsiness Dose 1<br>[N=51;52;52;51;51]       | 16 |  |  |  |
| Any Irritability Dose 1<br>[N=51;52;52;51;51]         | 23 |  |  |  |
| Grade 3 Irritability Dose 1<br>[N=51;52;52;51;51]     | 0  |  |  |  |
| Related Irritability Dose 1<br>[N=51;52;52;51;51]     | 14 |  |  |  |
| Any Loss of appetite Dose 1<br>[N=51;52;52;51;51]     | 14 |  |  |  |
| Grade 3 Loss of appetite Dose 1<br>[N=51;52;52;51;51] | 0  |  |  |  |
| Related Loss of appetite Dose 1<br>[N=51;52;52;51;51] | 7  |  |  |  |
| Any Fever Dose 1 [N=51;52;52;51;51]                   | 12 |  |  |  |
| Grade 3 Fever Dose 1<br>[N=51;52;52;51;51]            | 0  |  |  |  |
| Related Fever Dose 1<br>[N=51;52;52;51;51]            | 9  |  |  |  |
| Any Drowsiness Dose 2<br>[N=51;52;52;51;50]           | 23 |  |  |  |
| Grade 3 Drowsiness Dose 2<br>[N=51;52;52;51;50]       | 0  |  |  |  |
| Related Drowsiness Dose 2<br>[N=51;52;52;51;50]       | 18 |  |  |  |
| Any Irritability Dose 2<br>[N=51;52;52;51;50]         | 27 |  |  |  |
| Grade 3 Irritability Dose 2<br>[N=51;52;52;51;50]     | 1  |  |  |  |
| Related Irritability Dose 2<br>[N=51;52;52;51;50]     | 21 |  |  |  |
| Any Loss of appetite Dose 2<br>[N=51;52;52;51;50]     | 13 |  |  |  |
| Grade 3 Loss of appetite Dose 2<br>[N=51;52;52;51;50] | 0  |  |  |  |
| Related Loss of appetite Dose 2<br>[N=51;52;52;51;50] | 7  |  |  |  |
| Any Fever Dose 2 [N=51;52;52;51;50]                   | 7  |  |  |  |
| Grade 3 Fever Dose 2<br>[N=51;52;52;51;50]            | 0  |  |  |  |
| Related Fever Dose 2<br>[N=51;52;52;51;50]            | 7  |  |  |  |
| Any Drowsiness Booster<br>[N=51;51;52;51;50]          | 17 |  |  |  |
| Grade 3 Drowsiness Booster<br>[N=51;51;52;51;50]      | 0  |  |  |  |
| Related Drowsiness Booster<br>[N=51;51;52;51;50]      | 11 |  |  |  |
| Any Irritability Booster<br>[N=51;51;52;51;50]        | 19 |  |  |  |
| Grade 3 Irritability Booster<br>[N=51;51;52;51;50]    | 1  |  |  |  |
| Related Irritability Booster<br>[N=51;51;52;51;50]    | 13 |  |  |  |
| Any Loss of appetite Booster<br>[N=51;51;52;51;50]    | 8  |  |  |  |

|                                                        |   |  |  |  |
|--------------------------------------------------------|---|--|--|--|
| Grade 3 Loss of appetite Booster<br>[N=51;51;52;51;50] | 1 |  |  |  |
| Related Loss of appetite Booster<br>[N=51;51;52;51;50] | 6 |  |  |  |
| Any Fever Booster [N=51;51;52;51;50]                   | 7 |  |  |  |
| Grade 3 Fever Booster<br>[N=51;51;52;51;50]            | 0 |  |  |  |
| Related Fever Dose 3 Booster<br>[N=51;51;52;51;50]     | 3 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with unsolicited adverse events (AEs)

|                                                                                                                                                                                                                                                                                                                          |                                                          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                          | Number of subjects with unsolicited adverse events (AEs) |
| End point description:                                                                                                                                                                                                                                                                                                   |                                                          |
| An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined as an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. |                                                          |
| End point type                                                                                                                                                                                                                                                                                                           | Secondary                                                |
| End point timeframe:                                                                                                                                                                                                                                                                                                     |                                                          |
| During the 31-day (Days 0-30) follow-up period after each primary dose                                                                                                                                                                                                                                                   |                                                          |

| End point values            | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|-----------------------------|--------------------|--------------------|-------------------------|-------------------------|
| Subject group type          | Reporting group    | Reporting group    | Reporting group         | Reporting group         |
| Number of subjects analysed | 51                 | 52                 | 52                      | 51                      |
| Units: Subjects             |                    |                    |                         |                         |
| Any AE(s)                   | 25                 | 24                 | 31                      | 24                      |

| End point values            | 10Pn Group      |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 51              |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Any AE(s)                   | 22              |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with unsolicited adverse events (AEs)

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | Number of subjects with unsolicited adverse events (AEs) |
|-----------------|----------------------------------------------------------|

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined as an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

End point type Secondary

End point timeframe:

During the 31-day (Days 0-30) follow-up period after the booster dose

| End point values            | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|-----------------------------|--------------------|--------------------|-------------------------|-------------------------|
| Subject group type          | Reporting group    | Reporting group    | Reporting group         | Reporting group         |
| Number of subjects analysed | 51                 | 51                 | 52                      | 51                      |
| Units: Subjects             |                    |                    |                         |                         |
| Any AE(s)                   | 14                 | 12                 | 13                      | 4                       |

| End point values            | 10Pn Group      |  |  |  |
|-----------------------------|-----------------|--|--|--|
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 50              |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Any AE(s)                   | 9               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with serious adverse events (SAEs)

End point title Number of subjects with serious adverse events (SAEs)

End point description:

End point type Secondary

End point timeframe:

During the entire study period starting at the administration of the first vaccine dose up to study end

| End point values            | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|-----------------------------|--------------------|--------------------|-------------------------|-------------------------|
| Subject group type          | Reporting group    | Reporting group    | Reporting group         | Reporting group         |
| Number of subjects analysed | 51                 | 52                 | 52                      | 51                      |
| Units: Subjects             |                    |                    |                         |                         |
| Any SAE(s)                  | 5                  | 3                  | 5                       | 0                       |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | 10Pn Group      |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 51              |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Any SAE(s)                  | 4               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti- pneumococcal dPly and PhtD proteins antibody concentrations

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Anti- pneumococcal dPly and PhtD proteins antibody concentrations |
|-----------------|-------------------------------------------------------------------|

End point description:

Seropositivity status, defined as anti-pneumococcal dPly antibody concentrations  $\geq 599$  Luminex Units per millilitre (LU/mL) and anti-pneumococcal PhtD antibody concentrations  $\geq 391$  LU/mL .

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

End point timeframe:

one month post-dose 2, prior to the booster dose and one month post-booster:

| End point values                               | dPly-PhtD-LD Group                 | dPly-PhtD-HD Group                 | 10Pn-dPly-PhtD-LD Group            | 10Pn-dPly-PhtD-HD Group            |
|------------------------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|
| Subject group type                             | Reporting group                    | Reporting group                    | Reporting group                    | Reporting group                    |
| Number of subjects analysed                    | 45                                 | 45                                 | 47                                 | 41                                 |
| Units: LU/mL                                   |                                    |                                    |                                    |                                    |
| geometric mean (confidence interval 95%)       |                                    |                                    |                                    |                                    |
| Anti-dPly, Post-dose 2<br>[N=45;43;45;39;41]   | 135703.5<br>(95376.62 to 193081.3) | 148447.5<br>(101599.9 to 216896.7) | 32436.07<br>(25523.77 to 41220.35) | 57149.83<br>(44908.69 to 72727.64) |
| Anti-dPly, Pre-booster<br>[N=44;45;46;40;40]   | 100811.4<br>(74005.55 to 137326.8) | 96552.52<br>(73753.5 to 126399.3)  | 19573.55<br>(14948.37 to 25629.82) | 29592.91<br>(22065.25 to 39688.66) |
| Anti-dPly, Post-booster<br>[N=44;43;47;41;41]  | 224726.2<br>(178187.6 to 283419.8) | 305912.3<br>(248087.9 to 377214.4) | 44123.43<br>(34299.98 to 56760.29) | 85805.02<br>(67740.53 to 108686.8) |
| Anti-PhtD, Post-dose 2<br>[N=45;43;45;39;41]   | 30402.84<br>(20723.61 to 44602.88) | 35043.91<br>(24164.16 to 50822.19) | 23438.06<br>(16617.86 to 33057.36) | 22141.18<br>(15065.44 to 32540.15) |
| Anti- PhtD, Pre-booster<br>[N=44;45;46;40;40]  | 24350.58<br>(17056.09 to 34764.74) | 23918.77<br>(17724.59 to 32277.63) | 14375.59<br>(9338.31 to 22130.1)   | 12721.01<br>(8498 to 19042.62)     |
| Anti- PhtD, Post-booster<br>[N=44;43;47;41;41] | 65584.24<br>(50985.27 to 84363.43) | 77312.07<br>(58589.49 to 102017.6) | 32609.19<br>(23615.58 to 45027.88) | 36098.18<br>(26620.97 to 48949.34) |

|                                                |                                 |  |  |  |
|------------------------------------------------|---------------------------------|--|--|--|
| <b>End point values</b>                        | 10Pn Group                      |  |  |  |
| Subject group type                             | Reporting group                 |  |  |  |
| Number of subjects analysed                    | 41                              |  |  |  |
| Units: LU/mL                                   |                                 |  |  |  |
| geometric mean (confidence interval 95%)       |                                 |  |  |  |
| Anti-dPly, Post-dose 2<br>[N=45;43;45;39;41]   | 3759.82<br>(2376.77 to 5947.68) |  |  |  |
| Anti-dPly, Pre-booster<br>[N=44;45;46;40;40]   | 4654.16<br>(2879.42 to 7522.78) |  |  |  |
| Anti-dPly, Post-booster<br>[N=44;43;47;41;41]  | 4553.43<br>(2878.04 to 7204.12) |  |  |  |
| Anti-PhtD, Post-dose 2<br>[N=45;43;45;39;41]   | 3795.68<br>(2268.23 to 6351.73) |  |  |  |
| Anti- PhtD, Pre-booster<br>[N=44;45;46;40;40]  | 4814.97<br>(2881.25 to 8046.46) |  |  |  |
| Anti- PhtD, Post-booster<br>[N=44;43;47;41;41] | 5072.43<br>(3023.97 to 8508.53) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-pneumococcal serotypes and cross-reactive serotypes antibody concentrations

|                                                                                                                                                                                                                                                            |                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                            | Anti-pneumococcal serotypes and cross-reactive serotypes antibody concentrations |
| End point description:<br>Seropositivity status, defined as anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and cross-reactive serotype 6A and 19 antibody concentrations $\geq 0.05$ microgram per millilitre ( $\mu\text{g/mL}$ ). |                                                                                  |
| End point type                                                                                                                                                                                                                                             | Secondary                                                                        |
| End point timeframe:<br>One month post-dose 2, prior to the booster dose and one month post-booster                                                                                                                                                        |                                                                                  |

|                                          |                    |                    |                         |                         |
|------------------------------------------|--------------------|--------------------|-------------------------|-------------------------|
| <b>End point values</b>                  | dPly-PhtD-LD Group | dPly-PhtD-HD Group | 10Pn-dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
| Subject group type                       | Reporting group    | Reporting group    | Reporting group         | Reporting group         |
| Number of subjects analysed              | 43                 | 44                 | 47                      | 41                      |
| Units: $\mu\text{g/mL}$                  |                    |                    |                         |                         |
| geometric mean (confidence interval 95%) |                    |                    |                         |                         |

|                                              |                     |                     |                        |                        |
|----------------------------------------------|---------------------|---------------------|------------------------|------------------------|
| Anti-1, Post-Dose 2<br>[N=40;36;46;40;41]    | 0.04 (0.03 to 0.05) | 0.05 (0.04 to 0.06) | 2.5 (2.01 to 3.11)     | 2.08 (1.56 to 2.77)    |
| Anti-1, Pre-booster<br>[N=43;42;45;40;40]    | 0.05 (0.03 to 0.06) | 0.05 (0.04 to 0.07) | 0.87 (0.68 to 1.12)    | 0.75 (0.57 to 0.99)    |
| Anti-1, Post-booster<br>[N=40;41;47;41;41]   | 0.04 (0.03 to 0.06) | 0.05 (0.04 to 0.08) | 2.69 (2.13 to 3.39)    | 2.47 (2.03 to 3)       |
| Anti-4, Post-Dose 2<br>[N=37;37;46;40;41]    | 0.05 (0.03 to 0.08) | 0.03 (0.02 to 0.03) | 6.42 (5.23 to 7.87)    | 6.6 (5.12 to 8.52)     |
| Anti-4, Pre-booster<br>[N=41;41;46;41;40]    | 0.05 (0.03 to 0.07) | 0.03 (0.03 to 0.03) | 2.3 (1.82 to 2.91)     | 2.36 (1.79 to 3.11)    |
| Anti-4, Post-booster<br>[N=40;41;47;41;41]   | 0.05 (0.03 to 0.07) | 0.04 (0.03 to 0.05) | 5.26 (4.14 to 6.69)    | 5.61 (4.46 to 7.07)    |
| Anti-5, Post-Dose 2<br>[N=31;34;44;39;41]    | 0.06 (0.04 to 0.08) | 0.06 (0.05 to 0.08) | 2.42 (1.85 to 3.17)    | 2.41 (1.85 to 3.13)    |
| Anti-5, Pre-booster<br>[N=42;43;45;41;40]    | 0.07 (0.05 to 0.1)  | 0.06 (0.05 to 0.08) | 1.08 (0.83 to 1.41)    | 1.05 (0.81 to 1.36)    |
| Anti-5, Post-booster<br>[N=41;43;47;41;41]   | 0.07 (0.05 to 0.09) | 0.07 (0.05 to 0.09) | 3.57 (2.79 to 4.57)    | 3.45 (2.7 to 4.41)     |
| Anti-6B, Post-Dose 2<br>[N=43;39;46;40;41]   | 0.04 (0.03 to 0.05) | 0.03 (0.02 to 0.03) | 0.55 (0.37 to 0.81)    | 0.48 (0.32 to 0.72)    |
| Anti-6B, Pre-booster<br>[N=42;41;44;40;40]   | 0.04 (0.03 to 0.05) | 0.04 (0.03 to 0.05) | 0.39 (0.28 to 0.54)    | 0.42 (0.3 to 0.59)     |
| Anti-6B, Post-booster<br>[N=41;42;47;41;40]  | 0.04 (0.03 to 0.06) | 0.04 (0.03 to 0.06) | 1.08 (0.74 to 1.57)    | 1.14 (0.83 to 1.57)    |
| Anti-7F, Post-Dose 2<br>[N=37;38;46;40;41]   | 0.04 (0.03 to 0.06) | 0.04 (0.03 to 0.04) | 5.03 (4.16 to 6.09)    | 4.73 (3.89 to 5.74)    |
| Anti-7F, Pre-booster<br>[N=42;44;46;41;40]   | 0.04 (0.03 to 0.06) | 0.03 (0.03 to 0.04) | 2.6 (2.14 to 3.15)     | 2.36 (1.94 to 2.86)    |
| Anti-7F, Post-booster<br>[N=41;43;47;41;41]  | 0.04 (0.03 to 0.06) | 0.04 (0.03 to 0.05) | 5.9 (4.83 to 7.2)      | 5.25 (4.36 to 6.32)    |
| Anti-9V, Post-Dose 2<br>[N=42;40;46;40;41]   | 0.04 (0.03 to 0.06) | 0.03 (0.02 to 0.03) | 2.81 (2.24 to 3.51)    | 2.49 (1.95 to 3.19)    |
| Anti-9V, Pre-booster<br>[N=41;42;45;41;40]   | 0.04 (0.03 to 0.05) | 0.03 (0.03 to 0.04) | 1.44 (1.15 to 1.81)    | 1.26 (0.94 to 1.67)    |
| Anti-9V, Post-booster<br>[N=39;40;47;41;40]  | 0.04 (0.03 to 0.06) | 0.03 (0.02 to 0.04) | 3.13 (2.48 to 3.93)    | 3.21 (2.45 to 4.19)    |
| Anti-14, Post-Dose 2<br>[N=43;36;46;40;41]   | 0.1 (0.07 to 0.14)  | 0.09 (0.06 to 0.14) | 5.18 (3.91 to 6.86)    | 3.78 (2.92 to 4.91)    |
| Anti-14, Pre-booster<br>[N=40;40;46;40;40]   | 0.11 (0.08 to 0.17) | 0.11 (0.07 to 0.18) | 2.86 (2.25 to 3.65)    | 2.3 (1.81 to 2.91)     |
| Anti-14, Post-booster<br>[N=42;43;47;41;41]  | 0.13 (0.09 to 0.18) | 0.16 (0.1 to 0.26)  | 7.74 (6.03 to 9.94)    | 6.62 (5.22 to 8.4)     |
| Anti-18C, Post-Dose 2<br>[N=39;39;45;40;41]  | 0.04 (0.03 to 0.06) | 0.04 (0.03 to 0.05) | 13.92 (10.75 to 18.03) | 16.92 (13.61 to 21.03) |
| Anti-18C, Pre-booster<br>[N=41;42;45;41;40]  | 0.05 (0.03 to 0.07) | 0.04 (0.03 to 0.05) | 4.94 (3.83 to 6.38)    | 5.51 (4.3 to 7.05)     |
| Anti-18C, Post-booster<br>[N=42;44;47;41;40] | 0.05 (0.03 to 0.07) | 0.05 (0.03 to 0.07) | 16.12 (12.2 to 21.32)  | 21.98 (16.67 to 28.99) |
| Anti-19F, Post-Dose 2<br>[N=33;35;45;39;41]  | 0.05 (0.03 to 0.08) | 0.06 (0.03 to 0.12) | 8.6 (6.37 to 11.63)    | 10.08 (7.21 to 14.09)  |
| Anti-19F, Pre-booster<br>[N=38;40;46;41;40]  | 0.06 (0.04 to 0.1)  | 0.05 (0.03 to 0.09) | 4.15 (2.94 to 5.85)    | 4.72 (3.54 to 6.3)     |
| Anti-19F, Post-booster<br>[N=41;40;47;41;41] | 0.06 (0.04 to 0.09) | 0.07 (0.04 to 0.13) | 10.46 (7.35 to 14.88)  | 14.38 (10.53 to 19.63) |
| Anti-23F, Post-Dose 2<br>[N=38;38;45;39;41]  | 0.03 (0.03 to 0.04) | 0.04 (0.03 to 0.05) | 1.19 (0.82 to 1.74)    | 0.91 (0.62 to 1.33)    |
| Anti-23F, Pre-booster<br>[N=42;41;45;41;40]  | 0.03 (0.03 to 0.04) | 0.04 (0.03 to 0.06) | 0.71 (0.5 to 0.99)     | 0.62 (0.45 to 0.85)    |
| Anti-23F, Post-booster<br>[N=41;43;47;41;40] | 0.03 (0.03 to 0.04) | 0.05 (0.03 to 0.06) | 1.92 (1.42 to 2.6)     | 2.04 (1.56 to 2.65)    |
| Anti-6A, Post-Dose 2<br>[N=33;37;43;40;41]   | 0.04 (0.03 to 0.07) | 0.03 (0.03 to 0.04) | 0.32 (0.2 to 0.51)     | 0.27 (0.16 to 0.45)    |

|                                              |                     |                     |                     |                     |
|----------------------------------------------|---------------------|---------------------|---------------------|---------------------|
| Anti-6A, Pre-booster<br>[N=42;42;44;41;40]   | 0.04 (0.03 to 0.06) | 0.04 (0.03 to 0.04) | 0.24 (0.17 to 0.34) | 0.24 (0.15 to 0.38) |
| Anti-6A, Post-booster<br>[N=42;40;47;41;40]  | 0.04 (0.03 to 0.06) | 0.04 (0.03 to 0.06) | 0.53 (0.35 to 0.79) | 0.56 (0.36 to 0.87) |
| Anti-19A, Post-Dose 2<br>[N=33;35;43;39;41]  | 0.07 (0.04 to 0.12) | 0.05 (0.03 to 0.06) | 1.08 (0.71 to 1.62) | 0.97 (0.63 to 1.48) |
| Anti-19A, Pre-booster<br>[N=43;42;44;41;40]  | 0.07 (0.04 to 0.1)  | 0.05 (0.04 to 0.06) | 0.85 (0.61 to 1.17) | 0.68 (0.47 to 0.98) |
| Anti-19A, Post-booster<br>[N=41;39;47;41;41] | 0.07 (0.05 to 0.11) | 0.05 (0.04 to 0.07) | 2.76 (1.92 to 3.96) | 2.98 (2.08 to 4.26) |

| End point values                            | 10Pn Group          |  |  |  |
|---------------------------------------------|---------------------|--|--|--|
| Subject group type                          | Reporting group     |  |  |  |
| Number of subjects analysed                 | 41                  |  |  |  |
| Units: µg/mL                                |                     |  |  |  |
| geometric mean (confidence interval 95%)    |                     |  |  |  |
| Anti-1, Post-Dose 2<br>[N=40;36;46;40;41]   | 2.13 (1.62 to 2.79) |  |  |  |
| Anti-1, Pre-booster<br>[N=43;42;45;40;40]   | 0.73 (0.55 to 0.97) |  |  |  |
| Anti-1, Post-booster<br>[N=40;41;47;41;41]  | 2.4 (1.85 to 3.12)  |  |  |  |
| Anti-4, Post-Dose 2<br>[N=37;37;46;40;41]   | 5.67 (4.56 to 7.06) |  |  |  |
| Anti-4, Pre-booster<br>[N=41;41;46;41;40]   | 2.11 (1.68 to 2.64) |  |  |  |
| Anti-4, Post-booster<br>[N=40;41;47;41;41]  | 5.18 (4.05 to 6.63) |  |  |  |
| Anti-5, Post-Dose 2<br>[N=31;34;44;39;41]   | 2.36 (1.88 to 2.97) |  |  |  |
| Anti-5, Pre-booster<br>[N=42;43;45;41;40]   | 1.18 (0.94 to 1.48) |  |  |  |
| Anti-5, Post-booster<br>[N=41;43;47;41;41]  | 3.84 (2.98 to 4.95) |  |  |  |
| Anti-6B, Post-Dose 2<br>[N=43;39;46;40;41]  | 0.55 (0.39 to 0.78) |  |  |  |
| Anti-6B, Pre-booster<br>[N=42;41;44;40;40]  | 0.46 (0.34 to 0.62) |  |  |  |
| Anti-6B, Post-booster<br>[N=41;42;47;41;40] | 1.08 (0.78 to 1.52) |  |  |  |
| Anti-7F, Post-Dose 2<br>[N=37;38;46;40;41]  | 3.72 (3.17 to 4.36) |  |  |  |
| Anti-7F, Pre-booster<br>[N=42;44;46;41;40]  | 2.14 (1.82 to 2.51) |  |  |  |
| Anti-7F, Post-booster<br>[N=41;43;47;41;41] | 4.65 (3.77 to 5.72) |  |  |  |
| Anti-9V, Post-Dose 2<br>[N=42;40;46;40;41]  | 1.55 (1.21 to 2)    |  |  |  |
| Anti-9V, Pre-booster<br>[N=41;42;45;41;40]  | 0.95 (0.73 to 1.24) |  |  |  |
| Anti-9V, Post-booster<br>[N=39;40;47;41;40] | 2.18 (1.71 to 2.79) |  |  |  |
| Anti-14, Post-Dose 2<br>[N=43;36;46;40;41]  | 4.63 (3.71 to 5.77) |  |  |  |
| Anti-14, Pre-booster<br>[N=40;40;46;40;40]  | 2.71 (2.17 to 3.38) |  |  |  |

|                                              |                       |  |  |  |
|----------------------------------------------|-----------------------|--|--|--|
| Anti-14, Post-booster<br>[N=42;43;47;41;41]  | 5.98 (4.68 to 7.63)   |  |  |  |
| Anti-18C, Post-Dose 2<br>[N=39;39;45;40;41]  | 12.56 (9.8 to 16.1)   |  |  |  |
| Anti-18C, Pre-booster<br>[N=41;42;45;41;40]  | 4.79 (3.69 to 6.21)   |  |  |  |
| Anti-18C, Post-booster<br>[N=42;44;47;41;40] | 14.62 (10.9 to 19.6)  |  |  |  |
| Anti-19F, Post-Dose 2<br>[N=33;35;45;39;41]  | 8.87 (6.2 to 12.7)    |  |  |  |
| Anti-19F, Pre-booster<br>[N=38;40;46;41;40]  | 4.33 (3.06 to 6.12)   |  |  |  |
| Anti-19F, Post-booster<br>[N=41;40;47;41;41] | 11.32 (7.94 to 16.13) |  |  |  |
| Anti-23F, Post-Dose 2<br>[N=38;38;45;39;41]  | 0.73 (0.54 to 0.98)   |  |  |  |
| Anti-23F, Pre-booster<br>[N=42;41;45;41;40]  | 0.51 (0.39 to 0.67)   |  |  |  |
| Anti-23F, Post-booster<br>[N=41;43;47;41;40] | 1.47 (1.04 to 2.06)   |  |  |  |
| Anti-6A, Post-Dose 2<br>[N=33;37;43;40;41]   | 0.31 (0.2 to 0.48)    |  |  |  |
| Anti-6A, Pre-booster<br>[N=42;42;44;41;40]   | 0.27 (0.18 to 0.4)    |  |  |  |
| Anti-6A, Post-booster<br>[N=42;40;47;41;40]  | 0.58 (0.37 to 0.9)    |  |  |  |
| Anti-19A, Post-Dose 2<br>[N=33;35;43;39;41]  | 0.93 (0.61 to 1.43)   |  |  |  |
| Anti-19A, Pre-booster<br>[N=43;42;44;41;40]  | 0.62 (0.42 to 0.93)   |  |  |  |
| Anti-19A, Post-booster<br>[N=41;39;47;41;41] | 2.06 (1.3 to 3.25)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes and cross-reactive serotypes

|                 |                                                                                                    |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes and cross-reactive serotypes |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Seropositivity status, defined as Opsonophagocytic activity against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and cross-reactive serotypes 6A and 19A  $\geq 8$

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

End point timeframe:

one month post-dose 2, prior to the booster dose and one month post-booster

| End point values                           | dPly-PhtD-LD Group      | dPly-PhtD-HD Group      | 10Pn-dPly-PhtD-LD Group   | 10Pn-dPly-PhtD-HD Group   |
|--------------------------------------------|-------------------------|-------------------------|---------------------------|---------------------------|
| Subject group type                         | Reporting group         | Reporting group         | Reporting group           | Reporting group           |
| Number of subjects analysed                | 35                      | 36                      | 37                        | 36                        |
| Units: Titers                              |                         |                         |                           |                           |
| geometric mean (confidence interval 95%)   |                         |                         |                           |                           |
| OPSONO-1, Post-Dose 2 [N=27;33;35;30;30]   | 4 (4 to 4)              | 5.4 (3.8 to 7.8)        | 71.8 (40.9 to 126.1)      | 48.2 (26.5 to 87.6)       |
| OPSONO-1, Pre-booster [N=35;35;33;35;34]   | 4 (4 to 4)              | 4.3 (3.7 to 5)          | 23 (13.1 to 40.3)         | 12.4 (7.6 to 20.3)        |
| OPSONO-1, Post-booster [N=31;35;37;36;37]  | 5.2 (4 to 6.9)          | 8.1 (4.8 to 13.7)       | 169.5 (96.1 to 298.8)     | 200 (138.2 to 289.4)      |
| OPSONO-4, Post-Dose 2 [N=20;29;32;29;29]   | 7 (3.1 to 15.6)         | 8.9 (4.5 to 17.6)       | 1260.2 (856.1 to 1855.2)  | 1197.9 (784.1 to 1830.2)  |
| OPSONO-4, Pre-booster [N=28;29;29;33;30]   | 12.6 (5.6 to 28.4)      | 16.2 (7 to 37.2)        | 247.9 (117.4 to 523.2)    | 259.9 (120.6 to 560)      |
| OPSONO-4, Post-booster [N=24;31;35;32;34]  | 15.5 (6.1 to 39.5)      | 17.8 (7.3 to 43.4)      | 1206.2 (888.9 to 1636.8)  | 1385 (974.5 to 1968.4)    |
| OPSONO-5, Post-Dose 2 [N=27;33;33;30;31]   | 4 (4 to 4)              | 4.7 (3.4 to 6.5)        | 43.8 (27.1 to 70.8)       | 37.3 (21.7 to 64)         |
| OPSONO-5, Pre-booster [N=34;35;34;33;34]   | 4.5 (3.5 to 5.8)        | 4 (4 to 4)              | 12.8 (8.2 to 19.9)        | 14.8 (9.6 to 23)          |
| OPSONO-5, Post-booster [N=30;36;37;34;36]  | 4 (4 to 4)              | 5.1 (3.8 to 6.7)        | 99.3 (62.1 to 158.8)      | 110.4 (73.1 to 166.8)     |
| OPSONO-6B, Post-Dose 2 [N=16;21;27;25;28]  | 15 (4.2 to 53.1)        | 23.4 (6.1 to 90.3)      | 361.9 (120 to 1091.7)     | 527.5 (202.6 to 1372.9)   |
| OPSONO-6B, Pre-booster [N=23;27;30;30;30]  | 56.7 (16.2 to 198.4)    | 61.6 (19.2 to 197.3)    | 213.8 (79 to 578.1)       | 513.1 (243.9 to 1079.6)   |
| OPSONO-6B, Post-booster [N=24;33;33;34;35] | 26.1 (7.7 to 88.7)      | 30.8 (11.2 to 84.7)     | 804.6 (343.5 to 1884.9)   | 982.7 (527.6 to 1830.4)   |
| OPSONO-7F, Post-Dose 2 [N=27;33;33;29;30]  | 734.6 (369.7 to 1459.6) | 807.4 (445 to 1465.2)   | 5703.7 (4143.6 to 7851.2) | 4936.6 (3320.7 to 7338.7) |
| OPSONO-7F, Pre-booster [N=33;30;32;34;33]  | 670.4 (317.5 to 1415.6) | 462.3 (187.5 to 1139.8) | 2450.1 (1637.4 to 3666.2) | 2713.5 (1836.1 to 4010.1) |
| OPSONO-7F, Post-booster [N=30;35;35;33;36] | 936.8 (510 to 1720.7)   | 785.5 (428 to 1441.6)   | 4109.3 (3086.9 to 5470.3) | 5730.4 (4262 to 7704.7)   |
| OPSONO-9V, Post-Dose 2 [N=22;29;34;29;30]  | 26.5 (8.2 to 85.9)      | 50.1 (17.5 to 143.7)    | 4455 (2803.3 to 7079.9)   | 3542.8 (2271.5 to 5525.5) |
| OPSONO--9V, Pre-booster [N=30;28;32;33;32] | 172.4 (68.9 to 431.4)   | 172 (57.6 to 513.2)     | 2126.1 (1140.2 to 3964.4) | 2622.4 (1786.7 to 3849)   |
| OPSONO-9V, Post-booster [N=26;32;37;34;36] | 173.5 (59.1 to 509.8)   | 137.6 (51.7 to 366)     | 4643.1 (3418.3 to 6306.9) | 5802.4 (4453 to 7560.8)   |
| OPSONO-14, Post-Dose 2 [N=18;23;33;29;31]  | 21.1 (6.7 to 66.8)      | 11.9 (4.7 to 30.4)      | 3324.8 (2324.8 to 4754.8) | 2580.7 (1788.4 to 3724)   |
| OPSONO-14, Pre-booster [N=30;30;32;34;33]  | 21 (8.5 to 51.6)        | 27.9 (10.4 to 75.1)     | 1390.5 (615.7 to 3140.4)  | 1725.8 (972.1 to 3064)    |
| OPSONO-14, Post-booster [N=27;33;34;36;37] | 32.3 (11.5 to 90.9)     | 46.7 (17 to 127.8)      | 2911.6 (1841.3 to 4604)   | 3729.8 (2693.2 to 5165.4) |
| OPSONO-18C, Post-Dose 2 [N=24;29;33;28;27] | 4 (4 to 4)              | 7.4 (3.7 to 15.1)       | 1398.3 (810.6 to 2412)    | 2538.4 (1787.3 to 3605)   |
| OPSONO-18C, Pre-booster [N=33;33;31;34;34] | 5.4 (3.4 to 8.3)        | 5 (3.7 to 6.8)          | 420.1 (192.8 to 915.3)    | 1041 (699.6 to 1548.9)    |

|                                                |                      |                       |                           |                           |
|------------------------------------------------|----------------------|-----------------------|---------------------------|---------------------------|
| OPSONO-18C, Post-booster<br>[N=26;32;34;32;33] | 6 (3.3 to 10.7)      | 8 (4.4 to 14.6)       | 1764.6 (1243.6 to 2503.8) | 2640.6 (2083.3 to 3346.8) |
| OPSONO-19F, Pre-booster<br>[N=31;34;30;34;34]  | 5 (3.1 to 8.2)       | 8 (4.3 to 14.7)       | 794.3 (476.6 to 1324)     | 420.7 (197.4 to 896.4)    |
| OPSONO-19F, Post-booster<br>[N=30;36;36;34;34] | 4.9 (3.5 to 6.8)     | 4.4 (3.7 to 5.2)      | 173.3 (86.1 to 349)       | 210.1 (118.4 to 373)      |
| OPSONO-19F, Post-Dose 2<br>[N=17;28;32;28;27]  | 5.6 (3.4 to 9.1)     | 7.3 (4.3 to 12.6)     | 1248.5 (740.4 to 2105.3)  | 1823.7 (1252.9 to 2654.5) |
| OPSONO-23F, Post-Dose 2<br>[N=20;28;34;28;29]  | 17.9 (5.1 to 62.9)   | 107.8 (28.1 to 412.8) | 1735.5 (833.6 to 3613.3)  | 3621.8 (2431.4 to 5395.2) |
| OPSONO-23F, Pre-booster<br>[N=30;33;32;33;33]  | 23.2 (7.6 to 70.3)   | 136.3 (36.1 to 514.6) | 989.7 (419.2 to 2336.8)   | 1635.9 (691.7 to 3868.8)  |
| OPSONO-23F, Post-booster<br>[N=25;33;35;35;36] | 68.6 (17.3 to 271.2) | 106.7 (28.5 to 399.4) | 3598.5 (2422.2 to 5345.9) | 6108 (4335.9 to 8604.5)   |
| OPSONO-6A, Post-Dose 2<br>[N=19;26;31;21;27]   | 9.3 (3.5 to 24.7)    | 5.7 (3.4 to 9.5)      | 225.3 (83.3 to 608.8)     | 186.2 (55.3 to 627.2)     |
| OPSONO-6A, Pre-booster<br>[N=27;30;31;33;32]   | 18.4 (7.6 to 44.5)   | 9.4 (4.5 to 19.5)     | 58.9 (21.6 to 160.3)      | 99.4 (39.9 to 247.8)      |
| OPSONO-6A, Post-booster<br>[N=22;32;34;31;32]  | 11.8 (4.7 to 29.5)   | 17.3 (7.9 to 37.9)    | 308 (141 to 672.9)        | 348.2 (154.9 to 782.5)    |
| OPSONO-19A, Post-Dose 2<br>[N=25;31;34;28;29]  | 5.8 (3.4 to 9.9)     | 4.6 (3.7 to 5.6)      | 246 (109.7 to 551.7)      | 363.2 (202.1 to 652.8)    |
| OPSONO-19A, Pre-booster<br>[N=35;35;33;35;32]  | 6 (4 to 9.1)         | 4.5 (3.8 to 5.3)      | 56.7 (25.2 to 127.9)      | 76.4 (36.3 to 160.7)      |
| OPSONO-19A, Post-booster<br>[N=30;36;34;34;34] | 6.7 (4.3 to 10.3)    | 6.3 (4.4 to 9.1)      | 746.3 (407.8 to 1365.6)   | 989.3 (652.5 to 1500)     |

| End point values                             | 10Pn Group               |  |  |  |
|----------------------------------------------|--------------------------|--|--|--|
| Subject group type                           | Reporting group          |  |  |  |
| Number of subjects analysed                  | 37                       |  |  |  |
| Units: Titers                                |                          |  |  |  |
| geometric mean (confidence interval 95%)     |                          |  |  |  |
| OPSONO-1, Post-Dose 2<br>[N=27;33;35;30;30]  | 90 (52.9 to 153)         |  |  |  |
| OPSONO-1, Pre-booster<br>[N=35;35;33;35;34]  | 19.3 (11.1 to 33.6)      |  |  |  |
| OPSONO-1, Post-booster<br>[N=31;35;37;36;37] | 206.9 (123.1 to 347.5)   |  |  |  |
| OPSONO-4, Post-Dose 2<br>[N=20;29;32;29;29]  | 1220.4 (913.8 to 1629.9) |  |  |  |
| OPSONO-4, Pre-booster<br>[N=28;29;29;33;30]  | 478.9 (309.3 to 741.3)   |  |  |  |
| OPSONO-4, Post-booster<br>[N=24;31;35;32;34] | 1476 (1076 to 2024.6)    |  |  |  |
| OPSONO-5, Post-Dose 2<br>[N=27;33;33;30;31]  | 42 (26.6 to 66.4)        |  |  |  |
| OPSONO-5, Pre-booster<br>[N=34;35;34;33;34]  | 17 (10.9 to 26.4)        |  |  |  |
| OPSONO-5, Post-booster<br>[N=30;36;37;34;36] | 160.7 (113 to 228.7)     |  |  |  |
| OPSONO-6B, Post-Dose 2<br>[N=16;21;27;25;28] | 915.3 (543.4 to 1541.8)  |  |  |  |

|                                                |                               |  |  |  |
|------------------------------------------------|-------------------------------|--|--|--|
| OPSONO-6B, Pre-booster<br>[N=23;27;30;30;30]   | 371.9 (172.5<br>to 801.8)     |  |  |  |
| OPSONO-6B, Post-booster<br>[N=24;33;33;34;35]  | 1523.1 (875.8<br>to 2649)     |  |  |  |
| OPSONO-7F, Post-Dose 2<br>[N=27;33;33;29;30]   | 6154.4 (4244.4<br>to 8923.7)  |  |  |  |
| OPSONO-7F, Pre-booster<br>[N=33;30;32;34;33]   | 3844.5 (2725.7<br>to 5422.4)  |  |  |  |
| OPSONO-7F, Post-booster<br>[N=30;35;35;33;36]  | 7404.7 (5271.1<br>to 10401.8) |  |  |  |
| OPSONO-9V, Post-Dose 2<br>[N=22;29;34;29;30]   | 3947.2 (2612.7<br>to 5963.5)  |  |  |  |
| OPSONO--9V, Pre-booster<br>[N=30;28;32;33;32]  | 3450 (2357.5<br>to 5048.7)    |  |  |  |
| OPSONO-9V, Post-booster<br>[N=26;32;37;34;36]  | 6016.6 (4617.2<br>to 7840)    |  |  |  |
| OPSONO-14, Post-Dose 2<br>[N=18;23;33;29;31]   | 2487.6 (1703.4<br>to 3632.7)  |  |  |  |
| OPSONO-14, Pre-booster<br>[N=30;30;32;34;33]   | 1776.6 (1009.5<br>to 3126.5)  |  |  |  |
| OPSONO-14, Post-booster<br>[N=27;33;34;36;37]  | 3094 (2353.3<br>to 4068)      |  |  |  |
| OPSONO-18C, Post-Dose 2<br>[N=24;29;33;28;27]  | 1905.4 (1271.4<br>to 2855.6)  |  |  |  |
| OPSONO-18C, Pre-booster<br>[N=33;33;31;34;34]  | 766.4 (468.4<br>to 1253.8)    |  |  |  |
| OPSONO-18C, Post-booster<br>[N=26;32;34;32;33] | 2123.4 (1493<br>to 3020.1)    |  |  |  |
| OPSONO-19F, Pre-booster<br>[N=31;34;30;34;34]  | 625.4 (266.5<br>to 1467.7)    |  |  |  |
| OPSONO-19F, Post-booster<br>[N=30;36;36;34;34] | 260.7 (138 to<br>492.5)       |  |  |  |
| OPSONO-19F, Post-Dose 2<br>[N=17;28;32;28;27]  | 1625.3 (931.7<br>to 2835.3)   |  |  |  |
| OPSONO-23F, Post-Dose 2<br>[N=20;28;34;28;29]  | 2502.5 (1610.5<br>to 3888.6)  |  |  |  |
| OPSONO-23F, Pre-booster<br>[N=30;33;32;33;33]  | 897.4 (381.6<br>to 2110.4)    |  |  |  |
| OPSONO-23F, Post-booster<br>[N=25;33;35;35;36] | 5296.1 (3857.9<br>to 7270.4)  |  |  |  |
| OPSONO-6A, Post-Dose 2<br>[N=19;26;31;21;27]   | 364.5 (158.7<br>to 837.1)     |  |  |  |
| OPSONO-6A, Pre-booster<br>[N=27;30;31;33;32]   | 221.7 (93.8 to<br>524)        |  |  |  |
| OPSONO-6A, Post-booster<br>[N=22;32;34;31;32]  | 554.3 (248.3<br>to 1237.6)    |  |  |  |
| OPSONO-19A, Post-Dose 2<br>[N=25;31;34;28;29]  | 349.9 (177.1<br>to 691.6)     |  |  |  |
| OPSONO-19A, Pre-booster<br>[N=35;35;33;35;32]  | 87.8 (40.6 to<br>189.7)       |  |  |  |
| OPSONO-19A, Post-booster<br>[N=30;36;34;34;34] | 725.9 (367.8<br>to 1432.6)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Antibody concentrations to protein D (Anti-PD)

|                                                                                                                   |                                                |
|-------------------------------------------------------------------------------------------------------------------|------------------------------------------------|
| End point title                                                                                                   | Antibody concentrations to protein D (Anti-PD) |
| End point description:                                                                                            |                                                |
| Seropositivity status, defined as anti-PD antibody concentrations $\geq 100$ ELISA units per millilitre (EL.U/mL) |                                                |
| End point type                                                                                                    | Secondary                                      |
| End point timeframe:                                                                                              |                                                |
| One month post-dose 2, prior to the booster dose and one month post-booster                                       |                                                |

| End point values                           | dPly-PhtD-LD Group   | dPly-PhtD-HD Group    | 10Pn-dPly-PhtD-LD Group   | 10Pn-dPly-PhtD-HD Group   |
|--------------------------------------------|----------------------|-----------------------|---------------------------|---------------------------|
| Subject group type                         | Reporting group      | Reporting group       | Reporting group           | Reporting group           |
| Number of subjects analysed                | 45                   | 45                    | 47                        | 41                        |
| Units: EL.U/mL                             |                      |                       |                           |                           |
| geometric mean (confidence interval 95%)   |                      |                       |                           |                           |
| Anti-PD Post-Dose 2<br>[N=45;43;45;39;41]  | 90.9 (71.1 to 116.3) | 100.4 (76.3 to 132.1) | 1105.4 (833.7 to 1465.7)  | 600.2 (426.5 to 844.7)    |
| Anti-PD Pre-booster<br>[N=44;45;46;40;40]  | 89.1 (71.8 to 110.7) | 118.2 (89.6 to 155.9) | 734.6 (523.9 to 1030.1)   | 463 (330.2 to 649.3)      |
| Anti-PD Post-booster<br>[N=44;43;47;41;41] | 97.9 (78 to 122.9)   | 130.6 (93.1 to 183.3) | 1882.6 (1407.4 to 2518.1) | 1474.6 (1103.7 to 1970.3) |

| End point values                           | 10Pn Group              |  |  |  |
|--------------------------------------------|-------------------------|--|--|--|
| Subject group type                         | Reporting group         |  |  |  |
| Number of subjects analysed                | 41                      |  |  |  |
| Units: EL.U/mL                             |                         |  |  |  |
| geometric mean (confidence interval 95%)   |                         |  |  |  |
| Anti-PD Post-Dose 2<br>[N=45;43;45;39;41]  | 860 (659.2 to 1121.9)   |  |  |  |
| Anti-PD Pre-booster<br>[N=44;45;46;40;40]  | 691.8 (527.6 to 907.1)  |  |  |  |
| Anti-PD Post-booster<br>[N=44;43;47;41;41] | 1963.8 (1560.1 to 2472) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Level of anti-dPly antibodies inhibiting Ply haemolysis activity

|                 |                                                                  |
|-----------------|------------------------------------------------------------------|
| End point title | Level of anti-dPly antibodies inhibiting Ply haemolysis activity |
|-----------------|------------------------------------------------------------------|

End point description:

Inhibition of haemolysis activity of pneumolysin (Ply) by anti-dPly antibodies was measured in vitro by mean of a haemolytic assay. The haemolysis activity could be followed by measuring the level of haemoglobin released. Anti-dPly titres (for inhibition of haemolytic activity)  $\geq 140$

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

End point timeframe:

one month post-dose 2, prior to the booster dose and one month post-booster

| End point values                               | dPly-PhtD-LD Group        | dPly-PhtD-HD Group        | 10Pn-dPly-PhtD-LD Group   | 10Pn-dPly-PhtD-HD Group   |
|------------------------------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Subject group type                             | Reporting group           | Reporting group           | Reporting group           | Reporting group           |
| Number of subjects analysed                    | 43                        | 38                        | 43                        | 39                        |
| Units: % of inhibition                         |                           |                           |                           |                           |
| geometric mean (confidence interval 95%)       |                           |                           |                           |                           |
| Anti-Hem-dPly Post-Dose 2 [N=43;38;43;39;40]   | 3080 (2555.3 to 3712.5)   | 2988.7 (2410.1 to 3706.2) | 1278.9 (1048.2 to 1560.3) | 1814 (1495.3 to 2200.8)   |
| Anti- Hem-dPly Pre-booster [N=37;37;37;34;35]  | 2441.1 (1867.1 to 3191.7) | 2193.7 (1737.3 to 2770)   | 1141.5 (950.6 to 1370.6)  | 1344.2 (1087.6 to 1661.3) |
| Anti- Hem-dPly Post-booster [N=31;32;36;32;30] | 4332.4 (3327.6 to 5640.4) | 5931.9 (4744.5 to 7416.4) | 1346.2 (1068.2 to 1696.5) | 2388.3 (1830.6 to 3115.9) |

| End point values                               | 10Pn Group              |  |  |  |
|------------------------------------------------|-------------------------|--|--|--|
| Subject group type                             | Reporting group         |  |  |  |
| Number of subjects analysed                    | 40                      |  |  |  |
| Units: % of inhibition                         |                         |  |  |  |
| geometric mean (confidence interval 95%)       |                         |  |  |  |
| Anti-Hem-dPly Post-Dose 2 [N=43;38;43;39;40]   | 913.2 (699.1 to 1192.8) |  |  |  |
| Anti- Hem-dPly Pre-booster [N=37;37;37;34;35]  | 995.9 (788.3 to 1258.2) |  |  |  |
| Anti- Hem-dPly Post-booster [N=31;32;36;32;30] | 818.6 (662.5 to 1011.5) |  |  |  |

## **Statistical analyses**

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms during the 4-day post-primary and post booster vaccination period; Unsolicited AEs during the 31-day post-primary and post-booster vaccination period; SAEs: during the whole study period.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | dPly-PhtD-HD Group |
|-----------------------|--------------------|

Reporting group description: -

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | dPly-PhtD-LD Group |
|-----------------------|--------------------|

Reporting group description: -

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | 10Pn-dPly-PhtD-HD Group |
|-----------------------|-------------------------|

Reporting group description: -

|                       |            |
|-----------------------|------------|
| Reporting group title | 10Pn Group |
|-----------------------|------------|

Reporting group description: -

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | 10Pn-dPly-PhtD-LD Group |
|-----------------------|-------------------------|

Reporting group description: -

| <b>Serious adverse events</b>                     | dPly-PhtD-HD Group | dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|---------------------------------------------------|--------------------|--------------------|-------------------------|
| Total subjects affected by serious adverse events |                    |                    |                         |
| subjects affected / exposed                       | 3 / 52 (5.77%)     | 5 / 51 (9.80%)     | 0 / 51 (0.00%)          |
| number of deaths (all causes)                     | 0                  | 0                  | 0                       |
| number of deaths resulting from adverse events    |                    |                    |                         |
| Injury, poisoning and procedural complications    |                    |                    |                         |
| Concussion                                        |                    |                    |                         |
| subjects affected / exposed                       | 0 / 52 (0.00%)     | 0 / 51 (0.00%)     | 0 / 51 (0.00%)          |
| occurrences causally related to treatment / all   | 0 / 0              | 0 / 0              | 0 / 0                   |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0              | 0 / 0                   |
| Accidental exposure                               |                    |                    |                         |
| subjects affected / exposed                       | 0 / 52 (0.00%)     | 0 / 51 (0.00%)     | 0 / 51 (0.00%)          |
| occurrences causally related to treatment / all   | 0 / 0              | 0 / 0              | 0 / 0                   |
| deaths causally related to treatment / all        | 0 / 0              | 0 / 0              | 0 / 0                   |
| Foreign body                                      |                    |                    |                         |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 52 (0.00%) | 1 / 51 (1.96%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Open wound                                           |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders                                   |                |                |                |
| Haematoma                                            |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 1 / 51 (1.96%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                             |                |                |                |
| Febrile convulsion                                   |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Pyrexia                                              |                |                |                |
| subjects affected / exposed                          | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Ear and labyrinth disorders                          |                |                |                |
| Ear haemorrhage                                      |                |                |                |
| subjects affected / exposed                          | 1 / 52 (1.92%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                           |                |                |                |
| Enterocolitis                                        |                |                |                |
| subjects affected / exposed                          | 1 / 52 (1.92%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders      |                |                |                |
| Adenoidal hypertrophy                                |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| Affective disorder                              |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 51 (1.96%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Gastroenteritis salmonella                      |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 51 (1.96%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 51 (1.96%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchopneumonia                                |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Laryngitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 1 / 51 (1.96%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oral herpes                                     |                |                |                |
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pharyngo-tonsillitis                            |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 52 (1.92%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Type 1 diabetes mellitus                        |                |                |                |
| subjects affected / exposed                     | 0 / 52 (0.00%) | 0 / 51 (0.00%) | 0 / 51 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | 10Pn Group     | 10Pn-dPly-PhtD-LD Group |  |
|---------------------------------------------------|----------------|-------------------------|--|
| Total subjects affected by serious adverse events |                |                         |  |
| subjects affected / exposed                       | 4 / 51 (7.84%) | 5 / 52 (9.62%)          |  |
| number of deaths (all causes)                     | 0              | 0                       |  |
| number of deaths resulting from adverse events    |                |                         |  |
| Injury, poisoning and procedural complications    |                |                         |  |
| Concussion                                        |                |                         |  |
| subjects affected / exposed                       | 1 / 51 (1.96%) | 1 / 52 (1.92%)          |  |
| occurrences causally related to treatment / all   | 0 / 1          | 0 / 1                   |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0                   |  |
| Accidental exposure                               |                |                         |  |
| subjects affected / exposed                       | 0 / 51 (0.00%) | 1 / 52 (1.92%)          |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1                   |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0                   |  |
| Foreign body                                      |                |                         |  |
| subjects affected / exposed                       | 0 / 51 (0.00%) | 0 / 52 (0.00%)          |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0                   |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0                   |  |
| Open wound                                        |                |                         |  |

|                                                      |                |                |  |
|------------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                          | 1 / 51 (1.96%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Vascular disorders                                   |                |                |  |
| Haematoma                                            |                |                |  |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                             |                |                |  |
| Febrile convulsion                                   |                |                |  |
| subjects affected / exposed                          | 1 / 51 (1.96%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Pyrexia                                              |                |                |  |
| subjects affected / exposed                          | 1 / 51 (1.96%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Ear and labyrinth disorders                          |                |                |  |
| Ear haemorrhage                                      |                |                |  |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                           |                |                |  |
| Enterocolitis                                        |                |                |  |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders      |                |                |  |
| Adenoidal hypertrophy                                |                |                |  |
| subjects affected / exposed                          | 0 / 51 (0.00%) | 1 / 52 (1.92%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                                |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Affective disorder                              |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Gastroenteritis salmonella                      |                |                |  |
| subjects affected / exposed                     | 1 / 51 (1.96%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchitis                                      |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchopneumonia                                |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 1 / 52 (1.92%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastroenteritis                                 |                |                |  |
| subjects affected / exposed                     | 1 / 51 (1.96%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Laryngitis                                      |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Oral herpes                                     |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pharyngo-tonsillitis                            |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 0 / 52 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Viral infection                                 |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 51 (0.00%) | 1 / 52 (1.92%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Type 1 diabetes mellitus                        |                |                |  |
| subjects affected / exposed                     | 0 / 51 (0.00%) | 1 / 52 (1.92%) |  |
| 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>                     | dPly-PhtD-HD Group | dPly-PhtD-LD Group | 10Pn-dPly-PhtD-HD Group |
|-------------------------------------------------------|--------------------|--------------------|-------------------------|
| Total subjects affected by non-serious adverse events |                    |                    |                         |
| subjects affected / exposed                           | 30 / 52 (57.69%)   | 27 / 51 (52.94%)   | 36 / 51 (70.59%)        |
| General disorders and administration site conditions  |                    |                    |                         |
| Pain Primary                                          |                    |                    |                         |
| alternative assessment type: Systematic               |                    |                    |                         |
| subjects affected / exposed                           | 28 / 52 (53.85%)   | 27 / 51 (52.94%)   | 33 / 51 (64.71%)        |
| occurrences (all)                                     | 28                 | 27                 | 33                      |
| Redness Primary                                       |                    |                    |                         |
| alternative assessment type: Systematic               |                    |                    |                         |
| subjects affected / exposed                           | 30 / 52 (57.69%)   | 24 / 51 (47.06%)   | 33 / 51 (64.71%)        |
| occurrences (all)                                     | 30                 | 24                 | 33                      |
| Swelling Primary                                      |                    |                    |                         |
| alternative assessment type: Systematic               |                    |                    |                         |
| subjects affected / exposed                           | 11 / 52 (21.15%)   | 17 / 51 (33.33%)   | 21 / 51 (41.18%)        |
| occurrences (all)                                     | 11                 | 17                 | 21                      |
| Pain Booster                                          |                    |                    |                         |
| alternative assessment type: Systematic               |                    |                    |                         |
| subjects affected / exposed                           | 22 / 52 (42.31%)   | 18 / 51 (35.29%)   | 26 / 51 (50.98%)        |
| occurrences (all)                                     | 22                 | 18                 | 26                      |
| Redness Booster                                       |                    |                    |                         |
| alternative assessment type: Systematic               |                    |                    |                         |

|                                            |                  |                  |                  |
|--------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                | 20 / 52 (38.46%) | 19 / 51 (37.25%) | 22 / 51 (43.14%) |
| occurrences (all)                          | 20               | 19               | 22               |
| Swelling Booster                           |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 8 / 52 (15.38%)  | 11 / 51 (21.57%) | 15 / 51 (29.41%) |
| occurrences (all)                          | 8                | 11               | 15               |
| Drowsiness Primary                         |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 21 / 52 (40.38%) | 25 / 51 (49.02%) | 28 / 51 (54.90%) |
| occurrences (all)                          | 21               | 25               | 28               |
| Irritability Primary                       |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 23 / 52 (44.23%) | 26 / 51 (50.98%) | 36 / 51 (70.59%) |
| occurrences (all)                          | 23               | 26               | 36               |
| Loss of appetite Primary                   |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 15 / 52 (28.85%) | 19 / 51 (37.25%) | 19 / 51 (37.25%) |
| occurrences (all)                          | 15               | 19               | 19               |
| Temperature/Rectally Primary               |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 16 / 52 (30.77%) | 13 / 51 (25.49%) | 18 / 51 (35.29%) |
| occurrences (all)                          | 16               | 13               | 18               |
| Drowsiness Booster                         |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 13 / 52 (25.00%) | 13 / 51 (25.49%) | 12 / 51 (23.53%) |
| occurrences (all)                          | 13               | 13               | 12               |
| Irritability Booster                       |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 17 / 52 (32.69%) | 15 / 51 (29.41%) | 17 / 51 (33.33%) |
| occurrences (all)                          | 17               | 15               | 17               |
| Loss of appetite Booster                   |                  |                  |                  |
| alternative assessment type:<br>Systematic |                  |                  |                  |
| subjects affected / exposed                | 10 / 52 (19.23%) | 6 / 51 (11.76%)  | 15 / 51 (29.41%) |
| occurrences (all)                          | 10               | 6                | 15               |

|                                                                                                                                |                        |                      |                     |
|--------------------------------------------------------------------------------------------------------------------------------|------------------------|----------------------|---------------------|
| Temperature/Rectally Booster<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 10 / 52 (19.23%)<br>10 | 8 / 51 (15.69%)<br>8 | 5 / 51 (9.80%)<br>5 |
| Eye disorders<br>Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 52 (0.00%)<br>0    | 0 / 51 (0.00%)<br>0  | 0 / 51 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal<br>disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)                | 3 / 52 (5.77%)<br>3    | 6 / 51 (11.76%)<br>6 | 1 / 51 (1.96%)<br>1 |
| Infections and infestations<br>Nasopharyngitis Primary<br>subjects affected / exposed<br>occurrences (all)                     | 8 / 52 (15.38%)<br>8   | 4 / 51 (7.84%)<br>4  | 4 / 51 (7.84%)<br>4 |
| Nasopharyngitis Booster<br>subjects affected / exposed<br>occurrences (all)                                                    | 3 / 52 (5.77%)<br>3    | 3 / 51 (5.88%)<br>3  | 0 / 51 (0.00%)<br>0 |
| Rhinitis Primary<br>subjects affected / exposed<br>occurrences (all)                                                           | 1 / 52 (1.92%)<br>1    | 3 / 51 (5.88%)<br>3  | 1 / 51 (1.96%)<br>1 |
| Rhinitis Booster<br>subjects affected / exposed<br>occurrences (all)                                                           | 1 / 52 (1.92%)<br>1    | 4 / 51 (7.84%)<br>4  | 1 / 51 (1.96%)<br>1 |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                                                                 | 3 / 52 (5.77%)<br>3    | 0 / 51 (0.00%)<br>0  | 4 / 51 (7.84%)<br>4 |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                                                            | 2 / 52 (3.85%)<br>2    | 2 / 51 (3.92%)<br>2  | 0 / 51 (0.00%)<br>0 |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                                                            | 1 / 52 (1.92%)<br>1    | 1 / 51 (1.96%)<br>1  | 3 / 51 (5.88%)<br>3 |
| Laryngitis                                                                                                                     |                        |                      |                     |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 51 (0.00%) | 4 / 51 (7.84%) |
| occurrences (all)           | 1              | 0              | 4              |
| Varicella                   |                |                |                |
| subjects affected / exposed | 1 / 52 (1.92%) | 0 / 51 (0.00%) | 3 / 51 (5.88%) |
| occurrences (all)           | 1              | 0              | 3              |

| <b>Non-serious adverse events</b>                     | 10Pn Group       | 10Pn-dPly-PhtD-LD Group |  |
|-------------------------------------------------------|------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events |                  |                         |  |
| subjects affected / exposed                           | 35 / 51 (68.63%) | 36 / 52 (69.23%)        |  |
| General disorders and administration site conditions  |                  |                         |  |
| Pain Primary                                          |                  |                         |  |
| alternative assessment type: Systematic               |                  |                         |  |
| subjects affected / exposed                           | 34 / 51 (66.67%) | 34 / 52 (65.38%)        |  |
| occurrences (all)                                     | 34               | 34                      |  |
| Redness Primary                                       |                  |                         |  |
| alternative assessment type: Systematic               |                  |                         |  |
| subjects affected / exposed                           | 30 / 51 (58.82%) | 36 / 52 (69.23%)        |  |
| occurrences (all)                                     | 30               | 36                      |  |
| Swelling Primary                                      |                  |                         |  |
| alternative assessment type: Systematic               |                  |                         |  |
| subjects affected / exposed                           | 26 / 51 (50.98%) | 25 / 52 (48.08%)        |  |
| occurrences (all)                                     | 26               | 25                      |  |
| Pain Booster                                          |                  |                         |  |
| alternative assessment type: Systematic               |                  |                         |  |
| subjects affected / exposed                           | 25 / 51 (49.02%) | 32 / 52 (61.54%)        |  |
| occurrences (all)                                     | 25               | 32                      |  |
| Redness Booster                                       |                  |                         |  |
| alternative assessment type: Systematic               |                  |                         |  |
| subjects affected / exposed                           | 21 / 51 (41.18%) | 28 / 52 (53.85%)        |  |
| occurrences (all)                                     | 21               | 28                      |  |
| Swelling Booster                                      |                  |                         |  |
| alternative assessment type: Systematic               |                  |                         |  |
| subjects affected / exposed                           | 13 / 51 (25.49%) | 18 / 52 (34.62%)        |  |
| occurrences (all)                                     | 13               | 18                      |  |
| Drowsiness Primary                                    |                  |                         |  |

|                                            |                  |                  |  |
|--------------------------------------------|------------------|------------------|--|
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 35 / 51 (68.63%) | 34 / 52 (65.38%) |  |
| occurrences (all)                          | 35               | 34               |  |
| Irritability Primary                       |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 35 / 51 (68.63%) | 35 / 52 (67.31%) |  |
| occurrences (all)                          | 35               | 35               |  |
| Loss of appetite Primary                   |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 23 / 51 (45.10%) | 20 / 52 (38.46%) |  |
| occurrences (all)                          | 23               | 20               |  |
| Temperature/Rectally Primary               |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 17 / 51 (33.33%) | 18 / 52 (34.62%) |  |
| occurrences (all)                          | 17               | 18               |  |
| Drowsiness Booster                         |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 17 / 51 (33.33%) | 18 / 52 (34.62%) |  |
| occurrences (all)                          | 17               | 18               |  |
| Irritability Booster                       |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 19 / 51 (37.25%) | 26 / 52 (50.00%) |  |
| occurrences (all)                          | 19               | 26               |  |
| Loss of appetite Booster                   |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 8 / 51 (15.69%)  | 13 / 52 (25.00%) |  |
| occurrences (all)                          | 8                | 13               |  |
| Temperature/Rectally Booster               |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 7 / 51 (13.73%)  | 10 / 52 (19.23%) |  |
| occurrences (all)                          | 7                | 10               |  |
| Eye disorders                              |                  |                  |  |
| Conjunctivitis                             |                  |                  |  |

|                                                                                                              |                      |                      |  |
|--------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                             | 0 / 51 (0.00%)<br>0  | 3 / 52 (5.77%)<br>3  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 4 / 51 (7.84%)<br>4  | 2 / 52 (3.85%)<br>2  |  |
| Infections and infestations<br>Nasopharyngitis Primary<br>subjects affected / exposed<br>occurrences (all)   | 7 / 51 (13.73%)<br>7 | 9 / 52 (17.31%)<br>9 |  |
| Nasopharyngitis Booster<br>subjects affected / exposed<br>occurrences (all)                                  | 2 / 51 (3.92%)<br>2  | 2 / 52 (3.85%)<br>2  |  |
| Rhinitis Primary<br>subjects affected / exposed<br>occurrences (all)                                         | 1 / 51 (1.96%)<br>1  | 4 / 52 (7.69%)<br>4  |  |
| Rhinitis Booster<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 51 (0.00%)<br>0  | 1 / 52 (1.92%)<br>1  |  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                                               | 3 / 51 (5.88%)<br>3  | 4 / 52 (7.69%)<br>4  |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 51 (1.96%)<br>1  | 3 / 52 (5.77%)<br>3  |  |
| Viral infection<br>subjects affected / exposed<br>occurrences (all)                                          | 1 / 51 (1.96%)<br>1  | 4 / 52 (7.69%)<br>4  |  |
| Laryngitis<br>subjects affected / exposed<br>occurrences (all)                                               | 2 / 51 (3.92%)<br>2  | 1 / 52 (1.92%)<br>1  |  |
| Varicella<br>subjects affected / exposed<br>occurrences (all)                                                | 2 / 51 (3.92%)<br>2  | 1 / 52 (1.92%)<br>1  |  |



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported