



## Clinical trial results:

### A Randomised, Double-blind, Parallel Group Phase III Study to Assess the Efficacy and Safety of 100 mg SC Depemokimab in Patients With Chronic Rhinosinusitis With Nasal Polyps (CRSwNP) - ANCHOR-1 (depemokimAb iN CHrOnic Rhinosinusitis)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-005037-16 |
| Trial protocol           | FR BE DE ES    |
| Global end of trial date | 27 August 2024 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1             |
| This version publication date  | 15 August 2025 |
| First version publication date | 15 August 2025 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 217095 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05274750 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline  |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS               |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 8664357343, 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? | No |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 01 October 2024 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 30 July 2024    |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 27 August 2024  |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of depemokimab 100 milligram (mg) subcutaneous + standard of care (SOC) compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 22 April 2022 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Belgium: 4        |
| Country: Number of subjects enrolled | France: 15        |
| Country: Number of subjects enrolled | Germany: 29       |
| Country: Number of subjects enrolled | Netherlands: 18   |
| Country: Number of subjects enrolled | Spain: 22         |
| Country: Number of subjects enrolled | United Kingdom: 9 |
| Country: Number of subjects enrolled | United States: 21 |
| Country: Number of subjects enrolled | Argentina: 71     |
| Country: Number of subjects enrolled | Canada: 18        |
| Country: Number of subjects enrolled | China: 31         |
| Country: Number of subjects enrolled | Japan: 38         |
| Worldwide total number of subjects   | 276               |
| EEA total number of subjects         | 88                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |

|  |     |
|--|-----|
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 219 |
| From 65 to 84 years                      | 57  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

A total of 276 participants were randomized, of which 271 participants were included in Full analysis set (FAS). The FAS included all randomized participants who received at least 1 dose of study drug excluding 4 participants from 1 site with GCP/data integrity issues. One participant was randomized in error and did not receive any study drug.

### Pre-assignment

Screening details:

A total of 276 participants were enrolled in the study.

### Period 1

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

### Arms

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

Arm description:

Participants received a 100 milligram (mg) dose of depemokimab SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) standard of care (SOC) treatment throughout the study.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | GSK3511294             |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

100 milligram (mg) once every 26 weeks

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

Arm description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for CRSwNP SOC treatment throughout the study.

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

Dosage and administration details:

Matching Placebo once every 26 weeks

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Depemokimab | Placebo |
|---|-------------|---------|
| Started   | 143         | 128     |
| Completed   | 128         | 115     |
| Not completed                                       | 15          | 13      |
| Consent withdrawn by subject                        | 10          | 9       |
| Physician decision                                  | 3           | -       |
| Adverse event, non-fatal                            | -           | 1       |
| Lost to follow-up                                   | 2           | 3       |

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Notes:

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

Justification: Of 276 participants who were randomized, 4 participants from 1 site was excluded from the full analysis population due to data integrity concerns & GCP violations, and one randomized participant did not receive any study intervention. Hence, a total of 271 participants were included in the Full analysis set population

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Depemokimab |
|-----------------------|-------------|

Reporting group description:

Participants received a 100 milligram (mg) dose of depemokimab SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) standard of care (SOC) treatment throughout the study.

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

Reporting group description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for CRSwNP SOC treatment throughout the study.

| Reporting group values             | Depemokimab | Placebo | Total |
|------------------------------------|-------------|---------|-------|
| Number of subjects                 | 143         | 128     | 271   |
| Age categorical<br>Units: Subjects |             |         |       |

|   |                 |                 |     |
|---|-----------------|-----------------|-----|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | 54.1<br>± 13.37 | 52.9<br>± 13.49 | -   |
| Sex: Female, Male<br>Units: Participants  |                 |                 |     |
| Female  | 45              | 38              | 83  |
| Male  | 98              | 90              | 188 |
| Race/Ethnicity, Customized  |                 |                 |     |
| "All Other Races" category (Black or African American or Asian and Unknown where 0<n<11) are combined into one category to maintain participant confidentiality and privacy |                 |                 |     |
| Units: Subjects   |                 |                 |     |
| WHITE   | 97              | 88              | 185 |
| All Other Races   | 42              | 36              | 78  |
| Missing   | 4               | 4               | 8   |

### Subject analysis sets

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Pooled Depemokimab |
|----------------------------|--------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

This reporting arm contains the pooled population of treated participants from the clinical trial groups "Depemokimab" study intervention from protocol 217095 (2021-005037-16) and protocol 218079 (2021-005055-36). Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

|                            |                |
|----------------------------|----------------|
| Subject analysis set title | Pooled Placebo |
|----------------------------|----------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

This reporting arm contains the pooled population of participants from the clinical trial groups "Placebo" study intervention from protocol 217095 (2021-005037-16) and protocol 218079 (2021-005055-36). Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and

week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

| <b>Reporting group values</b>   | Pooled Depemokimab | Pooled Placebo  |  |
|---|--------------------|-----------------|--|
| Number of subjects  | 272                | 256             |  |
| Age categorical<br>Units: Subjects  |                    |                 |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | 52.4<br>± 13.27    | 51.6<br>± 13.27 |  |
| Sex: Female, Male<br>Units: Participants  |                    |                 |  |
| Female  | 85                 | 78              |  |
| Male  | 187                | 178             |  |
| Race/Ethnicity, Customized  |                    |                 |  |
| "All Other Races" category (Black or African American or Asian and Unknown where 0<n<11) are combined into one category to maintain participant confidentiality and privacy |                    |                 |  |
| Units: Subjects   |                    |                 |  |
| WHITE   | 196                | 186             |  |
| All Other Races   | 72                 | 66              |  |
| Missing   | 4                  | 4               |  |

## End points

### End points reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Depemokimab |
|-----------------------|-------------|

Reporting group description:

Participants received a 100 milligram (mg) dose of depemokimab SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) standard of care (SOC) treatment throughout the study.

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

Reporting group description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period of 52 weeks. Participants were to be maintained on their existing baseline maintenance for CRSwNP SOC treatment throughout the study.

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Pooled Depemokimab |
|----------------------------|--------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

This reporting arm contains the pooled population of treated participants from the clinical trial groups "Depemokimab" study intervention from protocol 217095 (2021-005037-16) and protocol 218079 (2021-005055-36). Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

|                            |                |
|----------------------------|----------------|
| Subject analysis set title | Pooled Placebo |
|----------------------------|----------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

This reporting arm contains the pooled population of participants from the clinical trial groups "Placebo" study intervention from protocol 217095 (2021-005037-16) and protocol 218079 (2021-005055-36). Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and week 26). Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

### Primary: Change From Baseline in Total Endoscopic Nasal Polyps (NP) Score at Week 52 (Centrally Read)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Total Endoscopic Nasal Polyps (NP) Score at Week 52 (Centrally Read) |
|-----------------|--|

End point description:

Total endoscopic nasal polyps (NP) score evaluated the size and extent of nasal polyps via endoscopy. The assessments were performed by central video image recordings. The right & left nostrils were scored from 0 to 4 (0 = No polyps; 1 = Small polyps in the middle meatus; 2 = Polyps reaching below the lower border of the middle turbinate; 3 = Large polyps reaching the lower border of the inferior turbinate; and 4 = Large polyps causing complete obstruction of the inferior meatus). The scores were graded based on NP size, recorded as sum of the right and left nostril scores & ranges from 0 (no polyps) to 8 (large polyps), calculated by summing the scores in each nostril; with higher scores indicating worse status. Baseline=Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. FAS population excluding participants from 1 site with GCP violation. Only those participants with data available at specified time points have been analyzed.

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

End point timeframe:

Baseline (Day 1) and at Week 52

| <b>End point values</b>             | Depemokimab     | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 139             | 127             |  |  |
| Units: Scores on a Scale            |                 |                 |  |  |
| least squares mean (standard error) | -0.6 (± 0.14)   | 0.2 (± 0.15)    |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 1           |
|--|----------------------------------|
| Statistical analysis description:  |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups  | Depemokimab v Placebo            |
| Number of subjects included in analysis  | 266                              |
| Analysis specification   | Pre-specified                    |
| Analysis type  |                                  |
| P-value  | < 0.001                          |
| Method   | Mixed models analysis            |
| Parameter estimate   | Difference in Least Square Means |
| Point estimate   | -0.7                             |
| Confidence interval  |                                  |
| level  | 95 %                             |
| sides  | 2-sided                          |
| lower limit  | -1.1                             |
| upper limit  | -0.3                             |

## Primary: Change from Baseline in Mean Nasal Obstruction Score Using Verbal Response Scale from Week 49 Through to Week 52

| <b>End point title</b>   | Change from Baseline in Mean Nasal Obstruction Score Using Verbal Response Scale from Week 49 Through to Week 52 |
|--|--|
| End point description:   |  |
| This endpoint evaluated change from baseline in the mean nasal obstruction score using a Verbal Response Scale (VRS) from Week 49 through to Week 52. Participants used VRS to rate nasal obstruction severity, with scores averaged over the specified period to assess treatment impact on nasal obstruction symptoms. Participants were asked to indicate the severity of nasal obstruction at their worst over the last 24 hours using a 4-point VRS, with options of no symptoms, mild symptoms, moderate and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). The average of daily scores in 4-weekly intervals were calculated & data are for Weeks 49-52. Baseline was defined as the average score from the 28 days of eDairy data collected prior to Day 1. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on FAS population. The number of participants analyzed represents evaluable participants at specified time points. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| Baseline (Day 1) and from Week 49 to Week 52   |  |

| <b>End point values</b>             | Depemokimab     | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 142             | 128             |  |  |
| Units: Scores on a Scale            |                 |                 |  |  |
| least squares mean (standard error) | -0.76 (± 0.079) | -0.53 (± 0.083) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 1           |
|--|----------------------------------|
| Statistical analysis description:  |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups  | Placebo v Depemokimab            |
| Number of subjects included in analysis  | 270                              |
| Analysis specification   | Pre-specified                    |
| Analysis type  |                                  |
| P-value  | = 0.047                          |
| Method   | Mixed models analysis            |
| Parameter estimate   | Difference in Least Square Means |
| Point estimate   | -0.23                            |
| Confidence interval  |                                  |
| level  | 95 %                             |
| sides  | 2-sided                          |
| lower limit  | -0.46                            |
| upper limit  | 0                                |

## Secondary: Change from Baseline in Mean Symptom Score for Rhinorrhea (Runny Nose) Using Verbal Response Scale from Week 49 Through to Week 52

|   |  |
|---|--|
| End point title   | Change from Baseline in Mean Symptom Score for Rhinorrhea (Runny Nose) Using Verbal Response Scale from Week 49 Through to Week 52 |
| End point description:  |  |
| Participants were asked to indicate the severity of rhinorrhea (runny nose) at their worst over the last 24 hours using a 4-point VRS, with options of no symptoms, mild symptoms, moderate symptoms, and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). Higher scores indicate the worse status. The average of daily scores in 4-weekly intervals were calculated and data are presented for Weeks 49-52. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at specified time points. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline (Day 1) and from Week 49 to Week 52  |  |

| <b>End point values</b>             | Depemokimab     | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 142             | 128             |  |  |
| Units: Scores on a Scale            |                 |                 |  |  |
| least squares mean (standard error) | -0.71 (± 0.084) | -0.49 (± 0.087) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Statistical Analysis 3           |
|---|----------------------------------|
| Statistical analysis description:   |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 49 to Week 52 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups   | Placebo v Depemokimab            |
| Number of subjects included in analysis   | 270                              |
| Analysis specification  | Pre-specified                    |
| Analysis type   |                                  |
| P-value   | = 0.074                          |
| Method  | Mixed models analysis            |
| Parameter estimate  | Difference in Least Square Means |
| Point estimate  | -0.22                            |
| Confidence interval   |                                  |
| level   | 95 %                             |
| sides   | 2-sided                          |
| lower limit   | -0.46                            |
| upper limit   | 0.02                             |

## Secondary: Change from Baseline in Mean Symptom Score for Loss of Smell Using Verbal Response Scale from Week 49 Through to Week 52

| <b>End point title</b>  | Change from Baseline in Mean Symptom Score for Loss of Smell Using Verbal Response Scale from Week 49 Through to Week 52 |
|---|--|
| End point description:  |  |
| Participants were asked to indicate the severity of loss of smell at their worst over the last 24 hours using a 4-point VRS, with options of no symptoms, mild symptoms, moderate symptoms, and severe symptoms. This was scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). Higher score indicates worse status. The average of daily scores in 4-weekly intervals were calculated and data are presented for Weeks 49-52. Baseline was defined as the average score from the 28 days of eDiary data collected prior to Day 1. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at specified time points. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline (Day 1) and from Week 49 to Week 52  |  |

| <b>End point values</b>             | Depemokimab     | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 142             | 128             |  |  |
| Units: Scores on a Scale            |                 |                 |  |  |
| least squares mean (standard error) | -0.48 (± 0.069) | -0.29 (± 0.072) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Statistical Analysis 4           |
|---|----------------------------------|
| Statistical analysis description:   |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 49 to Week 52 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups   | Placebo v Depemokimab            |
| Number of subjects included in analysis   | 270                              |
| Analysis specification  | Pre-specified                    |
| Analysis type   |                                  |
| P-value   | = 0.055                          |
| Method  | Mixed models analysis            |
| Parameter estimate  | Difference in Least Square Means |
| Point estimate  | -0.19                            |
| Confidence interval   |                                  |
| level   | 95 %                             |
| sides   | 2-sided                          |
| lower limit   | -0.39                            |
| upper limit   | 0                                |

## Secondary: Change from Baseline in Lund Mackay Computerized Tomography (CT) Score at Week 52

| <b>End point title</b>   | Change from Baseline in Lund Mackay Computerized Tomography (CT) Score at Week 52 |
|--|---|
| End point description:   |   |
| <p>The LMK CT scoring system is based on CT imaging of the sinuses with points given for degree of opacification: 0 =normal, 1 = partial opacification, 2 = total opacification. These points were applied to the maxillary, anterior ethmoid, posterior ethmoid, sphenoid, frontal sinus on each side (right and left). The osteomeatal complex (OC) is graded as 0 = not occluded, or 2 = occluded. The range for the total LMK CT score is therefore 0 (normal) to 24 (total opacification) when summed across both sides. Higher scores indicated more severe disease. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at specified time points.</p> |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline (Day 1) and at Week 52  |   |

| <b>End point values</b>             | Depemokimab        | Placebo            |  |  |
|-------------------------------------|--------------------|--------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed         | 127                | 119                |  |  |
| Units: Scores on a Scale            |                    |                    |  |  |
| least squares mean (standard error) | -2.8 ( $\pm$ 0.45) | -0.8 ( $\pm$ 0.46) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 5           |
|--|----------------------------------|
| Statistical analysis description:  |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups  | Placebo v Depemokimab            |
| Number of subjects included in analysis  | 246                              |
| Analysis specification   | Pre-specified                    |
| Analysis type  |                                  |
| P-value  | = 0.002                          |
| Method   | ANCOVA                           |
| Parameter estimate   | Difference in Least Square Means |
| Point estimate   | -2                               |
| Confidence interval  |                                  |
| level  | 95 %                             |
| sides  | 2-sided                          |
| lower limit  | -3.3                             |
| upper limit  | -0.8                             |

## Secondary: Change from Baseline in Sino-nasal Outcome Test (SNOT)-22 Total Score at Week 52

| <b>End point title</b>   | Change from Baseline in Sino-nasal Outcome Test (SNOT)-22 Total Score at Week 52 |
|--|--|
| End point description:   |  |
| Sino-nasal outcome test-22 is a 22-item measure of disease specific health related quality of life (HRQoL). Participants were asked to rate the severity of their condition on each of the 22 items over the previous 2 weeks using a 6-point rating scale of 0-5 including: 0 = Not present/no problem; 1 = Very mild problem; 2 = Mild or slight problem; 3 = Moderate problem; 4 = Severe problem; 5 = Problem as "bad as it can be". The scores for each question were summed up to derive the total score range for the SNOT-22 was from 0 (high quality of life) to 110 (worst quality of life), where higher scores indicate worse quality of life. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at specified time points. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline (Day 1) and at Week 52  |  |

| <b>End point values</b>             | Depemokimab         | Placebo            |  |  |
|-------------------------------------|---------------------|--------------------|--|--|
| Subject group type                  | Reporting group     | Reporting group    |  |  |
| Number of subjects analysed         | 139                 | 125                |  |  |
| Units: Scores on a Scale            |                     |                    |  |  |
| least squares mean (standard error) | -13.3 ( $\pm$ 2.96) | -6.5 ( $\pm$ 3.08) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 6           |
|--|----------------------------------|
| Statistical analysis description:  |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups  | Placebo v Depemokimab            |
| Number of subjects included in analysis  | 264                              |
| Analysis specification   | Pre-specified                    |
| Analysis type  |                                  |
| P-value  | = 0.113                          |
| Method   | Mixed models analysis            |
| Parameter estimate   | Difference in Least Square Means |
| Point estimate   | -6.8                             |
| Confidence interval  |                                  |
| level  | 95 %                             |
| sides  | 2-sided                          |
| lower limit  | -15.2                            |
| upper limit  | 1.6                              |

## Secondary: Change from Baseline in Mean Nasal Obstruction Score from Week 21 Through to Week 24

| <b>End point title</b>   | Change from Baseline in Mean Nasal Obstruction Score from Week 21 Through to Week 24 |
|--|--|
| End point description:   |  |
| Participants were asked to indicate the severity of nasal obstruction at its worst over the previous 24 hours using a 4-point VRS. The response options were no symptoms, mild symptoms, moderate symptoms, and severe symptoms, scored on a scale ranging from 0 (no symptoms) to 3 (severe symptoms). Higher score indicated more severe status. The average of daily scores in 4-weekly intervals were calculated and data are presented for Weeks 21-24. Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. The analysis was performed on the FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable participants at specified time points. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline (Day 1) and from Week 21 to Week 24   |  |

| <b>End point values</b>             | Depemokimab     | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 142             | 128             |  |  |
| Units: Scores on a Scale            |                 |                 |  |  |
| least squares mean (standard error) | -0.74 (± 0.071) | -0.57 (± 0.074) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>   | Statistical Analysis 7           |
|---|----------------------------------|
| Statistical analysis description:   |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 21 to Week 24 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups   | Placebo v Depemokimab            |
| Number of subjects included in analysis   | 270                              |
| Analysis specification  | Pre-specified                    |
| Analysis type   |                                  |
| P-value   | = 0.094                          |
| Method  | Mixed models analysis            |
| Parameter estimate  | Difference in Least Square Means |
| Point estimate  | -0.17                            |
| Confidence interval   |                                  |
| level   | 95 %                             |
| sides   | 2-sided                          |
| lower limit   | -0.37                            |
| upper limit   | 0.03                             |

## Secondary: Change from Baseline in Total Endoscopic Nasal Polyp Score at Week 26

| <b>End point title</b>  | Change from Baseline in Total Endoscopic Nasal Polyp Score at Week 26 |
|---|---|
| End point description:  |   |
| Total endoscopic nasal polyps score evaluated the size and extent of nasal polyps via endoscopy. The right & left nostrils were scored from 0 - 4 (0 = No polyps; 1 = Small polyps in the middle meatus not reaching below the inferior border of the middle concha; 2 = Polyps reaching below the lower border of the middle turbinate; 3 = Large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle concha; and 4 = Large polyps causing complete obstruction of the inferior meatus). The scores were recorded as sum of the right & left nostril scores ranging from 0 (no polyps) to 8 (large polyps), calculated by summing scores (0 - 4) in each nostril; with higher scores indicating worse status. Change from Baseline = Post-baseline value minus Baseline value. FAS population excluding participants from 1 site due to GCP violation. The number of participants analyzed represents evaluable subjects at specified time points. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Baseline (Day 1) and at Week 26   |   |

| <b>End point values</b>             | Depemokimab        | Placebo           |  |  |
|-------------------------------------|--------------------|-------------------|--|--|
| Subject group type                  | Reporting group    | Reporting group   |  |  |
| Number of subjects analysed         | 139                | 127               |  |  |
| Units: Scores on a Scale            |                    |                   |  |  |
| least squares mean (standard error) | -0.6 ( $\pm$ 0.13) | 0.1 ( $\pm$ 0.13) |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 8           |
|--|----------------------------------|
| Statistical analysis description:  |                                  |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 26 in participants with a diagnosis of CRSwNP |                                  |
| Comparison groups  | Placebo v Depemokimab            |
| Number of subjects included in analysis  | 266                              |
| Analysis specification   | Pre-specified                    |
| Analysis type  |                                  |
| P-value  | < 0.001                          |
| Method   | Mixed models analysis            |
| Parameter estimate   | Difference in Least Square Means |
| Point estimate   | -0.8                             |
| Confidence interval  |                                  |
| level  | 95 %                             |
| sides  | 2-sided                          |
| lower limit  | -1.1                             |
| upper limit  | -0.4                             |

## Secondary: Percentage of Participants Requiring First Nasal Surgery (Actual or Entry on Waiting List) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps up to Week 52

|  |  |
|--|--|
| End point title  | Percentage of Participants Requiring First Nasal Surgery (Actual or Entry on Waiting List) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps up to Week 52 |
| End point description:   |  |
| Nasal polyp surgery is defined as any procedure involving instruments resulting in incision & removal of tissue from the nasal cavity. Time to first nasal surgery (actual or entry on waiting list) or disease-modulating medication for CRSwNP up to Week 52 was assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). Percentage of participants with nasal surgery or course of systemic CS for CRSwNP and corresponding 95% CI have been presented, calculated using the Kaplan-Meier method. For pooled studies of 217095 and 218079, the analysis was performed on the FAS population. The FAS included all randomized participants who took at least 1 dose of study treatment excluding participants from 1 site for 217095 and 2 sites for 218079 respectively with GCP violation. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Up to Week 52  |  |

| <b>End point values</b>           | Pooled Depemokimab   | Pooled Placebo       |  |  |
|-----------------------------------|----------------------|----------------------|--|--|
| Subject group type                | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed       | 272                  | 256                  |  |  |
| Units: Percentage of participants |                      |                      |  |  |
| number (confidence interval 95%)  | 15.0 (11.3 to 19.9)  | 21.9 (17.2 to 27.7)  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 9              |
|--|-------------------------------------|
| Statistical analysis description:  |                                     |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis) |                                     |
| Comparison groups  | Pooled Depemokimab v Pooled Placebo |
| Number of subjects included in analysis  | 528                                 |
| Analysis specification   | Pre-specified                       |
| Analysis type  | other <sup>[1]</sup>                |
| P-value  | = 0.128                             |
| Method   | Cox proportional hazards            |
| Parameter estimate   | Hazard ratio (HR)                   |
| Point estimate   | 0.735                               |
| Confidence interval  |                                     |
| level  | 95 %                                |
| sides  | 2-sided                             |
| lower limit  | 0.495                               |
| upper limit  | 1.092                               |

Notes:

[1] - Cox Proportional Hazards Model with covariates of treatment, baseline total endoscopic nasal polyps score, baseline nasal obstruction score (VRS), log(e) baseline blood eosinophil count, region, study and previous surgery for nasal polyps. The covariate for study is removed for the individual-study analyses. If the hierarchy is broken, subsequent endpoints will be evaluated for nominal significance in a descriptive manner, using a 5% reference level.

## Secondary: Percentage of Participants Requiring First Nasal Surgery (Actual) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps up to Week 52

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Requiring First Nasal Surgery (Actual) or Disease-Modulating Medication for Chronic Rhinosinusitis with Nasal Polyps up to Week 52 |
|-----------------|---|

End point description:

Nasal polyp surgery is defined as any procedure involving instruments resulting in incision & removal of tissue from the nasal cavity. Time to first nasal surgery (actual) or disease-modulating medication for CRSwNP up to week 52 was assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). Percentage of participants with nasal surgery or course of systemic CS for CRSwNP and corresponding 95% CI have been presented, calculated using the Kaplan-Meier method. For pooled studies of 217095 and 218079, the analysis was performed on the FAS population. The FAS included all randomized participants who took at least 1 dose of study treatment excluding participants from 1 site for 217095 and 2 sites for 218079 respectively with GCP violation.

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

End point timeframe:

Up to Week 52

| <b>End point values</b>           | Pooled Depemokimab   | Pooled Placebo       |  |  |
|-----------------------------------|----------------------|----------------------|--|--|
| Subject group type                | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed       | 272                  | 256                  |  |  |
| Units: Percentage of Participants |                      |                      |  |  |
| number (confidence interval 95%)  | 12.2 (8.8 to 16.8)   | 16.7 (12.6 to 22.0)  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 10             |
|--|-------------------------------------|
| Statistical analysis description:  |                                     |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis) |                                     |
| Comparison groups  | Pooled Depemokimab v Pooled Placebo |
| Number of subjects included in analysis  | 528                                 |
| Analysis specification   | Pre-specified                       |
| Analysis type  |                                     |
| P-value  | = 0.146                             |
| Method   | Cox proportional hazards            |
| Parameter estimate   | Hazard ratio (HR)                   |
| Point estimate   | 0.713                               |
| Confidence interval  |                                     |
| level  | 95 %                                |
| sides  | 2-sided                             |
| lower limit  | 0.453                               |
| upper limit  | 1.124                               |

## **Secondary: Percentage of Participants Requiring at Least One Course of Systemic Corticosteroids or Disease-Modulating Medication for CRSwNP or Nasal Surgery (Actual) During the Week 52 Treatment Period**

|  |  |
|--|--|
| End point title  | Percentage of Participants Requiring at Least One Course of Systemic Corticosteroids or Disease-Modulating Medication for CRSwNP or Nasal Surgery (Actual) During the Week 52 Treatment Period |
| End point description:   |  |
| Percentage of participants requiring at least 1 course of systemic corticosteroids or disease-modulating medication for CRSwNP or nasal surgery (actual) during the Week 52 treatment period will be assessed in a pre-specified pooled analysis across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). For pooled studies of 217095 and 218079, the analysis was performed on the FAS population. The FAS included all randomized participants who took at least 1 dose of study treatment excluding participants from 1 site for 217095 and 2 sites for 218079 respectively with GCP violation. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Up to Week 52  |  |

| <b>End point values</b>           | Pooled Depemokimab   | Pooled Placebo       |  |  |
|-----------------------------------|----------------------|----------------------|--|--|
| Subject group type                | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed       | 272                  | 256                  |  |  |
| Units: Percentage of participants | 26                   | 36                   |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 11             |
|--|-------------------------------------|
| Statistical analysis description:  |                                     |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis) |                                     |
| Comparison groups  | Pooled Depemokimab v Pooled Placebo |
| Number of subjects included in analysis  | 528                                 |
| Analysis specification   | Pre-specified                       |
| Analysis type  |                                     |
| P-value  | = 0.006                             |
| Method   | Regression, Logistic                |
| Parameter estimate   | Odds ratio (OR)                     |
| Point estimate   | 0.58                                |
| Confidence interval  |                                     |
| level  | 95 %                                |
| sides  | 2-sided                             |
| lower limit  | 0.4                                 |
| upper limit  | 0.86                                |

## Secondary: Change from Baseline in Asthma Control Questionnaire (ACQ-5) Score at Week 52

| <b>End point title</b>   | Change from Baseline in Asthma Control Questionnaire (ACQ-5) Score at Week 52 |
|--|---|
| End point description:   |   |
| <p>The ACQ-5 is a 5-item questionnaire which enquires about the frequency and/or severity of asthma signs over the previous week (nocturnal awakening on waking in morning, activity limitation, &amp; shortness of breath, wheeze). Each question is scored from 0 (no impairment) to 6 (total impairment). Higher scores indicate more limitations. Impact on asthma control in participants with an ACQ-5 score &gt;0.75(i.e. partially or not well-controlled asthma) at baseline was assessed across replicate studies 217095 (2021-005037-16) and 218079 (2021-005055-36). Baseline was defined as Day 1 value. Change from Baseline = Post-baseline value minus Baseline value. FAS population from study 217095 &amp; 218079 excluding participants from 3 sites with GCP violation. Participants analyzed represents evaluable participants at specified time points.</p> |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline (Day 1) and at Week 52  |   |

| <b>End point values</b>             | Pooled Depemokimab   | Pooled Placebo       |  |  |
|-------------------------------------|----------------------|----------------------|--|--|
| Subject group type                  | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed         | 104                  | 102                  |  |  |
| Units: Scores on a Scale            |                      |                      |  |  |
| least squares mean (standard error) | -0.75 ( $\pm$ 0.182) | 0.00 ( $\pm$ 0.182)  |  |  |

## Statistical analyses

| <b>Statistical analysis title</b>  | Statistical Analysis 12             |
|--|-------------------------------------|
| Statistical analysis description:  |                                     |
| To assess the efficacy of depemokimab 100mg SC + SoC compared to placebo + SoC at Week 52 in participants with a diagnosis of CRSwNP (pooled analysis) |                                     |
| Comparison groups  | Pooled Depemokimab v Pooled Placebo |
| Number of subjects included in analysis  | 206                                 |
| Analysis specification   | Pre-specified                       |
| Analysis type  |                                     |
| P-value  | = 0.004                             |
| Method   | Mixed models analysis               |
| Parameter estimate   | Difference in Least Square Means    |
| Point estimate   | -0.75                               |
| Confidence interval  |                                     |
| level  | 95 %                                |
| sides  | 2-sided                             |
| lower limit  | -1.26                               |
| upper limit  | -0.25                               |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, Serious adverse events (SAEs) and non-serious adverse events (Non-SAEs) were collected from the start of the study intervention (Day 1) until follow up week 56.

Adverse event reporting additional description:

All-cause mortality, SAEs and Non-SAEs were reported for the Safety Population which included all randomized participants who received at least 1 dose of study treatment excluding participants from 1 site with GCP violation. AEs were reported treatment-wise.

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

### Dictionary used

|                    |      |
|--------------------|------|
| Dictionary name    | 27.1 |
| Dictionary version | 27.1 |

### Reporting groups

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

Reporting group description:

Participants received placebo SC injection once every 26 weeks (week 0 and week 26) over a treatment period for 52 weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Depemokimab |
|-----------------------|-------------|

Reporting group description:

Participants received a 100 mg dose of depemokimab SC injection once every 26 weeks (week 0 and week 26) over a treatment period for 52 weeks. Participants were to be maintained on their existing baseline maintenance CRSwNP SOC treatment throughout the study.

| <b>Serious adverse events</b>                     | Placebo         | Depemokimab     |  |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events |                 |                 |  |
| subjects affected / exposed                       | 6 / 128 (4.69%) | 5 / 143 (3.50%) |  |
| number of deaths (all causes)                     | 0               | 0               |  |
| number of deaths resulting from adverse events    | 0               | 0               |  |
| Injury, poisoning and procedural complications    |                 |                 |  |
| Humerus fracture                                  |                 |                 |  |
| subjects affected / exposed                       | 1 / 128 (0.78%) | 0 / 143 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Hand fracture                                     |                 |                 |  |
| subjects affected / exposed                       | 1 / 128 (0.78%) | 0 / 143 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Subdural haematoma                                |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 128 (0.00%) | 1 / 143 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Nervous system disorders</b>                 |                 |                 |  |
| Parkinson's disease                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 128 (0.78%) | 0 / 143 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Immune system disorders</b>                  |                 |                 |  |
| Drug hypersensitivity                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 128 (0.78%) | 0 / 143 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Gastrointestinal disorders</b>               |                 |                 |  |
| Pancreatitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 128 (0.00%) | 1 / 143 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Hepatobiliary disorders</b>                  |                 |                 |  |
| Cholecystitis acute                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 128 (0.00%) | 1 / 143 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| <b>Infections and infestations</b>              |                 |                 |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 128 (0.78%) | 0 / 143 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 128 (0.78%) | 0 / 143 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infective exacerbation of bronchiectasis        |                 |                 |  |

|   |                 |                 |
|---|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 128 (0.00%) | 1 / 143 (0.70%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |
| Otitis media                                    |                 |                 |
| subjects affected / exposed                     | 0 / 128 (0.00%) | 1 / 143 (0.70%) |
| 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: 3 %

| <b>Non-serious adverse events</b>                     | Placebo           | Depemokimab       |  |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 72 / 128 (56.25%) | 71 / 143 (49.65%) |  |
| Nervous system disorders                              |                   |                   |  |
| Headache  |                   |                   |  |
| subjects affected / exposed                           | 8 / 128 (6.25%)   | 6 / 143 (4.20%)   |  |
| occurrences (all)                                     | 12                | 6                 |  |
| Gastrointestinal disorders                            |                   |                   |  |
| Toothache   |                   |                   |  |
| subjects affected / exposed                           | 4 / 128 (3.13%)   | 4 / 143 (2.80%)   |  |
| occurrences (all)                                     | 4                 | 4                 |  |
| Respiratory, thoracic and mediastinal disorders       |                   |                   |  |
| Cough   |                   |                   |  |
| subjects affected / exposed                           | 6 / 128 (4.69%)   | 3 / 143 (2.10%)   |  |
| occurrences (all)                                     | 8                 | 4                 |  |
| Epistaxis   |                   |                   |  |
| subjects affected / exposed                           | 1 / 128 (0.78%)   | 5 / 143 (3.50%)   |  |
| occurrences (all)                                     | 1                 | 6                 |  |
| Nasal congestion                                      |                   |                   |  |
| subjects affected / exposed                           | 4 / 128 (3.13%)   | 4 / 143 (2.80%)   |  |
| occurrences (all)                                     | 5                 | 5                 |  |
| Nasal polyps  |                   |                   |  |
| subjects affected / exposed                           | 8 / 128 (6.25%)   | 8 / 143 (5.59%)   |  |
| occurrences (all)                                     | 10                | 11                |  |
| Musculoskeletal and connective tissue disorders       |                   |                   |  |

|   |                         |                         |  |
|---|-------------------------|-------------------------|--|
| Back pain<br>subjects affected / exposed<br>occurrences (all)                         | 4 / 128 (3.13%)<br>4    | 3 / 143 (2.10%)<br>3    |  |
| <b>Infections and infestations</b>  |                         |                         |  |
| Acute sinusitis<br>subjects affected / exposed<br>occurrences (all)                   | 4 / 128 (3.13%)<br>4    | 7 / 143 (4.90%)<br>9    |  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                        | 4 / 128 (3.13%)<br>4    | 6 / 143 (4.20%)<br>6    |  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)                          | 9 / 128 (7.03%)<br>9    | 12 / 143 (8.39%)<br>12  |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                   | 4 / 128 (3.13%)<br>5    | 2 / 143 (1.40%)<br>2    |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 10 / 128 (7.81%)<br>13  | 3 / 143 (2.10%)<br>4    |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 23 / 128 (17.97%)<br>26 | 21 / 143 (14.69%)<br>28 |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 7 / 128 (5.47%)<br>8    | 5 / 143 (3.50%)<br>7    |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 14 / 128 (10.94%)<br>17 | 14 / 143 (9.79%)<br>18  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment            |
|------------------|----------------------|
| 09 February 2022 | Protocol Amendment 1 |
| 26 October 2022  | Protocol Amendment 2 |
| 18 October 2023  | Protocol Amendment 3 |
| 12 March 2024    | Protocol Amendment 4 |
| 26 June 2024     | Protocol Amendment 5 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported