



## Clinical trial results:

### A Phase 2a, Open-label, Single-arm, 2-Part Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of VX-147 in Adults With APOL1-mediated Focal Segmental Glomerulosclerosis.

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2020-000185-42   |
| Trial protocol           | GB FR            |
| Global end of trial date | 09 December 2021 |

#### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 27 July 2023  |
| First version publication date | 25 December 2022  |
| Version creation reason        | • New data added to full data set<br>Update to match CT.gov |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | VX19-147-101 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04340362 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Vertex Pharmaceuticals Incorporated   |
| Sponsor organisation address | 50 Northern Avenue, Boston, Massachusetts, United States,                                   |
| Public contact               | Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.com |
| Scientific contact           | Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-341-6777, medicalinfo@vrtx.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                       | 14 February 2022 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 11 November 2021 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 09 December 2021 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy, safety and pharmacokinetics (PK) of VX-147 in subjects with apolipoprotein L1 (APOL1)-mediated focal segmental glomerulosclerosis (FSGS).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 08 June 2020 |
| 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 | France: 2         |
| Country: Number of subjects enrolled | United States: 11 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Worldwide total number of subjects   | 16                |
| EEA total number of subjects         | 2                 |

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)                      | 15 |
| From 65 to 84 years                       | 1  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This study was planned in 2 parts: Part A (Treatment Period), which consisted of 2 cohorts (i.e., cohort 1 and 2) and Part B (Optional Exploratory Off-treatment Follow-up Period). The primary and secondary efficacy analyses and safety analyses were planned for only Part A.

### Pre-assignment

Screening details:

This study was conducted on adult subjects who had APOL1-mediated focal segmental glomerulosclerosis (FSGS).

### Period 1

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

### Arms

|           |        |
|-----------|--------|
| Arm title | VX-147 |
|-----------|--------|

Arm description:

All subjects received VX-147 at a dosage of 15 mg once daily (qd) for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately greater than or equal to ( $\geq$ ) 3 g/g ( $\pm$  10%) and less than ( $<$ ) 10 g/g and estimated glomerular filtration rate (eGFR) approximately  $\geq$ 30 mL/min/1.73 m<sup>2</sup> ( $\pm$  10%). Cohort 2 included subjects with UPCR approximately  $\geq$ 0.8 g/g ( $\pm$  10%) and  $<$ 2.7 g/g and eGFR approximately  $\geq$ 30 mL/min/1.73 m<sup>2</sup>.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Inaxaplin    |
| Investigational medicinal product code | VX-147       |
| Other name                             | IXP          |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subject received VX-147 once daily.

|  |                   |
|--|-------------------|
| <b>Number of subjects in period 1</b>            | VX-147            |
| Started  | 16                |
| Cohort 1   | 3 <sup>[1]</sup>  |
| Cohort 2   | 13 <sup>[2]</sup> |
| Completed  | 15                |
| Not completed                                    | 1                 |
| Withdrawal of consent (not due to adverse event) | 1                 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The milestone represents the number of subjects in Cohort 1.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The milestone represents the number of subjects in Cohort 2.

## Baseline characteristics

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | VX-147 |
|-----------------------|--------|

Reporting group description:

All subjects received VX-147 at a dosage of 15 mg once daily (qd) for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately greater than or equal to ( $\geq$ ) 3 g/g ( $\pm$  10%) and less than ( $<$ ) 10 g/g and estimated glomerular filtration rate (eGFR) approximately  $\geq$ 30 mL/min/1.73 m<sup>2</sup> ( $\pm$  10%). Cohort 2 included subjects with UPCR approximately  $\geq$ 0.8 g/g ( $\pm$  10%) and  $<$ 2.7 g/g and eGFR approximately  $\geq$ 30 mL/min/1.73 m<sup>2</sup>.

| Reporting group values                    | VX-147     | Total |  |
|---|------------|-------|--|
| Number of subjects                        | 16         | 16    |  |
| Age categorical                           |            |       |  |
| Units: Subjects                           |            |       |  |
| Age continuous                            |            |       |  |
| Units: years                              |            |       |  |
| arithmetic mean                           | 38.8       |       |  |
| standard deviation                        | $\pm$ 14.5 | -     |  |
| Gender categorical                        |            |       |  |
| Units: Subjects                           |            |       |  |
| Female                                    | 9          | 9     |  |
| Male                                      | 7          | 7     |  |
| Ethnicity                                 |            |       |  |
| Units: Subjects                           |            |       |  |
| Hispanic or Latino                        | 0          | 0     |  |
| Not Hispanic or Latino                    | 16         | 16    |  |
| Unknown or Not Reported                   | 0          | 0     |  |
| Race                                      |            |       |  |
| Units: Subjects                           |            |       |  |
| American Indian or Alaska Native          | 0          | 0     |  |
| Asian                                     | 0          | 0     |  |
| Native Hawaiian or Other Pacific Islander | 0          | 0     |  |
| Black or African American                 | 16         | 16    |  |
| White                                     | 0          | 0     |  |
| More than one Race                        | 0          | 0     |  |
| Unknown or Not Reported                   | 0          | 0     |  |
| Urine Protein to Creatinine Ratio (UPCR)  |            |       |  |
| Units: g/g                                |            |       |  |
| arithmetic mean                           | 2.08       |       |  |
| standard deviation                        | $\pm$ 0.90 | -     |  |

## End points

### End points reporting groups

|  |        |
|--|--------|
| Reporting group title  | VX-147 |
| Reporting group description:   |        |
| All subjects received VX-147 at a dosage of 15 mg once daily (qd) for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately greater than or equal to ( $\geq$ ) 3 g/g ( $\pm$ 10%) and less than ( $<$ ) 10 g/g and estimated glomerular filtration rate (eGFR) approximately $\geq$ 30 mL/min/1.73 m <sup>2</sup> ( $\pm$ 10%). Cohort 2 included subjects with UPCR approximately $\geq$ 0.8 g/g ( $\pm$ 10%) and $<$ 2.7 g/g and eGFR approximately $\geq$ 30 mL/min/1.73 m <sup>2</sup> . |        |

### Primary: Percent Change From Baseline in UPCR

|                        |   |
|------------------------|---|
| End point title        | Percent Change From Baseline in UPCR <sup>[1]</sup> |
| End point description: |   |

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

End point timeframe:

From Baseline up to Week 13

Notes:

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

Justification: This is a single arm study. Only descriptive statistics for geometric mean percent change from baseline were planned . No statistical comparisons were planned for this endpoint.

| End point values                         | VX-147                 |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                       | Reporting group        |  |  |  |
| Number of subjects analysed              | 13                     |  |  |  |
| Units: Percent Change                    |                        |  |  |  |
| geometric mean (confidence interval 95%) |                        |  |  |  |
| Cohort 1 (n=3)                           | -47.7 (-70.1 to -8.5)  |  |  |  |
| Cohort 2 (n=10)                          | -47.5 (-63.4 to -24.6) |  |  |  |
| Total (n=13)                             | -47.6 (-60.0 to -31.3) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

|                 |  |
|-----------------|--|
| End point title | Safety and Tolerability as Assessed by Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) |
|-----------------|--|

End point description:

Safety set included all subjects who received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified cohorts.

|                             |           |
|-----------------------------|-----------|
| End point type              | Secondary |
| End point timeframe:        |           |
| From Baseline up to Week 17 |           |

|                                       |                 |  |  |  |
|---------------------------------------|-----------------|--|--|--|
| <b>End point values</b>               | VX-147          |  |  |  |
| Subject group type                    | Reporting group |  |  |  |
| Number of subjects analysed           | 16              |  |  |  |
| Units: Subjects                       |                 |  |  |  |
| Cohort 1 : Subjects with TEAEs (n=3)  | 3               |  |  |  |
| Cohort 1 : Subjects with SAEs (n=3)   | 0               |  |  |  |
| Cohort 2 : Subjects with TEAEs (n=13) | 12              |  |  |  |
| Cohort 2 : Subjects with SAEs (n=13)  | 1               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Concentration (Cmax) of VX-147

|   |   |
|---|---|
| End point title   | Maximum Observed Concentration (Cmax) of VX-147 |
| End point description:  |   |
| Pharmacokinetic (PK) set included all subjects who have received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified time point. |   |
| End point type  | Secondary                                       |
| End point timeframe:  |   |
| Pre-dose and at 0.25, 0.5, 1, 2, 4 and 12 hours post-dose on Day 1 and Week 5   |   |

|   |                  |  |  |  |
|---|------------------|--|--|--|
| <b>End point values</b>                   | VX-147           |  |  |  |
| Subject group type                        | Reporting group  |  |  |  |
| Number of subjects analysed               | 16               |  |  |  |
| Units: micrograms per milliliter (mcg/ml) |                  |  |  |  |
| arithmetic mean (standard deviation)      |                  |  |  |  |
| 15 mg qd: Day 1 (n=15)                    | 0.168 (± 0.0630) |  |  |  |
| 45 mg qd: Week 5 (n=14)                   | 0.846 (± 0.303)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Observed Pre-dose Concentration (Ctough) of VX-147

|                 |  |
|-----------------|--|
| End point title | Observed Pre-dose Concentration (Ctough) of VX-147 |
|-----------------|--|

End point description:

PK set included all subjects who have received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified time point.

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

End point timeframe:

Pre-dose and on Day 8, 15, Week 3, 5, 9 and 13

| End point values                     | VX-147           |  |  |  |
|--------------------------------------|------------------|--|--|--|
| Subject group type                   | Reporting group  |  |  |  |
| Number of subjects analysed          | 16               |  |  |  |
| Units: mcg/ml                        |                  |  |  |  |
| arithmetic mean (standard deviation) |                  |  |  |  |
| 15 mg qd: Day 8 (n=16)               | 0.153 (± 0.0984) |  |  |  |
| 15 mg qd: Day 15 (n=15)              | 0.123 (± 0.0796) |  |  |  |
| 45 mg qd: Week 3 (n=15)              | 0.379 (± 0.249)  |  |  |  |
| 45 mg qd: Week 5 (n=15)              | 0.492 (± 0.265)  |  |  |  |
| 45 mg qd: Week 9 (n=14)              | 0.446 (± 0.342)  |  |  |  |
| 45 mg qd: Week 13 (n=13)             | 0.529 (± 0.302)  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Area Under the Concentration Time-curve From 0 to 24 hours (AUC0-24hr) of VX-147

|                 |  |
|-----------------|--|
| End point title | Area Under the Concentration Time-curve From 0 to 24 hours (AUC0-24hr) of VX-147 |
|-----------------|--|

End point description:

PK set included all subjects who have received at least 1 dose of study drug in the treatment period. Here, the "n" signifies subjects who were evaluable for the specified time point.

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

End point timeframe:

Pre-dose and at 0.25, 0.5, 1, 2, 4, 12 and 24 hours Post-dose on Week 5



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| <b>End point values</b>                            | VX-147          |  |  |  |
| Subject group type                                 | Reporting group |  |  |  |
| Number of subjects analysed                        | 13              |  |  |  |
| Units: micrograms per hour<br>milliliter(mcg-h/ml) |                 |  |  |  |
| arithmetic mean (standard deviation)               | 15.3 (± 6.37)   |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 17

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | VX-147: Cohort 1 |
|-----------------------|------------------|

Reporting group description:

Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately  $\geq 3$  g/g ( $\pm 10\%$ ) and  $< 10$  g/g and estimated glomerular filtration rate (eGFR) approximately  $\geq 30$  mL/min/1.73 m<sup>2</sup> ( $\pm 10\%$ ).

|                       |                  |
|-----------------------|------------------|
| Reporting group title | VX-147: Cohort 2 |
|-----------------------|------------------|

Reporting group description:

Cohort 2 included subjects with UPCR approximately  $\geq 0.8$  g/g ( $\pm 10\%$ ) and  $< 2.7$  g/g and eGFR approximately  $\geq 30$  mL/min/1.73 m<sup>2</sup>.

|                       |               |
|-----------------------|---------------|
| Reporting group title | VX-147: Total |
|-----------------------|---------------|

Reporting group description:

All subjects received VX-147 at a dosage of 15 mg qd for 2 weeks and VX-147 at a dosage of 45 mg qd for 11 weeks. Part A was enrolled in 2 cohorts: Cohort 1 and Cohort 2. Cohort 1 included subjects with urine protein to creatinine ratio (UPCR) approximately  $\geq 3$  g/g ( $\pm 10\%$ ) and  $< 10$  g/g and estimated glomerular filtration rate (eGFR) approximately  $\geq 30$  mL/min/1.73 m<sup>2</sup> ( $\pm 10\%$ ). Cohort 2 included subjects with UPCR approximately  $\geq 0.8$  g/g ( $\pm 10\%$ ) and  $< 2.7$  g/g and eGFR approximately  $\geq 30$  mL/min/1.73 m<sup>2</sup>.

| Serious adverse events  | VX-147: Cohort 1 | VX-147: Cohort 2 | VX-147: Total  |
|---|------------------|------------------|----------------|
| Total subjects affected by serious adverse events                   |                  |                  |                |
| subjects affected / exposed   | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%) |
| number of deaths (all causes)                                       | 0                | 0                | 0              |
| number of deaths resulting from adverse events                      |                  |                  | 0              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |                |
| Uterine leiomyoma   |                  |                  |                |
| subjects affected / exposed   | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0          |
| Vascular disorders  |                  |                  |                |
| Deep vein thrombosis  |                  |                  |                |
| subjects affected / exposed   | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0          |

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

| <b>Non-serious adverse events</b>                     | VX-147: Cohort 1 | VX-147: Cohort 2 | VX-147: Total    |
|---|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events |                  |                  |                  |
| subjects affected / exposed                           | 3 / 3 (100.00%)  | 12 / 13 (92.31%) | 15 / 16 (93.75%) |
| Investigations  |                  |                  |                  |
| Blood bicarbonate decreased                           |                  |                  |                  |
| subjects affected / exposed                           | 0 / 3 (0.00%)    | 2 / 13 (15.38%)  | 2 / 16 (12.50%)  |
| occurrences (all)                                     | 0                | 3                | 3                |
| Blood creatine phosphokinase increased                |                  |                  |                  |
| subjects affected / exposed                           | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%)   |
| occurrences (all)                                     | 0                | 1                | 1                |
| Gamma-glutamyltransferase increased                   |                  |                  |                  |
| subjects affected / exposed                           | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%)   |
| occurrences (all)                                     | 0                | 1                | 1                |
| Electrocardiogram ST segment depression               |                  |                  |                  |
| subjects affected / exposed                           | 1 / 3 (33.33%)   | 0 / 13 (0.00%)   | 1 / 16 (6.25%)   |
| occurrences (all)                                     | 1                | 0                | 1                |
| Transaminases increased                               |                  |                  |                  |
| subjects affected / exposed                           | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%)   |
| occurrences (all)                                     | 0                | 1                | 1                |
| Injury, poisoning and procedural complications        |                  |                  |                  |
| Vaccination complication                              |                  |                  |                  |
| subjects affected / exposed                           | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%)   |
| occurrences (all)                                     | 0                | 1                | 1                |
| Cardiac disorders                                     |                  |                  |                  |
| Palpitations  |                  |                  |                  |
| subjects affected / exposed                           | 0 / 3 (0.00%)    | 1 / 13 (7.69%)   | 1 / 16 (6.25%)   |
| occurrences (all)                                     | 0                | 1                | 1                |
| Nervous system disorders                              |                  |                  |                  |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| Headache<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 3 (33.33%)<br>1 | 3 / 13 (23.08%)<br>4 | 4 / 16 (25.00%)<br>5 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 3 (0.00%)<br>0  | 2 / 13 (15.38%)<br>2 | 2 / 16 (12.50%)<br>2 |
| General disorders and administration<br>site conditions                              |                     |                      |                      |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 3 (0.00%)<br>0  | 2 / 13 (15.38%)<br>2 | 2 / 16 (12.50%)<br>2 |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)              | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 1 / 16 (6.25%)<br>1  |
| Gastrointestinal disorders   |                     |                      |                      |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 3 (33.33%)<br>1 | 0 / 13 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |
| Abdominal pain lower<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 1 / 16 (6.25%)<br>1  |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>2  | 1 / 16 (6.25%)<br>2  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 3 (0.00%)<br>0  | 2 / 13 (15.38%)<br>3 | 2 / 16 (12.50%)<br>3 |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 1 / 16 (6.25%)<br>1  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 3 (33.33%)<br>1 | 1 / 13 (7.69%)<br>1  | 2 / 16 (12.50%)<br>2 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 3 (33.33%)<br>1 | 0 / 13 (0.00%)<br>0  | 1 / 16 (6.25%)<br>1  |
| Nausea   |                     |                      |                      |

|   |   |   |   |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1   | 2 / 13 (15.38%)<br>2  | 3 / 16 (18.75%)<br>3  |
| Respiratory, thoracic and mediastinal disorders<br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1   | 0 / 13 (0.00%)<br>0   | 1 / 16 (6.25%)<br>1   |
| Skin and subcutaneous tissue disorders<br>Decubitus ulcer<br>subjects affected / exposed<br>occurrences (all)<br><br>Eczema<br>subjects affected / exposed<br>occurrences (all)<br><br>Dry skin<br>subjects affected / exposed<br>occurrences (all) | 1 / 3 (33.33%)<br>1<br><br>0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0 | 0 / 13 (0.00%)<br>0<br><br>1 / 13 (7.69%)<br>1<br><br>1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1<br><br>1 / 16 (6.25%)<br>1<br><br>1 / 16 (6.25%)<br>1 |
| Renal and urinary disorders<br>Pollakiuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1   | 1 / 16 (6.25%)<br>1   |
| Psychiatric disorders<br>Thinking abnormal<br>subjects affected / exposed<br>occurrences (all)<br><br>Depressed mood<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0                            | 1 / 13 (7.69%)<br>1<br><br>1 / 13 (7.69%)<br>1                            | 1 / 16 (6.25%)<br>1<br><br>1 / 16 (6.25%)<br>1                            |
| Musculoskeletal and connective tissue disorders<br>Muscle spasms<br>subjects affected / exposed<br>occurrences (all)<br><br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Musculoskeletal chest pain                         | 0 / 3 (0.00%)<br>0<br><br>0 / 3 (0.00%)<br>0                            | 1 / 13 (7.69%)<br>1<br><br>3 / 13 (23.08%)<br>3                           | 1 / 16 (6.25%)<br>1<br><br>3 / 16 (18.75%)<br>3                           |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                      | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Synovitis<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Infections and infestations   |                     |                     |                     |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Tinea pedis<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 3 (33.33%)<br>1 | 0 / 13 (0.00%)<br>0 | 1 / 16 (6.25%)<br>1 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |
| Vulvovaginal mycotic infection<br>subjects affected / exposed<br>occurrences (all)    | 0 / 3 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1 | 1 / 16 (6.25%)<br>1 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 05 March 2020     | Amended to specify the doses to be used, added optional Cohort 2 and modified the schedule of assessments and eligibility criteria.            |
| 23 September 2020 | Amended the eligibility criteria.  |
| 11 December 2020  | Amended the eligibility criteria and also specified that both cohorts will be analyzed for the primary endpoint.                               |
| 09 April 2021     | Amended the eligibility criteria, updated the study restrictions, and contraceptive requirements.  |
| 26 July 2021      | Amended to specify that Cohort 1 will enroll "up to 10 subjects" to clarify that enrollment could be stopped before 10 subjects were enrolled. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported