



## Clinical trial results:

### A Phase 3b Open-label Study Evaluating the Safety of Elexacaftor/Tezacaftor/Ivacaftor Combination Therapy in Subjects With Cystic Fibrosis

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2020-004885-21   |
| Trial protocol           | CZ BE NL ES      |
| Global end of trial date | 20 December 2022 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 05 July 2023 |
| First version publication date | 05 July 2023 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | VX20-445-121 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT05111145 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Vertex Pharmaceuticals Incorporated  |
| Sponsor organisation address | 50 Northern Avenue, Boston, 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? | Yes |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 06 February 2023 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 20 December 2022 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 20 December 2022 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of Elexacaftor (ELX)/Tezacaftor (TEZ)/Ivacaftor (IVA) in subjects with Cystic Fibrosis (CF).

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                          | 14 January 2022 |
| 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 | Australia: 24 |
| Country: Number of subjects enrolled | Canada: 1     |
| Country: Number of subjects enrolled | Spain: 20     |
| Country: Number of subjects enrolled | Belgium: 38   |
| Country: Number of subjects enrolled | Czechia: 3    |
| Worldwide total number of subjects   | 86            |
| EEA total number of subjects         | 61            |

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)                 | 27 |
| Adults (18-64 years)                      | 59 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Subjects from Parent Studies VX19-445-117(NCT04599465) and VX20-445-126(NCT04969224) were enrolled in this study. A total of 86 subjects were enrolled in this study.

### 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 | ELX/TEZ/IVA |
|-----------|-------------|

Arm description:

Subjects received Elexacaftor (ELX) 200 mg once daily (qd)/Tezacaftor (TEZ) 100 mg qd/Ivacaftor (IVA) 150 mg every 12 hours (q12h) in the treatment period for up to 36 weeks.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | ELX/TEZ/IVA                      |
| Investigational medicinal product code | VX-445/VX-661/VX-770             |
| Other name                             | Elexacaftor/Tezacaftor/Ivacaftor |
| Pharmaceutical forms                   | Tablet                           |
| Routes of administration               | Oral use                         |

Dosage and administration details:

Subjects received ELX/TEZ/IVA fixed-dose combination once daily in the morning.

|  |           |
|--|-----------|
| Investigational medicinal product name | IVA       |
| Investigational medicinal product code | VX-770    |
| Other name                             | Ivacaftor |
| Pharmaceutical forms                   | Tablet    |
| Routes of administration               | Oral use  |

Dosage and administration details:

Subjects received IVA once daily in the evening.

| Number of subjects in period 1                     | ELX/TEZ/IVA |
|--|-------------|
| Started  | 86          |
| Completed  | 0           |
| Not completed                                      | 86          |
| Commercial drug available to the subject           | 76          |
| Subject enrolled in another qualified Vertex study | 10          |



## Baseline characteristics

### Reporting groups

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Overall Trial (overall period) |
|-----------------------|--------------------------------|

Reporting group description:

Baseline data is based on the parent study baseline, which is defined as the most recent non-missing measurement collected before the first dose of study drug in the treatment period of parent studies. Baseline data is presented for subjects who received at least 1 dose of study drug in this study.

| Reporting group values  | Overall Trial (overall period) | Total |  |
|---|--------------------------------|-------|--|
| Number of subjects  | 86                             | 86    |  |
| Age categorical<br>Units: Subjects                                      |                                |       |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 25.3<br>± 9.9                  | -     |  |
| Gender categorical<br>Units: Subjects                                   |                                |       |  |
| Female  | 37                             | 37    |  |
| Male  | 49                             | 49    |  |
| Ethnicity<br>Units: Subjects  |                                |       |  |
| Hispanic or Latino  | 11                             | 11    |  |
| Not Hispanic or Latino  | 68                             | 68    |  |
| Not collected per local regulations                                     | 7                              | 7     |  |
| Race<br>Units: Subjects   |                                |       |  |
| White   | 79                             | 79    |  |
| Black or African American   | 0                              | 0     |  |
| Asian   | 0                              | 0     |  |
| American Indian or Alaska Native  | 0                              | 0     |  |
| Native Hawaiian or other Pacific Islander                               | 0                              | 0     |  |
| Other   | 0                              | 0     |  |
| Not collected per local regulations                                     | 7                              | 7     |  |

## End points

### End points reporting groups

|  |             |
|--|-------------|
| Reporting group title  | ELX/TEZ/IVA |
| Reporting group description:<br>Subjects received Elexacaftor (ELX) 200 mg once daily (qd)/Tezacaftor (TEZ) 100 mg qd/Ivacaftor (IVA) 150 mg every 12 hours (q12h) in the treatment period for up to 36 weeks. |             |

### Primary: 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) <sup>[1]</sup> |
|-----------------|---|

End point description:

Safety set included all subjects who received at least 1 dose of study drug in the treatment period.

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

End point timeframe:

Day 1 up to Week 36

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: Only descriptive statistics were planned. No statistical comparisons were planned for this endpoint.

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | ELX/TEZ/IVA     |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 86              |  |  |  |
| Units: Subjects             |                 |  |  |  |
| Subjects with TEAEs         | 61              |  |  |  |
| Subjects with SAEs          | 4               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 36

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | ELX/TEZ/IVA |
|-----------------------|-------------|

Reporting group description:

Subjects received ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h in the treatment period for up to 36 weeks.

| Serious adverse events                            | ELX/TEZ/IVA    |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 4 / 86 (4.65%) |  |  |
| number of deaths (all causes)                     | 0              |  |  |
| number of deaths resulting from adverse events    |                |  |  |
| Investigations                                    |                |  |  |
| Alanine aminotransferase increased                |                |  |  |
| subjects affected / exposed                       | 1 / 86 (1.16%) |  |  |
| occurrences causally related to treatment / all   | 1 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Aspartate aminotransferase increased              |                |  |  |
| subjects affected / exposed                       | 1 / 86 (1.16%) |  |  |
| occurrences causally related to treatment / all   | 1 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Psychiatric disorders                             |                |  |  |
| Anxiety   |                |  |  |
| subjects affected / exposed                       | 1 / 86 (1.16%) |  |  |
| occurrences causally related to treatment / all   | 0 / 1          |  |  |
| deaths causally related to treatment / all        | 0 / 0          |  |  |
| Infections and infestations                       |                |  |  |
| Gastroenteritis viral                             |                |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 86 (1.16%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Malnutrition                                    |                |  |  |
| subjects affected / exposed                     | 1 / 86 (1.16%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | ELX/TEZ/IVA      |  |  |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 33 / 86 (38.37%) |  |  |
| Infections and infestations                           |                  |  |  |
| COVID-19  |                  |  |  |
| subjects affected / exposed                           | 16 / 86 (18.60%) |  |  |
| occurrences (all)                                     | 16               |  |  |
| Infective pulmonary exacerbation of cystic fibrosis   |                  |  |  |
| subjects affected / exposed                           | 11 / 86 (12.79%) |  |  |
| occurrences (all)                                     | 14               |  |  |
| Nasopharyngitis                                       |                  |  |  |
| subjects affected / exposed                           | 9 / 86 (10.47%)  |  |  |
| occurrences (all)                                     | 9                |  |  |
| Upper respiratory tract infection                     |                  |  |  |
| subjects affected / exposed                           | 6 / 86 (6.98%)   |  |  |
| occurrences (all)                                     | 6                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 14 February 2022 | Updated that study drug does not need to be discontinued for a male subject whose female partner becomes pregnant during study participation; Removed parent study VX19-445-114 and updated the number of planned subjects. |

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported