



## Clinical trial results:

### A Multicentre Phase 2 Study of SFX-01 Treatment and Evaluation in Patients with Estrogen Receptor (ER) Positive and Human Epidermal Growth Factor Receptor 2 (HER2) Negative Metastatic Breast Cancer Progressing on either an Aromatase Inhibitor (AI) or Tamoxifen or Fulvestrant

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-004851-28  |
| Trial protocol           | GB ES FR        |
| Global end of trial date | 10 January 2019 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 29 February 2020 |
| First version publication date | 29 February 2020 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | EVG001BC |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02970682 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                                   |
|------------------------------|---------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Evgen Pharma PLC                                                                                  |
| Sponsor organisation address | Liverpool Science Park, Innovation Centre 2, 146 Brownlow Hill, Liverpool, United Kingdom, L3 5RF |
| Public contact               | Clinical Development Officer, Evgen Pharma PLC, 44 1625466591, enquiries@evgen.com                |
| Scientific contact           | Clinical Development Officer, Evgen Pharma PLC, 44 1625466591, enquiries@evgen.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:

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## Results analysis stage

|                                                      |                 |
|------------------------------------------------------|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 08 January 2020 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 10 January 2019 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 10 January 2019 |
| Was the trial ended prematurely?                     | No              |

Notes:

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## General information about the trial

Main objective of the trial:

1. To determine the safety and tolerability of SFX-01 in combination with AI, tamoxifen and fulvestrant
2. To determine clinical benefit rate (CBR) (complete response [CR] + partial response [PR] + stable disease [SD]) at 24 weeks using Response Evaluation Criteria in Solid Tumours (RECIST; version 1.1)

Protection of trial subjects:

Trial subjects were only eligible if they met all 17 inclusion criteria and were excluded for any one of 12 reasons. All patients had to sign an informed consent document, indicating that they understood the purpose of, and procedures required for the study and were willing to participate in the study. A patient could withdraw from the study at any time, and the physician responsible for the patient's wellbeing could also withdraw the patient at any time for an appropriate medical reason. Withdrawn patients were followed up for safety by the site staff. If a patient prematurely discontinued treatment, the reason for discontinuation was recorded.

Safety was assessed by means of clinical examination, vital signs (weight, heart rate, temperature, blood pressure and respiratory rate), performance status, laboratory evaluations (clinical chemistry and haematology), electrocardiograms (ECGs), recording of concurrent illness/therapy and documenting AEs.

Background therapy:

This study was a multi-centre study conducted over a 2-year period. Patients needed to have histologically confirmed ER-positive, HER2-negative, metastatic or locally advanced breast cancer (MBC) with at least 1 site of measurable disease. They previously were to be on either a third generation AI, tamoxifen or fulvestrant and had to have documented evidence of PD immediately prior to entry into this study, but were suitable for continuing the endocrine therapy (ET) they had progressed on according to the treating clinician. Patients continued to receive the same endocrine treatment with the addition of SFX-01.

Evidence for comparator:

Not applicable

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 22 December 2016 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Spain: 5           |
| Country: Number of subjects enrolled | United Kingdom: 27 |
| Country: Number of subjects enrolled | Belgium: 7         |
| Country: Number of subjects enrolled | France: 7          |

|                                    |    |
|------------------------------------|----|
| Worldwide total number of subjects | 46 |
| EEA total number of subjects       | 46 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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)                      | 27 |
| From 65 to 84 years                       | 19 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This study was a multi-centre study conducted over a 2-year period. Patients were recruited from those attending sites in the UK, France, Belgium and Spain for treatment of MBC.

### Pre-assignment

Screening details:

The Screening Phase was up to 28 days prior to enrolment. Patients previously were to be on either a third generation AI, tamoxifen or fulvestrant and had to have documented evidence of PD, but were suitable for continuing ET according to the treating clinician. Patients continued to receive the same treatment with the addition of SFX-01

### Period 1

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

### Arms

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

Arm description:

Aromatase inhibitor plus SFX-01

|                                        |               |
|----------------------------------------|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Sulforadex    |
| Investigational medicinal product code | SFX-01        |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

300mg SFX-01, one capsule taken twice daily, 12 hours apart after food, preferably within 2 hours of eating.

Aromatase inhibitor continued at the same dose prior to entry into the study.

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

Arm description:

Tamoxifen plus SFX-01

|                                        |               |
|----------------------------------------|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Sulforadex    |
| Investigational medicinal product code | SFX-01        |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

300mg SFX-01, one capsule taken twice daily, 12 hours apart after food, preferably within 2 hours of eating.

Tamoxifen continued at the same dose prior to entry into the study.

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

Arm description:

Fulvestrant plus SFX 01

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | Sulforadex    |
| Investigational medicinal product code | SFX-01        |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

300mg SFX-01, one capsule taken twice daily, 12 hours apart after food, preferably within 2 hours of eating.

Fulvestrant continued at 500mg injected intramuscularly every 28 days.

| <b>Number of subjects in period 1</b>     | Arm A | Arm B | Arm C |
|-------------------------------------------|-------|-------|-------|
| Started                                   | 31    | 8     | 7     |
| Completed                                 | 7     | 4     | 1     |
| Not completed                             | 24    | 4     | 6     |
| Consent withdrawn by subject              | 1     | -     | -     |
| Patient choice: progressive disease & AEs | 2     | -     | -     |
| Adverse event, non-fatal                  | 1     | -     | -     |
| progressive disease                       | 19    | 4     | 6     |
| noncompliance/protocol violation          | 1     | -     | -     |

## Baseline characteristics

### Reporting groups

|                                                                 |       |
|-----------------------------------------------------------------|-------|
| Reporting group title                                           | Arm A |
| Reporting group description:<br>Aromatase inhibitor plus SFX-01 |       |
| Reporting group title                                           | Arm B |
| Reporting group description:<br>Tamoxifen plus SFX-01           |       |
| Reporting group title                                           | Arm C |
| Reporting group description:<br>Fulvestrant plus SFX 01         |       |

| Reporting group values      | Arm A    | Arm B    | Arm C    |
|-----------------------------|----------|----------|----------|
| Number of subjects          | 31       | 8        | 7        |
| Age categorical             |          |          |          |
| Age category at study entry |          |          |          |
| Units: Subjects             |          |          |          |
| Adults (18-64 years)        | 16       | 6        | 5        |
| From 65-84 years            | 15       | 2        | 2        |
| Age continuous              |          |          |          |
| Age at study entry          |          |          |          |
| Units: years                |          |          |          |
| median                      | 64       | 55       | 62       |
| full range (min-max)        | 43 to 82 | 45 to 81 | 55 to 77 |
| Gender categorical          |          |          |          |
| Female only                 |          |          |          |
| Units: Subjects             |          |          |          |
| Female                      | 31       | 8        | 7        |
| Male                        | 0        | 0        | 0        |

| Reporting group values      | Total |  |  |
|-----------------------------|-------|--|--|
| Number of subjects          | 46    |  |  |
| Age categorical             |       |  |  |
| Age category at study entry |       |  |  |
| Units: Subjects             |       |  |  |
| Adults (18-64 years)        | 27    |  |  |
| From 65-84 years            | 19    |  |  |
| Age continuous              |       |  |  |
| Age at study entry          |       |  |  |
| Units: years                |       |  |  |
| median                      | -     |  |  |
| full range (min-max)        | -     |  |  |
| Gender categorical          |       |  |  |
| Female only                 |       |  |  |
| Units: Subjects             |       |  |  |
| Female                      | 46    |  |  |
| Male                        | 0     |  |  |

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**Subject analysis sets**

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | FAS           |
| Subject analysis set type  | Full analysis |

Subject analysis set description:

The full analysis set (FAS) included all patients who received any amount of the IP (SFX 01 or ET).

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Safety          |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

The safety population included all patients who received at least 1 dose of study treatment (SFX-01).

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| Reporting group values      | FAS      | Safety   |  |
|-----------------------------|----------|----------|--|
| Number of subjects          | 46       | 46       |  |
| Age categorical             |          |          |  |
| Age category at study entry |          |          |  |
| Units: Subjects             |          |          |  |
| Adults (18-64 years)        | 27       | 27       |  |
| From 65-84 years            | 19       | 19       |  |
| Age continuous              |          |          |  |
| Age at study entry          |          |          |  |
| Units: years                |          |          |  |
| median                      | 63       | 63       |  |
| full range (min-max)        | 43 to 82 | 43 to 82 |  |
| Gender categorical          |          |          |  |
| Female only                 |          |          |  |
| Units: Subjects             |          |          |  |
| Female                      | 46       | 46       |  |
| Male                        | 0        | 0        |  |

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## End points

### End points reporting groups

|                                                                                                                                            |                 |
|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| Reporting group title                                                                                                                      | Arm A           |
| Reporting group description:<br>Aromatase inhibitor plus SFX-01                                                                            |                 |
| Reporting group title                                                                                                                      | Arm B           |
| Reporting group description:<br>Tamoxifen plus SFX-01                                                                                      |                 |
| Reporting group title                                                                                                                      | Arm C           |
| Reporting group description:<br>Fulvestrant plus SFX 01                                                                                    |                 |
| Subject analysis set title                                                                                                                 | FAS             |
| Subject analysis set type                                                                                                                  | Full analysis   |
| Subject analysis set description:<br>The full analysis set (FAS) included all patients who received any amount of the IP (SFX 01 or ET).   |                 |
| Subject analysis set title                                                                                                                 | Safety          |
| Subject analysis set type                                                                                                                  | Safety analysis |
| Subject analysis set description:<br>The safety population included all patients who received at least 1 dose of study treatment (SFX-01). |                 |

### Primary: CBR (Clinical Benefit Rate)

|                                                                                                                                                                                                                                                                                                                    |                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                    | CBR (Clinical Benefit Rate) <sup>[1]</sup> |
| End point description:<br>Primary efficacy endpoint was CBR i.e. the percentage of patients who had a best overall response of confirmed CR or confirmed PR in the first 25 weeks, or who had SD for a minimum of 23 weeks according to RECIST v1.1, based on the investigator's assessments of radiological data. |                                            |
| End point type                                                                                                                                                                                                                                                                                                     | Primary                                    |
| End point timeframe:<br>CBR at Week 24 (FAS)                                                                                                                                                                                                                                                                       |                                            |

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: No formal stats analysis was pre-specified in the protocol / SAP

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: number of patients   | 7               | 4               | 0               | 11                   |

### Statistical analyses

No statistical analyses for this end point

### Secondary: ORR (Objective Response Rate)

|                                                                                       |                               |
|---------------------------------------------------------------------------------------|-------------------------------|
| End point title                                                                       | ORR (Objective Response Rate) |
| End point description:<br>Objective response rate (ORR) at 24 weeks using RECIST v1.1 |                               |

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| ORR at 24 weeks      |           |

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of patients   | 0               | 0               | 0               | 0                    |

### Statistical analyses

No statistical analyses for this end point

### Secondary: CR (Complete Response)

|                                                      |                        |
|------------------------------------------------------|------------------------|
| End point title                                      | CR (Complete Response) |
| End point description:                               |                        |
| Complete response (CR) at 24 weeks using RECIST v1.1 |                        |
| End point type                                       | Secondary              |
| End point timeframe:                                 |                        |
| CR (complete response) at 24 weeks                   |                        |

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of patients   | 0               | 0               | 0               | 0                    |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Confirmed PR (Partial Response)

|                                                               |                                 |
|---------------------------------------------------------------|---------------------------------|
| End point title                                               | Confirmed PR (Partial Response) |
| End point description:                                        |                                 |
| Confirmed partial response (PR) at 24 weeks using RECIST v1.1 |                                 |
| End point type                                                | Secondary                       |
| End point timeframe:                                          |                                 |
| Confirmed partial response (PR) at 24 weeks                   |                                 |

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of patients   | 0               | 0               | 0               | 0                    |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Unconfirmed PR (Partial Response)

|                        |                                                                 |
|------------------------|-----------------------------------------------------------------|
| End point title        | Unconfirmed PR (Partial Response)                               |
| End point description: | Unconfirmed partial response (PR) at 24 weeks using RECIST v1.1 |
| End point type         | Secondary                                                       |
| End point timeframe:   | Unconfirmed PR (partial response) at 24 weeks                   |

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of patients   | 0               | 1               | 1               | 2                    |

### Statistical analyses

No statistical analyses for this end point

### Secondary: SD (Stable Disease)

|                        |                                                   |
|------------------------|---------------------------------------------------|
| End point title        | SD (Stable Disease)                               |
| End point description: | Stable disease (SD) at 24 weeks using RECIST v1.1 |
| End point type         | Secondary                                         |
| End point timeframe:   | SD (stable disease) at 24 weeks                   |

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of patients   | 17              | 5               | 1               | 23                   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PD (Progressive Disease)

|                        |                                                        |
|------------------------|--------------------------------------------------------|
| End point title        | PD (Progressive Disease)                               |
| End point description: | Progressive Disease (PD) at 24 weeks using RECIST v1.1 |
| End point type         | Secondary                                              |
| End point timeframe:   | PD (progressive disease) at 24 weeks                   |

| End point values            | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of patients   | 13              | 2               | 4               | 19                   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Missing

|                        |                                                                  |
|------------------------|------------------------------------------------------------------|
| End point title        | Missing                                                          |
| End point description: | Missing RECIST v 1.1 tumor assessment response data at 24 weeks. |
| End point type         | Secondary                                                        |
| End point timeframe:   | Missing at 24 weeks                                              |

| <b>End point values</b>     | Arm A           | Arm B           | Arm C           | FAS                  |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 31              | 8               | 7               | 46                   |
| Units: Number of Patients   | 1               | 0               | 1               | 2                    |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

24 week study period plus 30 days after last dose of SFX-01 + ET

Adverse event reporting additional description:

All AEs were recorded, with details of the duration and the severity of each episode, the action taken with respect to IP, investigator's evaluation of its relationship to IP and the patient outcome. The intensity (severity of the AE) was assessed using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v4.03

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 20 |
|--------------------|----|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | Safety |
|-----------------------|--------|

Reporting group description: -

| Serious adverse events                            | Safety           |  |  |
|---------------------------------------------------|------------------|--|--|
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 10 / 46 (21.74%) |  |  |
| number of deaths (all causes)                     | 0                |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |
| Investigations                                    |                  |  |  |
| Fibrin D dimer increased                          |                  |  |  |
| subjects affected / exposed                       | 1 / 46 (2.17%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Injury, poisoning and procedural complications    |                  |  |  |
| Hip fracture                                      |                  |  |  |
| subjects affected / exposed                       | 1 / 46 (2.17%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Humerus fracture                                  |                  |  |  |
| subjects affected / exposed                       | 1 / 46 (2.17%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Ligament sprain                                   |                  |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Urinary tract stoma complication                     |                |  |  |
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Nervous system disorders                             |                |  |  |
| Spinal cord compression                              |                |  |  |
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Condition aggravated                                 |                |  |  |
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Pyrexia                                              |                |  |  |
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Blood and lymphatic system disorders                 |                |  |  |
| Anaemia                                              |                |  |  |
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Gastrointestinal disorders                           |                |  |  |
| Abdominal distension                                 |                |  |  |
| subjects affected / exposed                          | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Abdominal pain                                       |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Dyspepsia                                       |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal haemorrhage                    |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting                                        |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Pleuritic pain                                  |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pulmonary embolism                              |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Arthralgia                                      |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Infections and infestations                     |                |  |  |
| Urinary tract infection                         |                |  |  |
| subjects affected / exposed                     | 1 / 46 (2.17%) |  |  |
| 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>                     | Safety           |  |  |
|-------------------------------------------------------|------------------|--|--|
| Total subjects affected by non-serious adverse events |                  |  |  |
| subjects affected / exposed                           | 45 / 46 (97.83%) |  |  |
| Investigations                                        |                  |  |  |
| Blood alkaline phosphatase increased                  |                  |  |  |
| subjects affected / exposed                           | 6 / 46 (13.04%)  |  |  |
| occurrences (all)                                     | 7                |  |  |
| Alanine aminotransferase increased                    |                  |  |  |
| subjects affected / exposed                           | 5 / 46 (10.87%)  |  |  |
| occurrences (all)                                     | 5                |  |  |
| Blood lactate dehydrogenase increased                 |                  |  |  |
| subjects affected / exposed                           | 4 / 46 (8.70%)   |  |  |
| occurrences (all)                                     | 6                |  |  |
| Aspartate aminotransferase increased                  |                  |  |  |
| subjects affected / exposed                           | 3 / 46 (6.52%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Platelet count decreased                              |                  |  |  |
| subjects affected / exposed                           | 3 / 46 (6.52%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Weight decreased                                      |                  |  |  |
| subjects affected / exposed                           | 3 / 46 (6.52%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Nervous system disorders                              |                  |  |  |
| Dizziness                                             |                  |  |  |
| subjects affected / exposed                           | 3 / 46 (6.52%)   |  |  |
| occurrences (all)                                     | 3                |  |  |
| Dysgeusia                                             |                  |  |  |

|                                                         |                     |  |  |
|---------------------------------------------------------|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all)        | 3 / 46 (6.52%)<br>3 |  |  |
| General disorders and administration<br>site conditions |                     |  |  |
| Fatigue                                                 |                     |  |  |
| subjects affected / exposed                             | 9 / 46 (19.57%)     |  |  |
| occurrences (all)                                       | 13                  |  |  |
| Asthenia                                                |                     |  |  |
| subjects affected / exposed                             | 8 / 46 (17.39%)     |  |  |
| occurrences (all)                                       | 9                   |  |  |
| Pain                                                    |                     |  |  |
| subjects affected / exposed                             | 3 / 46 (6.52%)      |  |  |
| occurrences (all)                                       | 3                   |  |  |
| Blood and lymphatic system disorders                    |                     |  |  |
| Anaemia                                                 |                     |  |  |
| subjects affected / exposed                             | 4 / 46 (8.70%)      |  |  |
| occurrences (all)                                       | 7                   |  |  |
| Gastrointestinal disorders                              |                     |  |  |
| Nausea                                                  |                     |  |  |
| subjects affected / exposed                             | 25 / 46 (54.35%)    |  |  |
| occurrences (all)                                       | 28                  |  |  |
| Dyspepsia                                               |                     |  |  |
| subjects affected / exposed                             | 15 / 46 (32.61%)    |  |  |
| occurrences (all)                                       | 17                  |  |  |
| Diarrhoea                                               |                     |  |  |
| subjects affected / exposed                             | 12 / 46 (26.09%)    |  |  |
| occurrences (all)                                       | 12                  |  |  |
| Vomiting                                                |                     |  |  |
| subjects affected / exposed                             | 10 / 46 (21.74%)    |  |  |
| occurrences (all)                                       | 11                  |  |  |
| Abdominal pain                                          |                     |  |  |
| subjects affected / exposed                             | 7 / 46 (15.22%)     |  |  |
| occurrences (all)                                       | 7                   |  |  |
| Constipation                                            |                     |  |  |
| subjects affected / exposed                             | 4 / 46 (8.70%)      |  |  |
| occurrences (all)                                       | 4                   |  |  |
| Gastrooesophageal reflux disease                        |                     |  |  |

|                                                                                                                  |                        |  |  |
|------------------------------------------------------------------------------------------------------------------|------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                                                 | 4 / 46 (8.70%)<br>4    |  |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                                         | 3 / 46 (6.52%)<br>4    |  |  |
| Flatulence<br>subjects affected / exposed<br>occurrences (all)                                                   | 3 / 46 (6.52%)<br>3    |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)  | 4 / 46 (8.70%)<br>4    |  |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                            | 4 / 46 (8.70%)<br>4    |  |  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all) | 10 / 46 (21.74%)<br>10 |  |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                                                   | 5 / 46 (10.87%)<br>7   |  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                                            | 5 / 46 (10.87%)<br>5   |  |  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)                                         | 3 / 46 (6.52%)<br>4    |  |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all)     | 6 / 46 (13.04%)<br>7   |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 22 July 2016    | Amendment 01, Version 2.0<br>Inclusion criterion no. 12 revised to state that no more than 3 prior lines of ET for the MBC                                                                                                                                                                                                                                                                                                                                                                                           |
| 30 August 2016  | Amendment 02, Version 3.0<br>Added a pregnancy test as study Baseline Visit to the current pregnancy tests at Visit 2 and Visit 11<br>Amended schedule of events to include the Visit 11 pregnancy test and updated the description of Visit 11 assessments                                                                                                                                                                                                                                                          |
| 07 October 2016 | Amendment 03, Version 4.0<br>Removed tumour biopsy at week 16<br>Three exploratory objectives (based on: pharmacogenomics, tumour tissue or whole blood samples; liquid biopsy; proteomics) were deleted<br>Made provision for historical paraffin embedded tissue block (or slides derived from this) if available from a previous tumour biopsy to be collected at screening from consented patients<br>Made provision for patients who are receiving clinical benefit to continue to receive SFX-01 after week 24 |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The reported results only present the data from the 24-week main study period. Data from patients who continued SFX-01 + endocrine therapy beyond 24 weeks in the extended use phase of the study are not presented.

Notes: