Headline Results from STEM:
SFX-01 in the Treatment and Evaluation of Metastatic Breast Cancer (An Open-Label Phase II Study)

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Outline of the presentation

- Estrogen Receptor positive (ER+) metastatic breast cancer: the clinical need
- Rationale for SFX-01 in ER+ metastatic breast cancer
- STEM Phase IIa trial: objectives and trial design
- STEM Headline Results
- Patient case study
- Positioning of SFX-01 in tomorrow’s treatment paradigm and the next steps
ER+ metastatic breast cancer

- Breast cancer is the commonest cancer and the second most frequent cause of cancer death in women
- ER+ breast cancer is the most prevalent breast cancer sub-type (70%)
- Metastatic breast cancer (MBC) means that the cancer has spread to other parts of the body
- MBC is incurable with 5-year survival rates of 22%\(^1\)
- First-line endocrine therapy provides 9-15 months of progression free survival\(^2\)
- Combination with CDK4/6 inhibitors extends to c.25 months\(^2\)
- Limited options thereafter and novel, well tolerated therapies are urgently needed

\(^1\)American Cancer Society; \(^2\)Palbociclib and Letrozole in Advanced Breast Cancer (2016) N Engl J Med
Rationale for SFX-01 in ER+ MBC

- Treatment with endocrine therapies results in expansion of treatment resistant cancer stem-like cells (CSCs)
- In preclinical models using patient derived ER+ MBC samples, SFX-01 reduces CSC activity and metastasis
- Translating the preclinical findings with SFX-01 has the potential to delay the generation of resistance and to prolong the duration of sensitivity to endocrine therapy
- Since SFX-01 has so far proven to be well tolerated this would maintain quality of life whilst delaying the use of more toxic agents such as chemotherapy
- By adding SFX-01 to endocrine therapy that has become ineffective in the individual patient, a positive signal in the STEM trial would bode well for deferring resistance in subsequent trials in an earlier patient population
STEM trial objectives

- Exploratory trial with two objectives:
  - To assess the anti-tumour activity of SFX-01 after failure of at least one and up to three prior endocrine therapies
  - To assess the safety and tolerability of SFX-01 in combination with the three commonly used endocrine approaches and with long-term exposure
STEM trial design

- Open-label Phase II, multicentre study in patients taking either a third generation aromatase inhibitor (AI), tamoxifen or fulvestrant and have a documented evidence of progressive disease
- Patients had 6-weekly scans and were discontinued from the study upon clinical progression, up to a maximum of 28 weeks
- At the end of the trial, patients who continued to receive benefit entered the compassionate use phase and remained on drug until clinically indicated or progression
STEM clinical centres

- 14 centres were initiated across Europe: Belgium (5), France (1), Spain (3) and UK (5)
- Of these, 9 sites treated patients within the study: Belgium (7); France (7); Spain (5) and UK (27)

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Headline results:
SFX-01 meets both primary endpoints

- Primary Endpoint 1: Clinical Benefit Rate (CBR, where CBR = Complete Response + Partial Response + Stable Disease) at 24 weeks using RECIST v1.1
  - SFX-01 can both stabilise and shrink endocrine resistant metastatic breast cancer

- Primary Endpoint 2: Treatment-Emergent Adverse Events (Safety and Tolerability) to determine the safety and tolerability of SFX-01 in combination with AI, tamoxifen and fulvestrant
  - SFX-01 is well tolerated with no severe toxicity
Efficacy

- Clinical Benefit Rate across all patients was 23.9%: disease stabilisation seen in all participating countries

- Objective response seen in 2 patients (4%)

- Impressive data considering SFX-01 added to endocrine therapy on which the cancer had progressed
Safety and tolerability

- Adverse events related to SFX-01 seen in ≥10% were:
  - Dyspepsia (indigestion) in approximately one-quarter of patients
  - Nausea in approximately one-fifth of patients
- **No** severe adverse events causally related to SFX-01
- Significantly improved tolerability profile compared with everolimus and exemestane

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<td>SFX-01 N = 46</td>
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<tr>
<td>Nausea</td>
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Patient case study

- Diagnosed age 40 ER+ Her2- early BC
- Received surgery, chemotherapy and tamoxifen
- After 5 years diagnosed with pleural nodules
- Biopsy confirmed metastatic ER+ Her2- BC
- Enrolled into STEM trial May 2017 – tamoxifen + SFX-01
- Objective response to treatment, very well tolerated, able to continue her life caring for her 2 young children and husband with head and neck cancer
- Entered the compassionate use programme and had Stable Disease for a total of 448 days
SFX-01 presents a unique mechanism of action in the metastatic breast cancer therapy landscape.
Market landscape and positioning of SFX-01 in the future treatment paradigm

First-line therapy
- Aromatase Inhibitors (AI)¹
- CDK4/6²

Median PFS c.15 months for AI, extended to c.25 months in combination with CDK4/6²

Second-line therapy
- Fulvestrant/Exemestane
- Everolimus

Median PFS 3.7-6.5 months for Fulvestrant and 3.2 months for Exemestane, extended to 7.8 months for the combination of Everolimus with Exemestane⁴

Fulvestrant/Exemestane

SFX-01

Improved Median PFS?  
More favourable safety and tolerance?

Chemotherapy

¹First-line in post-menopausal – for premenopausal, tamoxifen can also be given as 1st-line therapy
²Palbociclib is approved in 1st and 2nd-line settings, Ribociclib is approved in the 1st-line setting, Abemaciclib is approved in the 1st-line setting and also later lines as monotherapy
Summary and next steps

- Significant clinical need associated with extending the utility of hormone therapies in ER+ mBC
- The commercial success of the CDK4/6 inhibitors validate that need but even those ultimately fail
- In the most difficult of settings, SFX-01 has demonstrated anti-tumour activity with excellent safety and tolerability
- Next step: a randomised, double-blind, placebo controlled Phase II study in ER+ breast cancer for second line treatment after the CDK4/6 inhibitors
- Complete data set to be submitted to ESMO 2019 Congress in Barcelona (27 September to 1 October)
Acknowledgements

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