



# 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%<sup>1</sup>
- First-line endocrine therapy provides 9-15 months of progression free survival<sup>2</sup>
- Combination with CDK4/6 inhibitors extends to c.25 months<sup>2</sup>
- Limited options thereafter and novel, well tolerated therapies are urgently needed

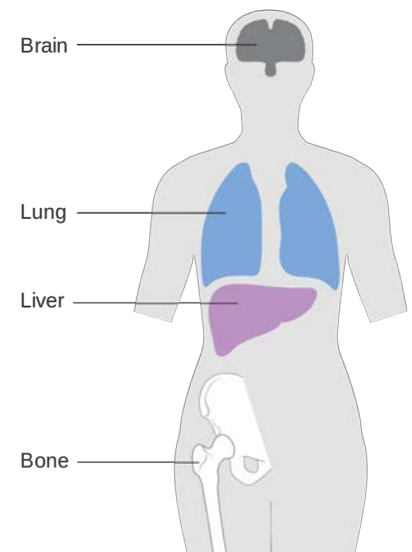


Image: Cancer Research UK

<sup>1</sup>American Cancer Society; <sup>2</sup>Palbociclib and Letrozole in Advanced Breast Cancer (2016) N Engl J Med



## Rationale for SFX-01 in ER+ MBC

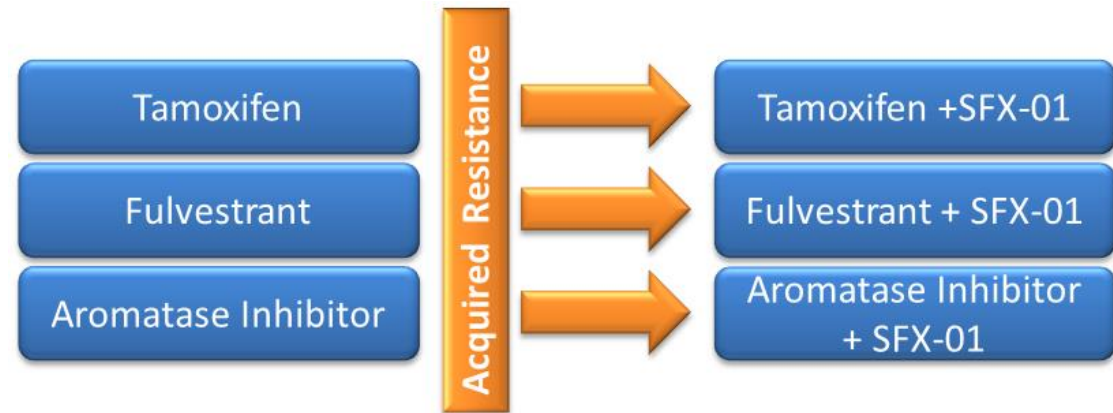
- Treatment with endocrine therapies results in expansion of treatment resistant cancer stem-like cells (CSCs)
- In preclinical models using patient derived ER+ MBC samples, SFX-01 reduces CSC activity and metastasis
- Translating the preclinical findings with SFX-01 has the potential to delay the generation 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) or 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 24 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)

Investigator	Country	No. Screened	No. Enrolled
Prof Duhoux	Belgium	6	6
Dr Canon	Belgium	1	1
Dr Altintas	Belgium	1	0
Prof Campone	France	7	7
Dr Perez	Spain	4	3
Dr Cortes	Spain	2	2
Dr Howell	UK	19	17
Dr Hickish	UK	4	4
Dr Takeuchi	UK	2	2
Dr Anwar	UK	5	5



## Headline results:

# SFX-01 meets both primary endpoints

- Primary Endpoint 1: Clinical Benefit Rate (CBR, where  $CBR = \text{Complete Response} + \text{Partial Response} + \text{Stable Disease}$ ) 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 or tamoxifen or fulvestrant
  - SFX-01 is well tolerated with no severe toxicity





## Efficacy

- Clinical Benefit Rate across all patients was 23.9%: disease stabilisation seen in patients from 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  $\geq 10\%$ 
  - 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

Adverse Event	Grade 3 or 4 (%)		
	SFX-01 N = 46	Eve + EXE N = 482	Placebo + EXE N = 238
Nausea	0	8	1
Dyspepsia	0	0	0
Diarrhoea	0	2	1
Vomiting	0	1	<1
Stomatitis	0	8	1
Rash	0	1	0

## 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

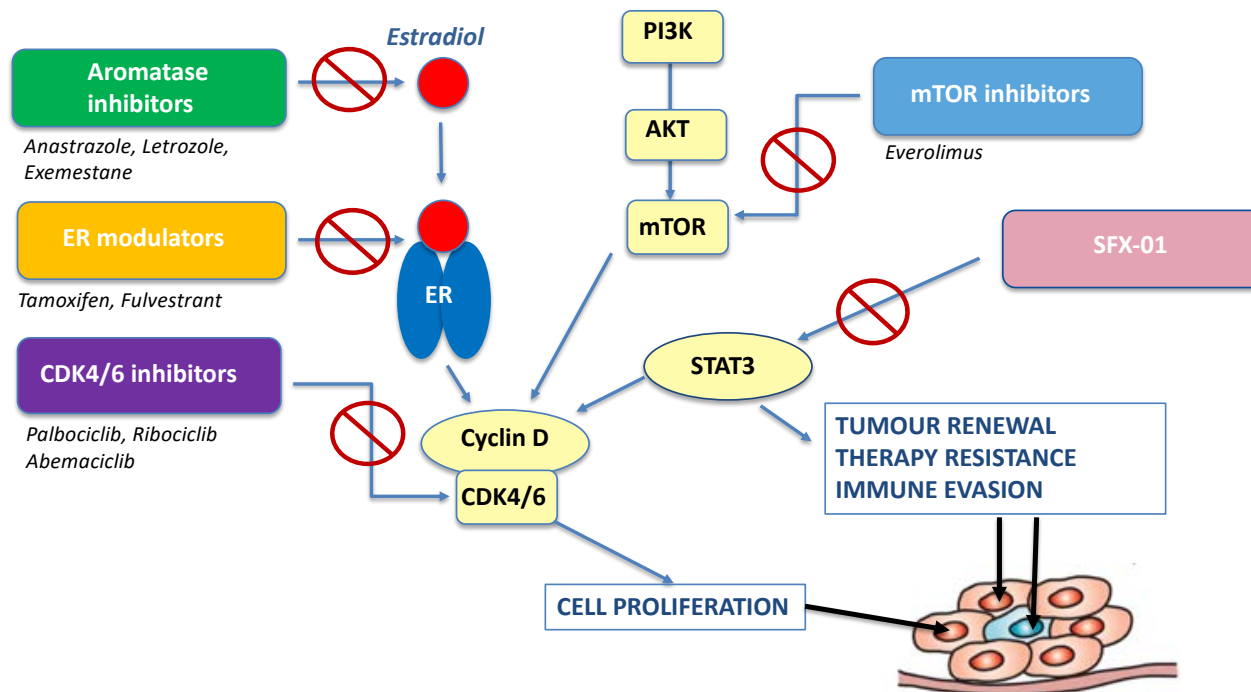
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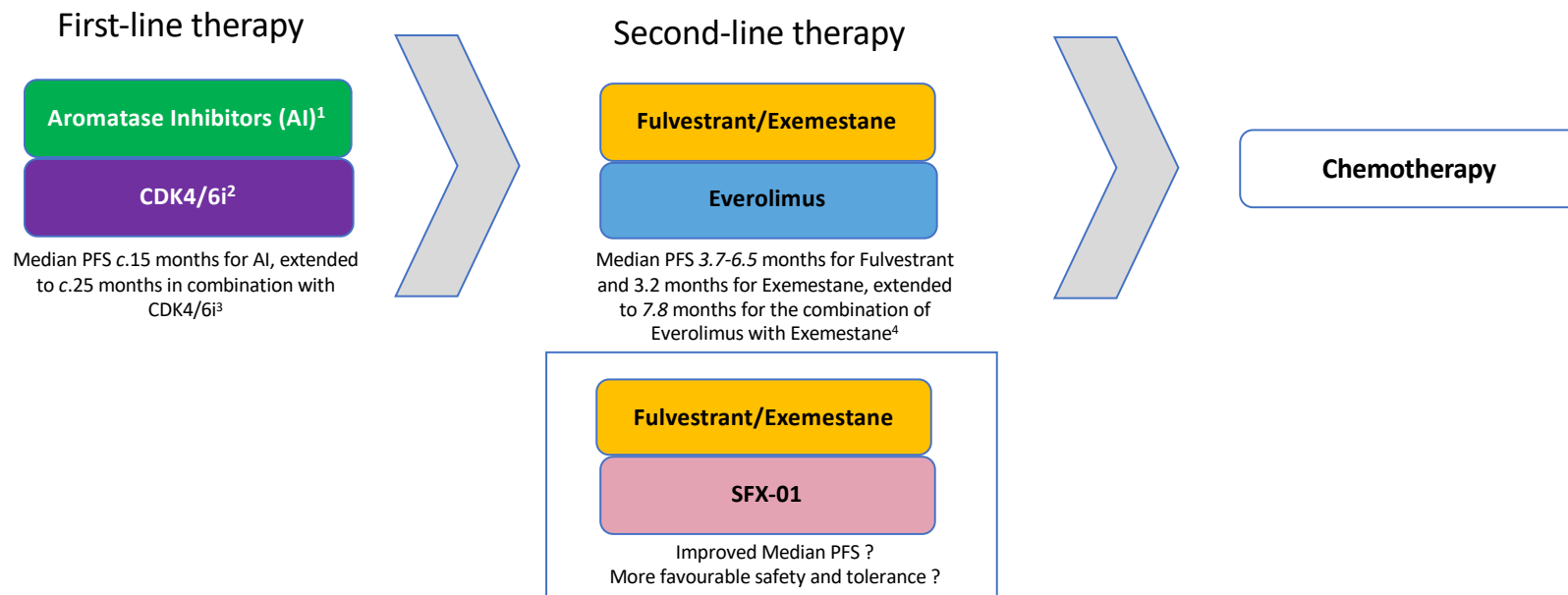
June 2018



# 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



<sup>1</sup>First-line in post-menopausal – for premenopausal, tamoxifen can also be given as 1<sup>st</sup>-line therapy

<sup>2</sup>Palbociclib is approved in 1<sup>st</sup> and 2<sup>nd</sup>-line settings, Ribociclib is approved in the 1<sup>st</sup>-line setting, Abemaciclib is approved in the 1<sup>st</sup>-line setting and also later lines as monotherapy

<sup>3</sup>Palbociclib and Letrozole in Advanced Breast Cancer (2016) N Engl J Med

<sup>4</sup>BOLERO-2: Everolimus in Postmenopausal Hormone-Receptor-Positive Advanced Breast Cancer N Engl J Med 2012; 366:520-529; Fulvestrant in advanced breast cancer: evidence to date and place in therapy (2017) Ther Adv Med Oncol



## 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+ metastatic 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)



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