Sulforaphane (SFN) is a plant secondary metabolite that was first identified as an anti-cancer agent in 1992. SFN is a highly unstable compound and thus the development of a practical pharmaceutical has been challenging. Some exploratory clinical trials have used plant extracts that are enzymatically-treated to release SFN and then subsequently frozen. However, these formulations are not practical for larger trials or subsequent commercialization. SFX-01 is a novel pharmaceutical based upon synthetic SFN stabilized with cyclodextrin, solving the manufacturing and economic barriers to subsequent commercialization. SFX-01 is a novel pharmaceutical based upon synthetic SFN stabilized with cyclodextrin, solving the manufacturing and economic barriers to subsequent commercialization. SFX-01 is a potential therapy for reducing resistance to hormone therapy in patients with mBC.

**SFX-01 in the Treatment and Evaluation of Metastatic breast cancer**

**BACKGROUND**

Sulforaphane (SFN) is a plant secondary metabolite that was first identified as an anti-cancer agent in 1992. SFN is a highly unstable compound and thus the development of a practical pharmaceutical has been challenging. Some exploratory clinical trials have used plant extracts that are enzymatically-treated to release SFN and then subsequently frozen. However, these formulations are not practical for larger trials or subsequent commercialization. SFX-01 is a novel pharmaceutical based upon synthetic SFN stabilized with cyclodextrin, solving the manufacturing and economic barriers to clinical development. Preclinical data show sulforaphane and SFX-01 inhibit breast cancer stem cells1,2 and SFX-01 potently suppresses STAT3 in ER+ metastatic breast cancer2,3. It is therefore hypothesised that SFX-01 could become a potential therapy for reducing resistance to hormone therapy in patients with mBC.

**KEY ELIGIBILITY CRITERIA**

- Male or female patients 18yrs or older
- Histological confirmation of ER+ HER2-negative breast cancer
- Clinical or histological confirmation of metastatic or locally advanced disease not amenable to curative surgical resection
- At least 1 site of measurable disease
- Must be on a third generation AI, Tam or Fulv and have evidence of emerging secondary endocrine resistance as evidenced by either:
  a) Progressive disease while on adjuvant ET but after the first 2 years, or b) Progressive disease within 12 months of completing adjuvant ET, or c) Progressive disease while on ET, 26 months after initiating ET for metastatic breast cancer
- No more than 3 lines of endocrine therapy including the treatment at the time of study entry
- No more than 1 prior line of chemotherapy for metastatically advanced breast cancer

**TRIAL DESIGN**

An open label trial with a maximum target of 60 patients with ER+ HER2-negative, mBC who are on a third generation aromatase inhibitor (AI), tamoxifen (Tam) or fulvestrant (Fulv) and have evidence of emerging secondary endocrine resistance. Participants remain on AI, Tam or Fulv and take this in combination with 300mg SFX-01 orally, twice-daily, and are scanned every 6 weeks (wks) until disease progression. Patients come off study upon progressive disease (PD) or at the full term of 24wks. Patients who are progression free as they approach 24wks can be enrolled in a compassionate use phase.

**STATISTICAL METHODS**

Demographic, baseline characteristics, safety and efficacy data will primarily be summarised descriptively. The sample size of 20 patients in each treatment cohort is such that if the observed CBR on any arm is 15%, it will provide a 90% exact binomial confidence interval (CI) for the true CBR of 4.2% to 34.4%. Duration of response will be compared to duration of response on prior ET.

**REFERENCES**

1. Li et al, Clin Cancer Res 2010 May1;16(9):2580-2590
3. Simões et al, 1st UK Interdisciplinary Breast Cancer Symposium 2018; Manchester, UK