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TFX06 shows remarkable safety and extracranial and intracranial efficacy in patients with ER+ /HER2- breast cancer in a phase 2 study

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Background

TFX06, a third-generation oral CERAN/SERD, was evaluated in a multicenter Phase 1a/b study (NCT05927779) involving patients with ER$^+$/HER2$^-$ locally advanced or metastatic breast cancer (Zhang J, et al., SABCS 2024). Throughout dose escalation, TFX06 was well tolerated at doses up to 200 mg/day, with no dose-limiting toxicities observed, and the maximum tolerated dose (MTD) was not reached. The recommended phase 2 dose was established as 150 mg once daily. A dose expansion study at 150 mg has been initiated, and this abstract summarizes our key findings.

Clinical Designs and Methods

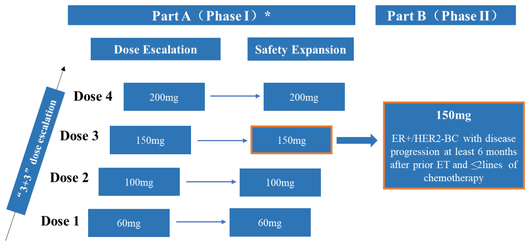
Study Design and Objectives

- An open-label, multicenter, Phase 1/2 clinical trial designed to evaluate the safety, efficacy, and pharmacokinetics of TFX06 tablets in patients with ER+/HER2- locally advanced or metastatic breast cancer.
- Patients received TFX06 tablets orally at a dose of 150 mg once a day (QD) in 28-day cycles until disease progression or unacceptable toxicity.

Key Inclusion Criteria

- ER+/HER2- locally advanced and/or metastatic breast cancer;
- Age ≥18 y old, regardless of menopausal status;
- ≥1 line of endocrine therapy (ET), prior treatments permitted including CDK4/6 inhibitor (CDK4/6i), fulvestrant or combinations;
- ≤2 prior lines of cytotoxic chemotherapy;
- At least one measurable lesion as per RECIST v1.1;
- With an ECOG performance status of 0 or 1.

Scheme 1: Summary of Current Clinical Designs



*According to the protocol, once the Recommended Phase 2 Dose (RP2D) has been confirmed by the SRC, subjects enrolled in the Phase I study are permitted to have their dose adjusted to the RP2D and continue treatment.

Clinical Results

Patient Baseline

As of the cutoff date (July 28, 2025), total 57 patients received TFX06 monotherapy at 150mg dose (median age 60 years [range: 34–74]; ECOG 0-1). 84.2% of patients had visceral metastasis, and 15.8% had brain metastasis. The median number of prior endocrine therapies was 2 (range: 1–4), including fulvestrant (56.1%), CDK4/6 inhibitors (61.4%), and combination of both (38.6%). Tumor assessments were performed by investigators every eight weeks according to RECIST v1.1.

Table 1. Demographics and Baseline Characteristics

Characteristics	Phase 2 @150mg (n=41)	150 mg TFX06 (RP2D) (n=57)
Age（median, range）	59 (41, 73)	60 (34, 74)
ECOG Score, n (%) 0 1	 10 (24.4%) 31 (75.6%)	 13 (22.8%) 44 (77.2%)
Measurable disease, n (%)	41 (100%)	57 (100)
Visceral metastasis, n (%) All (liver, lung, peritoneal, pleural, ascites) Liver	 34 (82.9%) 12 (29.3%)	 48 (84.2%) 17 (29.8%)
Brain metastasis, n (%)	6 (14.6%)	9 (15.8%)
Prior endocrine therapy lines, n (%) 1 2 ≥3	 15（36.6%） 20（48.8%） 6（14.6%）	 22（38.6%） 24（42.1%） 11（19.3%）
Previous types of anti-tumor treatment, n (%) Chemotherapy Aromatase inhibitor Fulvestrant CDK4/6 inhibitor	 37（90.2%） 33（80.5%） 26（63.4%） 28（68.2%）	 51（89.5%） 47（82.5%） 32（56.1%） 35（61.4%）
ESR1-m (ctDNA), n (%)	14（34.1%）	21（36.8%）

Safety

Table 2. Treatment-Related Adverse Events (TRAEs) Reported in ≥15% of Patients

	150 mg TFX06 (n=57)	
Grade	≥ 3	all
TRAEs, n (%)	10 (17.5)	46 (80.7)
Serious TRAEs, n (%)	1 (1.8)	2 (3.5)
TRAE (≥15%), n (%) Hypertriglyceridemia AST increased Anemia Lactate dehydrogenase increased Hypoalbuminemia ALT increased Lymphocyte count decreased White-cell count decreased Serum creatinine increased Creatine phosphokinase MB increased	 2 (3.5) 0 1 (1.8) 0 0 1 (1.8) 3 (5.3) 0 0 0	 22 (38.6) 19 (33.3) 16 (28.1) 12 (21.1) 12 (21.1) 11 (19.3) 10 (17.5) 9 (15.8) 9 (15.8) 9 (15.8)
GI TRAE，n (%) Nausea Constipation Diarrhea Vomiting	 0 0 0 0	 4 (7.0) 4 (7.0) 3 (5.3) 1 (1.8)
Ocular TRAE，n (%) Photopsia	 0	 0

- TFX06 was well tolerated in heavily treated population.
- The most common (≥15% of patients) treatment-related adverse events (TRAEs) were hypertriglyceridemia, AST increased, anemia, lactate dehydrogenase increased and hypoalbuminemia. Most of these events were Grade 1 or 2 in severity.
- The incidence of nausea, constipation, diarrhea and vomiting was low (7.0%, 7.0%, 5.3% and 1.8%, respectively).
- No ocular toxicity reported.

Clinical Results (cont'd)

Preliminary Efficacy

- Among 55 evaluable patients, there were 6 partial responses (ORR was 10.9%); clinical benefit rate (CBR) was 45.5% (Figure 2)
- The median progression-free survival (mPFS) was 5.5 months in the overall population and 5.7 months in patients with detectable ESR1 mutations (Figure 3)
- Among 21 patients who had prior fulvestrant+CDK4/6i combo treatment, CBR was 42.9% and mPFS was 3.7 months, while ESR1 detectable mutation patients, CBR was 55.6% and mPFS was 5.6 months (Figure 4)
- 3 of 8 brain metastasis patients had partial responses (ORR was 37.5%) and CBR of 75%; mPFS was 7.6 months. Notably, three patients with measurable brain lesions were evaluable for response: two showed >70% brain lesion reduction (PR), one had stable disease, suggesting TFX06 had intracranial activity (Table 3 and Figure 5)

Figure 2. Duration of Treatment in the Overall Population

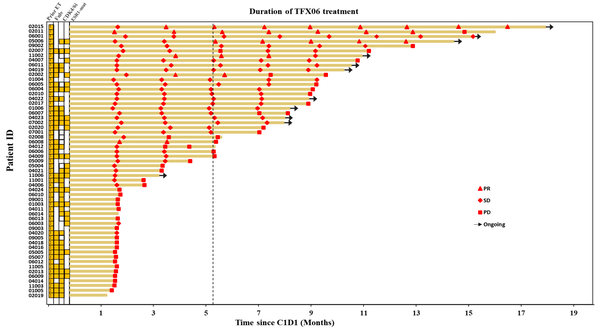
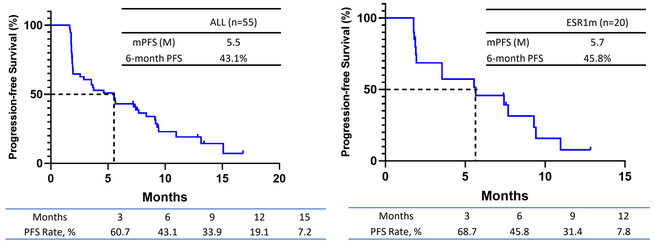


Figure 3. PFS Kaplan-Meier Curves (Overall and ESR1m Populations)



Clinical Results (cont'd)

Figure 4. PFS and Treatment Duration in Patients with Prior Fulvestrant plus CDK4/6 Inhibitor Therapy

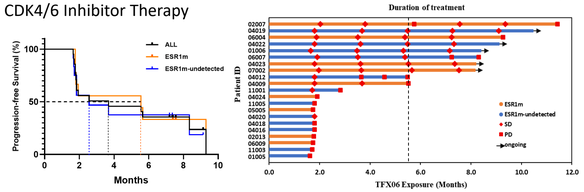
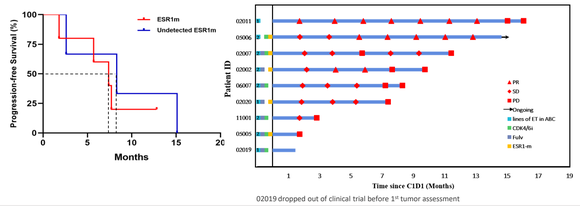


Table 3. TFX06 Clinical Response in Patients with Brain Metastasis

Best clinical response		02002 (60mg*)	02011 (150mg)	05006 (Ⅱ-150mg)	02007 (100mg*)	06007 (Ⅱ-150mg)	02020 (Ⅱ-150mg)	11001 (Ⅱ-150mg)	05005 (Ⅱ-150mg)
Baseline ESR1-m		D538G (36.29%)	not detected	Y537N (6.18%) D538G (0.93%)	D538G (2.77%)	not detected	Y537N (0.50%) D538G (2.79%)	not detected	R555H (54.46%)
Brain lesion	Target	-78.4%	-78.1%	NA	NA	NA	+2.7%	NA	NA
	Non-target	NA	**Disappeared**	**Disappeared**	Present/non-PD	Present/non-PD	Present/non-PD	Present/non-PD	Present/non-PD
	new	no	no	no	no	no	no	no	yes
	Response	**PR**	**PR**	**CR**	SD	SD	SD	SD	PD
Overall	Target	**-36%**	**-62.1%**	**-69.7%**	**-6.3%**	**+4.7%**	**-11.1%**	**-20.5%**	**+42.9%**
	Non-target	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD	Non-CR/Non-PD
	new	no	no	no	no	no	no	no	yes
	Response	PR	PR	PR	SD	SD	SD	SD	PD
Progression free survival (PFS), M		**7.7 M**	**15.1 M**	**14.8 M +**	**5.7 M**	**8.3 M**	**7.4 M**	**2.6 M**	**1.8 M**
Summary		Brain lesions：ORR（37.5%），DCR（87.5%），CBR（75%） Overall：ORR（37.5%），DCR（87.5%），CBR（75%），mPFS 7.55 months							

*: Two patients were transitioned from the phase I dose-escalation dose to the RP2D for continued treatment.

Figure 5. PFS and Treatment Duration in Patients with Brain Metastasis



02019 dropped out of clinical trial before 1st tumor assessment

Conclusions

- TFX06 is well tolerated with excellent safety profile; low GI tox, no photopsia.
- In heavily pretreated patients—including those who had progressed even after a combination of fulvestrant and a CDK4/6 inhibitor—TFX06 demonstrated favorable antitumor activity.
- Intracranial antitumor activity was observed in patients with brain metastases.
- TFX06 clinical trials including combination with CDK4/6i and everolimus are ongoing (NCT05927779). Full data will be disclosed in due course.

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Abbreviations not indicated in the context

- MTD, Maximum Tolerated Dose
- QD, Once a Day
- ET, Endocrine Therapy
- CDK4/6i, CDK4/6 inhibitor
- RP2D, Recommended Phase 2 Dose
- ECOG, Eastern Cooperative Oncology Group
- TRAEs, Treatment-Related Adverse Events
- ORR, Objective Response Rat
- CBR, Clinical Benefit Rate
- mPFS, Median Progression-Free Survival
- CR, Complete Response
- PR, Partial Response
- SD, Stable Disease
- PD, Progressive Disease
- DCR, Disease Control Rate
- ESR1, Estrogen Receptor Gene 1

References

1. Wu J., et al. 2023 AACR Annual Meeting
2. Fu Z., et al. 2023 SABCS
3. Zhang J, et al., SABCS 2024

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