CLAIMS

1. Use of lasofoxifene or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treatment in reducing the progression of estrogen receptor positive and human epidermal growth factor receptor 2 negative ($ER^+/HER2^-$) breast cancer in a patient whose breast cancer has progressed on an aromatase inhibitor, wherein the cancer is determined not to have a gain of function missense mutation within the ligand binding domain (LBD) of the Estrogen Receptor 1 (ESR1) gene.

2. Use according to claim 1, wherein the $ER^+/HER2^-$ cancer is locally advanced or metastatic breast cancer.

3. Use according to claim 1 or claim 2, wherein the aromatase inhibitor is exemestane, letrozole, or anastrozole.

4. Use according to any one of claims 1 to 3, further comprising a determination that the cancer does not have a gain of function missense mutation within the ligand binding domain (LBD) of the Estrogen Receptor 1 (ESR1) gene.

5. Use according to any one of claims 1 to 4, wherein the cancer has at least one variant in at least one gene as set forth below:

TNFRSF1B	CASP3	ABCA1	CYP19A1	NR2F6
RAB42	DNAH5	TRAF1	SETD1A	URI1
FCER1G	LIFR	ABCA2	CETP	MAP3K10
USH2A	MAP3K1	MYO3A	CTCF	CYP2F1
MYCN	HSD17B4	MMP8	PELP1	LILRB1
APOB	HLA-A	PTPN6	TP53	SRC
AFF3	MYB	KRT18	DNAH2	BMP7
VHL	SYNE1	KRT8	BCAS3	GGT1

WNT7A	GLI3	TPH2	TMC8	MN1
RASGEF1B	KMT2C	STAB2	DSG2	CYP2D7
PGRMC2	DEFA3	FLT3	SMAD4	RPGR
PALLD	PTPRD	AHNAK2	MUC16	
NEK1	SYK	HERC2	LDLR	

6. Use according to claim 5, further comprising a determination that the cancer has at least one variant in at least one of the genes set forth.

7. Use according to any one of claims 1 to 6, wherein the lasofoxifene is lasofoxifene tartrate.

8. Use according to claim 7, wherein lasofoxifene tartrate is for oral administration.

9. Use according to claim 8, wherein lasofoxifene tartrate is for oral administration in a dose of 5 mg lasofoxifene/day to 10 mg lasofoxifene/day.

10. Use according to claim 8, wherein lasofoxifene tartrate is for oral administration in a dose of 5 mg lasofoxifene/day.

11. Use according to any one of claims 1 to 10, wherein the treatment further comprises an effective amount of a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor.

12. Use according to claim 11, wherein the CDK4/6 inhibitor is palbociclib, abemaciclib, or ribociclib.

13. Use according to claim 12, wherein the CDK4/6 inhibitor is palbociclib.

14. Use according to claim 12, wherein the CDK4/6 inhibitor is abemaciclib.

15. Use according to claim 12, wherein the CDK4/6 inhibitor is ribociclib.

16. Use according to any one of claims 11 to 15, wherein the lasofoxifene and CDK4/6 inhibitor combination is for inhibiting metastasis of the breast cancer to the bone.

17. Use according to any one of claims 1 to 16, wherein the treatment further comprises an effective amount of an AKT inhibitor or mTor inhibitor.