CLAIMS

1. Use of capivasertib in the manufacture of a medicament for the treatment of a patient having hormone receptor-positive (HR+), HER2-negative locally advanced or metastatic breast cancer, wherein the capivasertib is to be administered as a combination therapy with a CDK4/6 inhibitor and fulvestrant.

2. The use of claim 1, wherein the CDK4/6 inhibitor is selected from palbociclib, ribociclib and abemaciclib.

3. The use of claim 1, wherein capivasertib is to be administered to the patient at an amount of 400 mg twice daily, the CDK4/6 inhibitor is palbociclib and the palbociclib is to be administered to the patient at an amount of 125 mg once daily.

4. The use of claim 1, wherein capivasertib is to be administered to the patient at an amount of 400 mg twice daily, the CDK4/6 inhibitor is palbociclib and the palbociclib is to be administered to the patient at an amount of 100 mg once daily.

5. The use of claim 1, wherein capivasertib is to be administered to the patient at an amount of 320 mg twice daily, the CDK4/6 inhibitor is ribociclib and the ribociclib is to be administered to the patient at an amount of 600 mg once daily.

6. The use of any one of claims 1 to 5, wherein fulvestrant is to be administered to the patient at an amount of 500 mg once monthly.

7. The use of claim 1, wherein the combination therapy is to be administered to the patient over a 28-day cycle in which 400 mg of capivasertib is to be orally administered to the patient twice daily on days 1 to 4, 8 to 11, 15 to 18, and 22 to 25; 125 mg of palbociclib is to be orally administered to the patient once daily on days 1 to 21; and 500 mg of fulvestrant is to be intramuscularly administered to the patient once daily on days 1 and 15 of the first 28-day cycle, and once on day 1 of the 28-day cycle thereafter.

8. The use of claim 1, wherein the combination therapy is to be administered to the patient over a 28-day cycle in which 400 mg of capivasertib is to be orally administered to the patient twice daily on days 1 to 4, 8 to 11, 15 to 18, and 22 to

25; 100 mg of palbociclib is to be orally administered to the patient once daily on days 1 to 21; and 500 mg of fulvestrant is to be intramuscularly administered to the patient once daily on days 1 and 15 of the first 28-day cycle, and once on day 1 of the 28-day cycle thereafter.

9. The use of claim 1, wherein the combination therapy is to be administered to the patient over a 28-day cycle in which 320 mg of capivasertib is to be orally administered to the patient twice daily on days 1 to 4, 8 to 11, 15 to 18, and 22 to 25; 600 mg of ribociclib is to be orally administered to the patient once daily on days 1 to 21; and 500 mg of fulvestrant is to be intramuscularly administered to the patient once daily on days 1 and 15 of the first 28-day cycle, and once on day 1 of the 28-day cycle thereafter.

10. The use of any one of claims 1 to 9, wherein the patient has previously received endocrine therapy.

11. The use of any one of claims 1 to 10, wherein the patient's breast cancer has recurred or progressed during, or within twelve months of the patient completing, adjuvant endocrine therapy.

12. The use of any one of claims 1 to 11, wherein the patient's breast cancer has progressed during endocrine therapy for locally advanced or metastatic breast cancer.

13. The use of claim 10, 11 or 12, wherein the endocrine therapy is tamoxifen or an aromatase inhibitor.

14. The use of any one of claims 1 to 13, wherein the patient has previously received
    (a) an oral SERD as an adjuvant therapy;
    (b) therapy with fulvestrant;
    (c) chemotherapy for advanced breast cancer; and/or
    (d) a CDK4/6 inhibitor as an adjuvant therapy.

15. The use of any one of claims 1 to 14, wherein the patient has not previously received a CDK4/6 inhibitor as a therapy for locally advanced or metastatic breast cancer.

16. The use of any one of claims 1 to 15, wherein the patient's tumour cells comprise any of the following mutations:
    i. E17K in the AKT1 gene;
    ii. any of the mutations in the PIK3CA gene listed in Table 2; and
    iii. any of the mutations in the PTEN gene listed in Table 3 or in Table 4.

17. The use of any one of claims 1 to 16, wherein (a) the patient exhibits a molecular response to the combination therapy after one 28-day cycle of treatment; or (b) the ctDNA burden of the patient is reduced by more than 50% after one 28-day cycle of treatment with the combination therapy.

18. Use of any one of claims 1 to 17, wherein the combination therapy provides (a) an ORR of 40% or more; and/or (b) a CBR at 24 weeks of 40% or more.