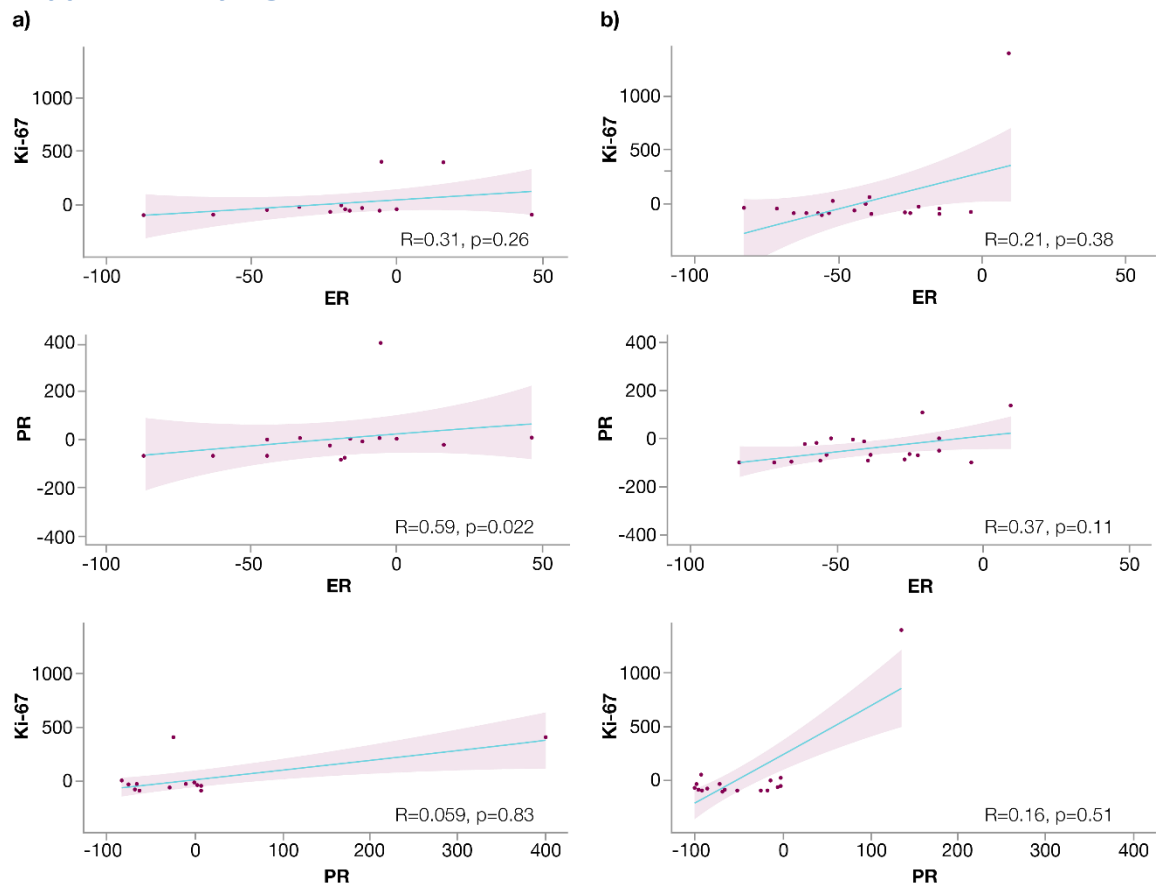


## Supplementary materials

### Supplementary Figure 1

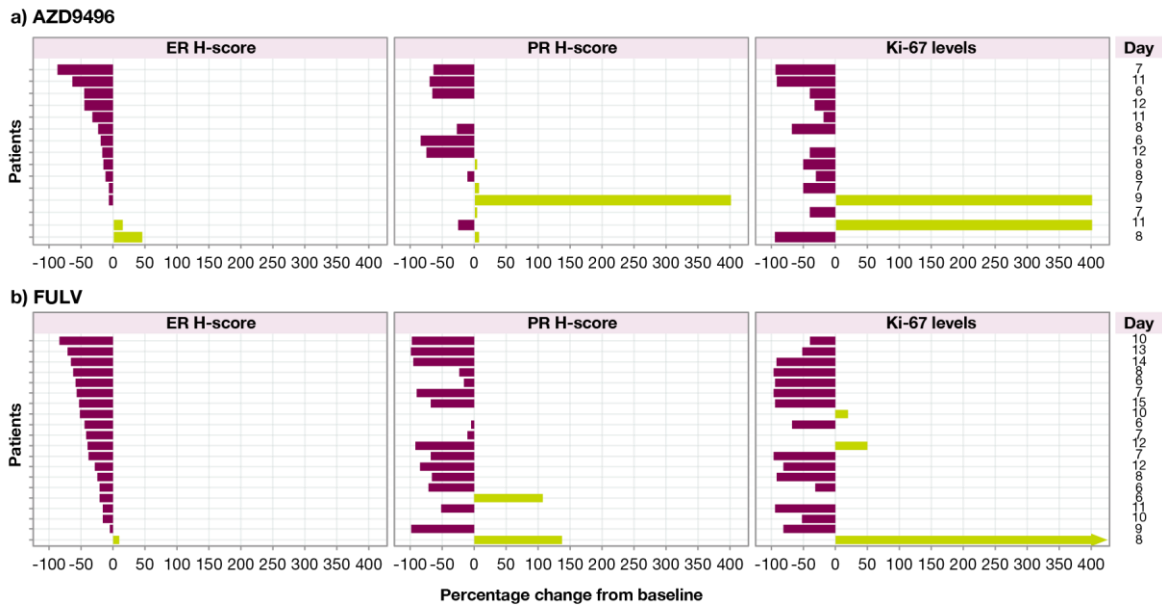


**Supplementary Figure 1:** Correlation between percentage changes in PD markers at on-treatment biopsy after treatment with a) AZD9496 and b) fulvestrant, by individual patient. Blue line represents the line of best fit by linear regression and shaded areas represent 80% CIs.

CI: confidence interval; ER: estrogen receptor; PD: pharmacodynamic; PR: progesterone receptor  
R: correlation coefficient

## Supplementary Figure 2

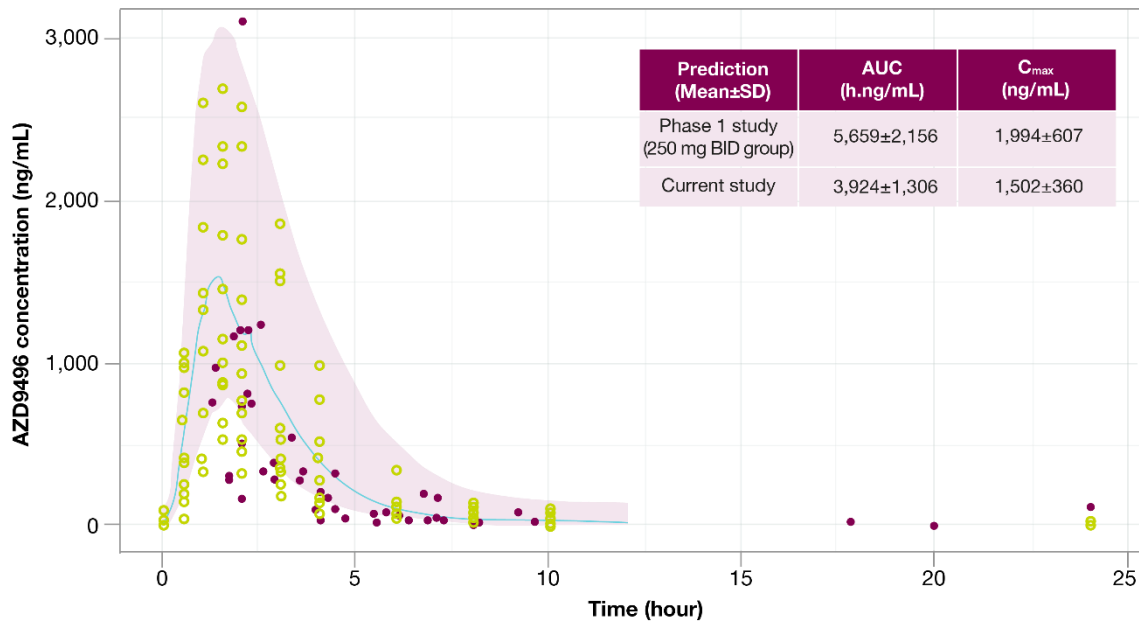
a)



**Supplementary Figure 2:** Pharmacodynamic marker percentage change by patient after receiving (a) AZD9496 or (b) fulvestrant. Each row represents the same patient. Right-hand 'Day' column represents the day of biopsy for each patient.

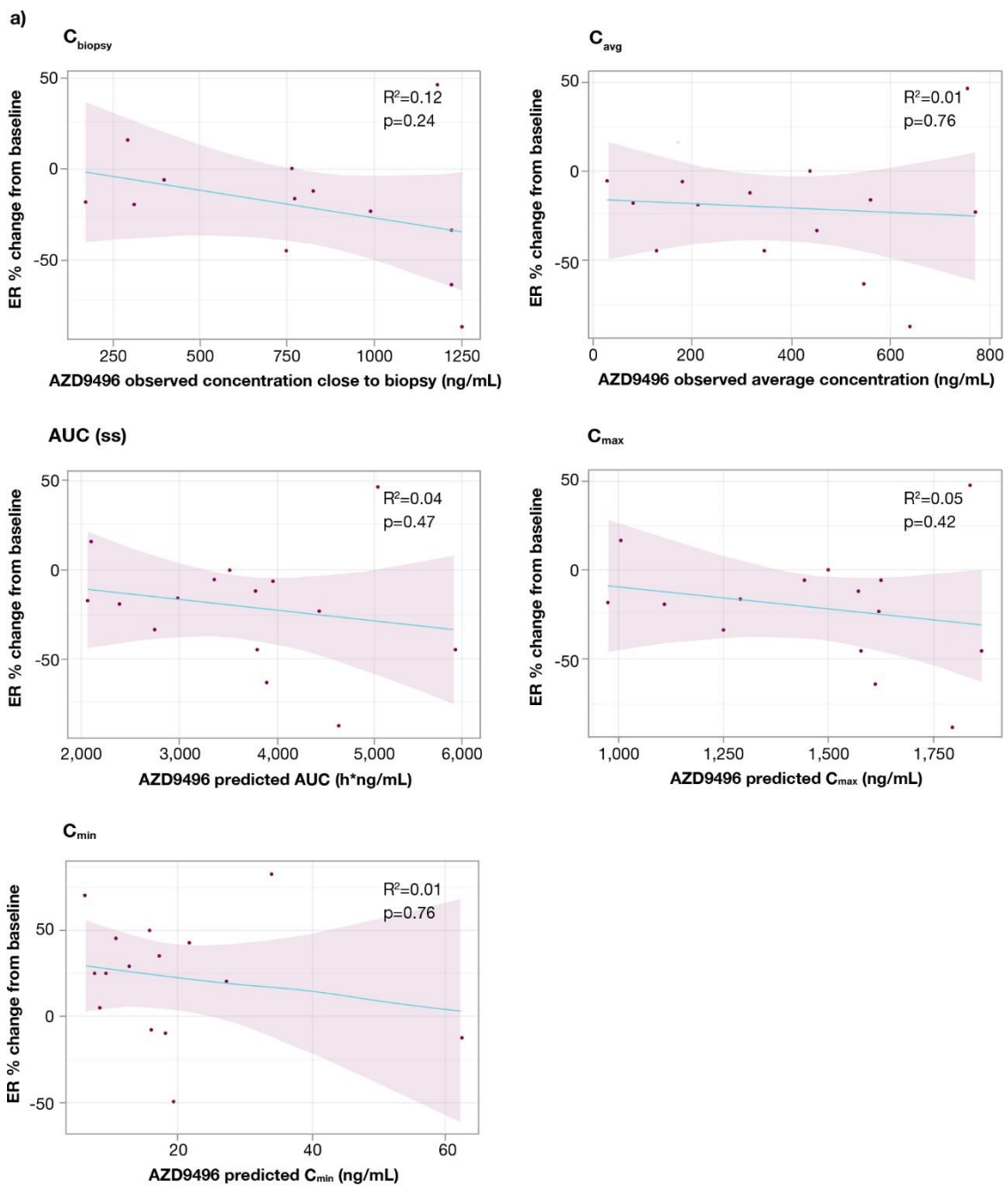
ER: estrogen receptor; PR: progesterone receptor

### Supplementary Figure 3

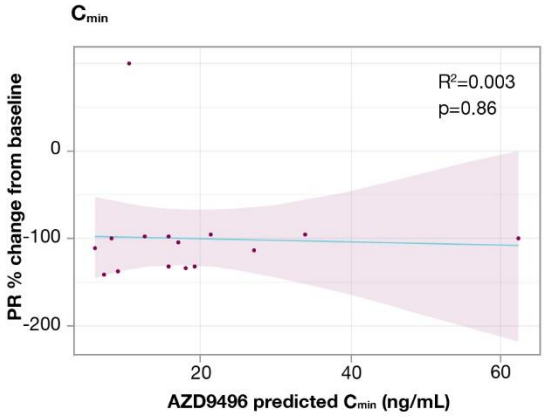
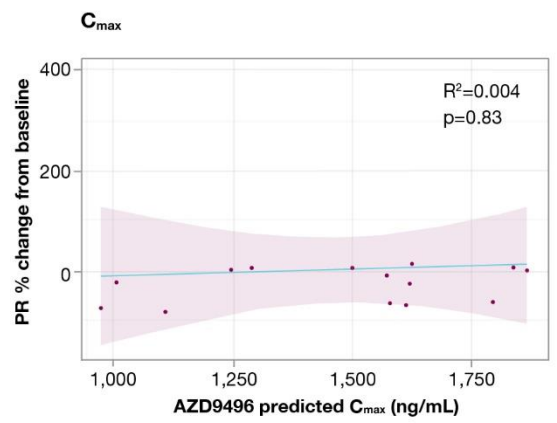
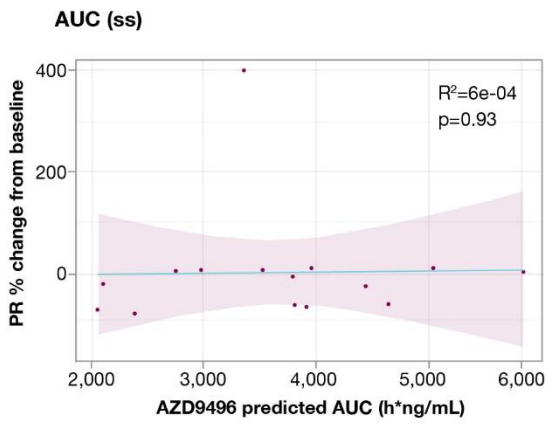
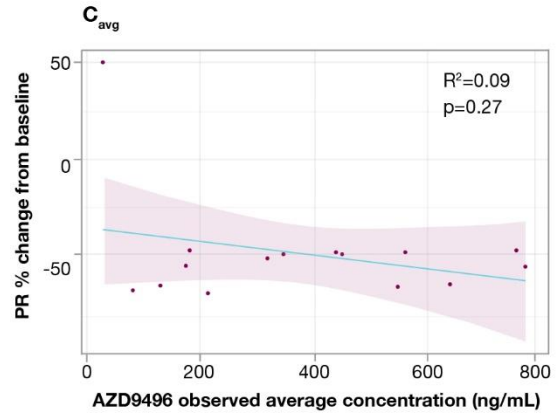
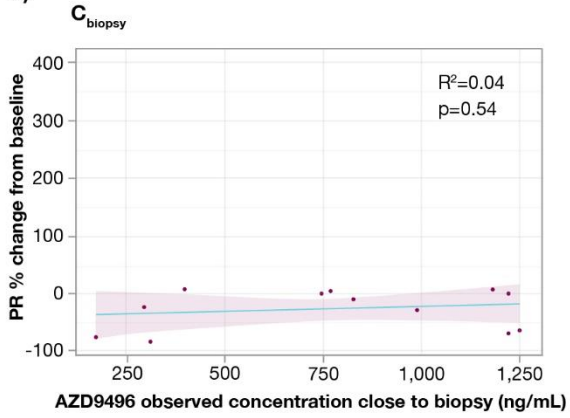


**Supplementary Figure 3:-** Plasma concentration of AZD9496, predicted *versus* observed. AZD9496 plasma concentration during current study (solid dots) compared with the predicted AZD9496 concentration based on the previous Phase 1 study<sup>1</sup> (hollow dots). Line represents the median prediction and the shaded area represents 95% CIs. AUC: area under the concentration–time curve; CI: confidence interval; C<sub>max</sub>: maximum plasma concentration; SD: standard deviation

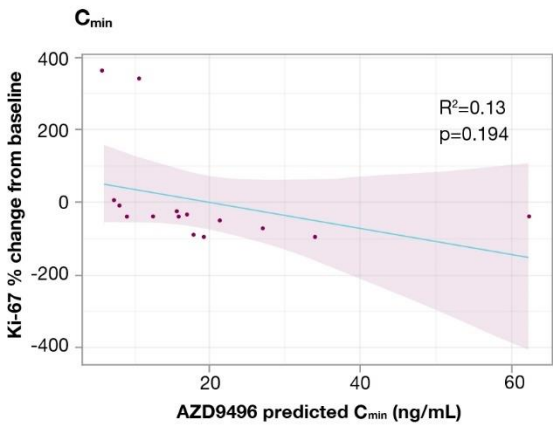
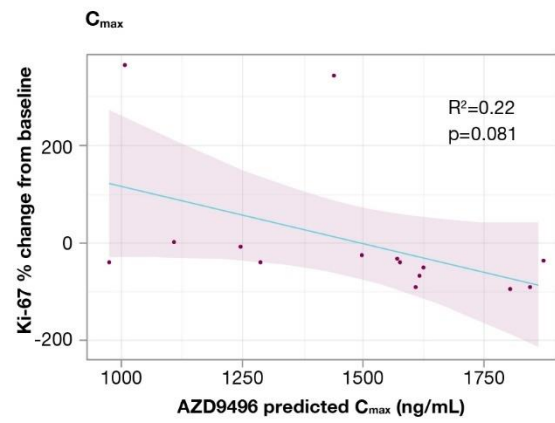
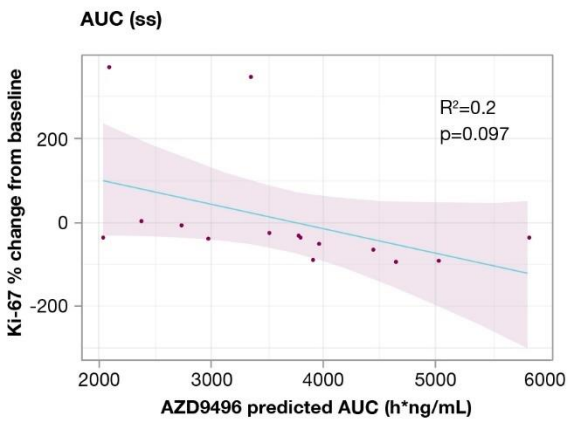
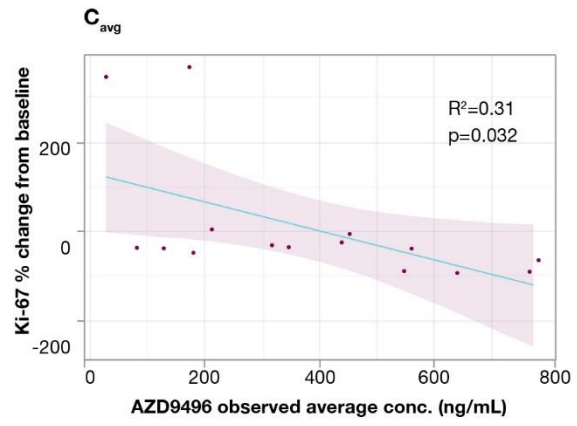
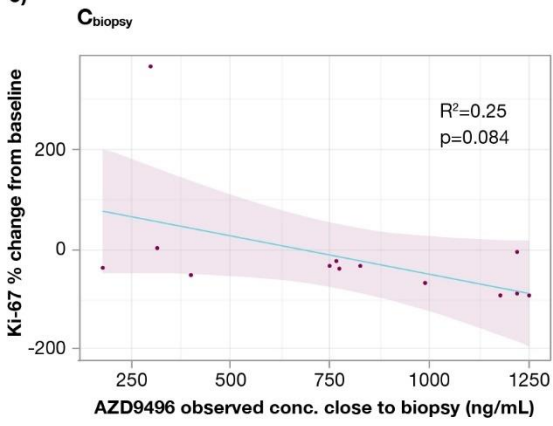
## Supplementary Figure 4



b)



c)



d)



**Supplementary figure 4:** PK/PD relationships at on-treatment biopsy between a) AZD9496 plasma concentration and ER percentage change from baseline, b) AZD9496 plasma concentration and PR percentage change from baseline, c) AZD9496 plasma concentration and Ki-67 percentage change from baseline, and d) observed fulvestrant concentration on day of biopsy and ER, PR, and Ki-67 levels. Blue line represents linear regression and shaded area represents 95% CIs.

AUC: area under the concentration–time curve; C: concentration;  $C_{avg}$ : average of all plasma concentrations; CI: confidence interval;  $C_{max}$ : maximum plasma concentration;  $C_{min}$ : minimum plasma concentration; ER: estrogen receptor; PD: pharmacodynamics; PK: pharmacokinetics; PR: progesterone receptor; ss: steady state

## Reference

1. Hamilton EP, Patel MR, Armstrong AC *et al.* A First-in-Human Study of the New Oral Selective Estrogen Receptor Degradar AZD9496 for ER<sup>+</sup>/HER2<sup>-</sup> Advanced Breast Cancer. *Clin Cancer Res* 2018; **24**: 3510–8.