Supplementary information for

Evaluation of the dual mTOR / PI3K inhibitors Gedatolisib (PF-05212384) and PF-04691502 against ovarian cancer xenograft models

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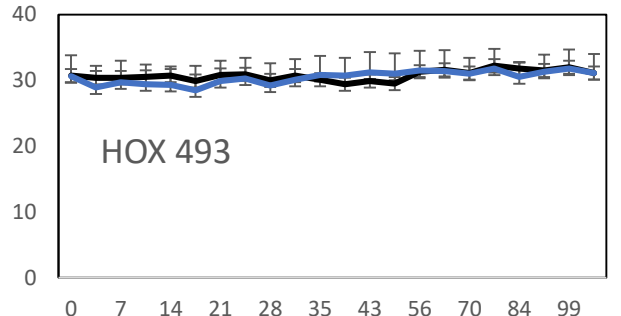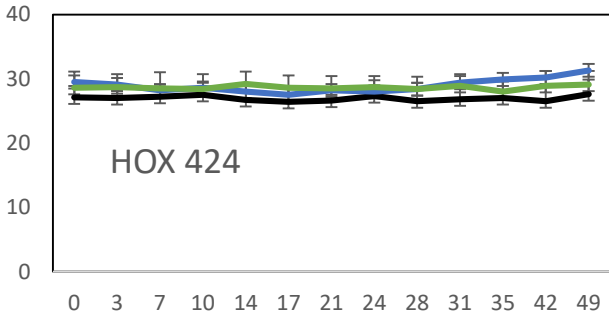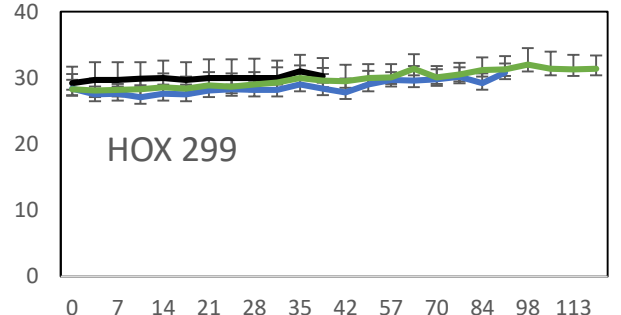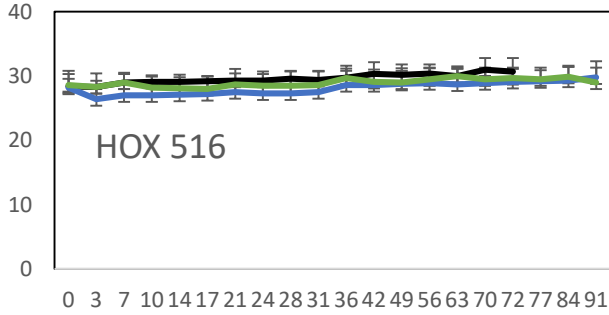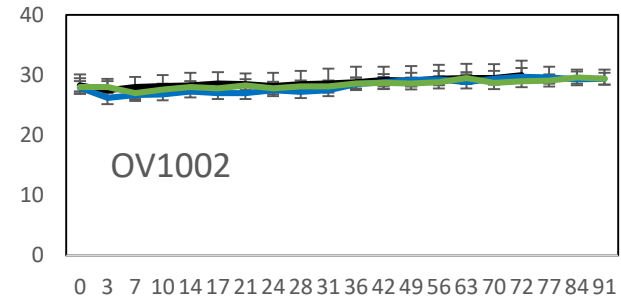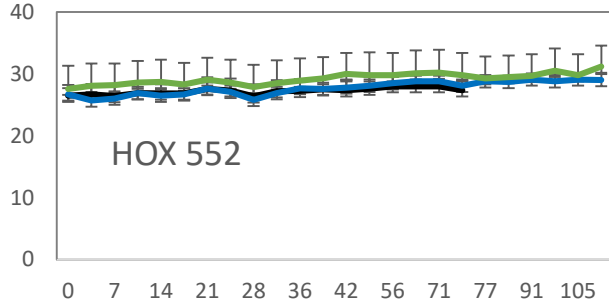
[4]Wyeth Translational Medicine Research Consortium, Sir James Black Centre, Dow Street, Dundee DD1 5EH, United Kingdom

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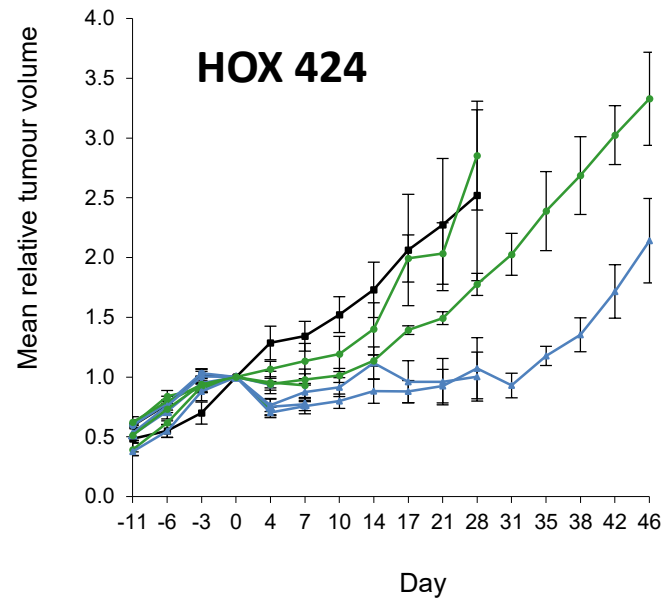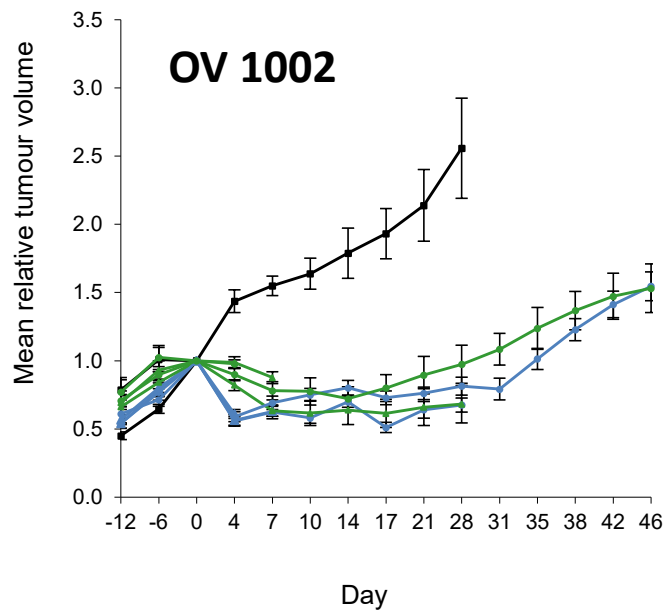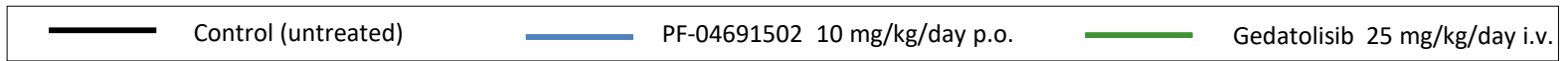
*Corresponding author: simon.langdon@ed.ac.uk
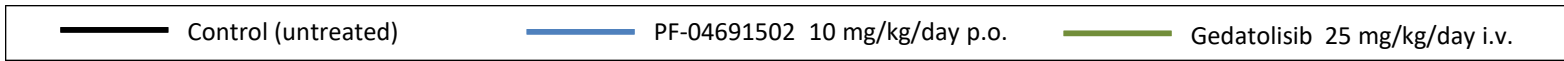
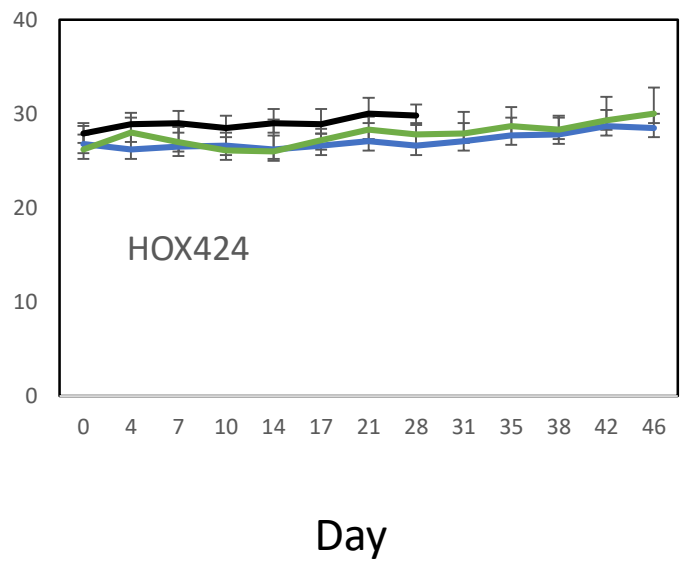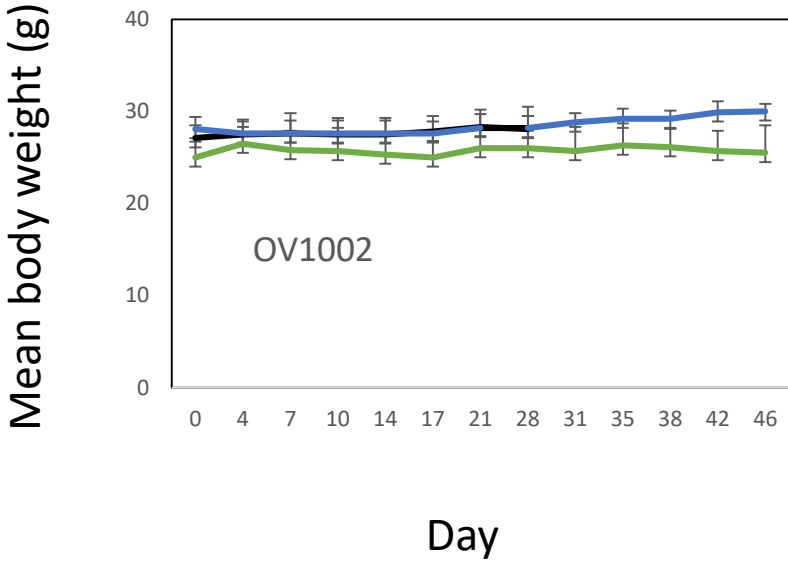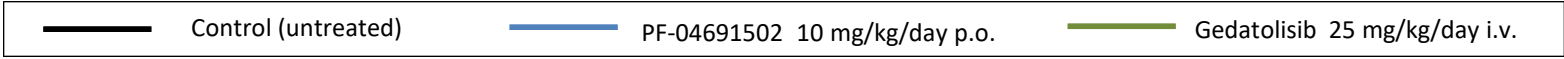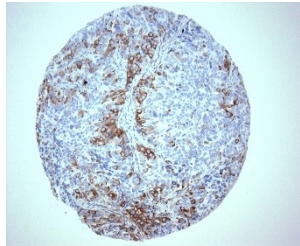**Supplementary Figure 1.** Mean body weights (+/- S.D.) for the antitumour studies

Supplementary Figure 2. Mean relative tumour volumes for the samples collected in the time course expression analysis.
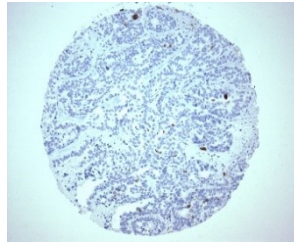
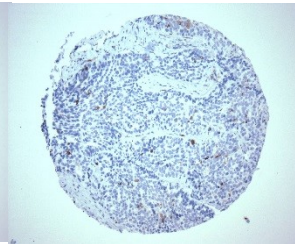**Supplementary Figure 3.** Mean body weights (+/- S.D.) for the animals used in the tumour collection study
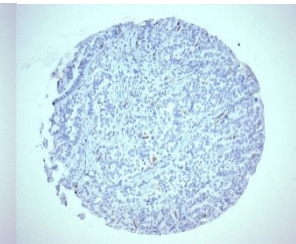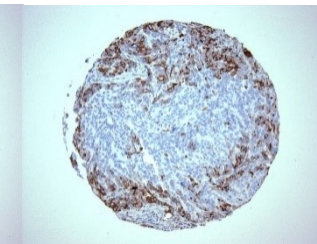
OV1002

Day 0 control

Day 4 PF-04691502

Day 7 PF-04691502

Day 29 PF-04691502

Day 46 PF-04691502

Day 4 Gedatolisib

Day 7 Gedatolisib

Day 29 Gedatolisib

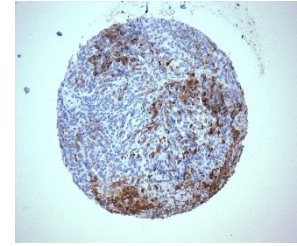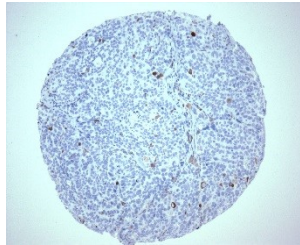Day 46 Gedatolisib

Day 29 Control

HOX424

Day 0 control

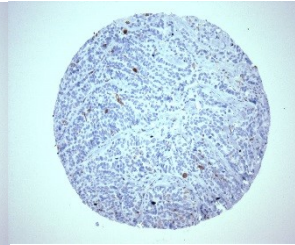Day 4 PF-04691502

Day 7 PF-04691502
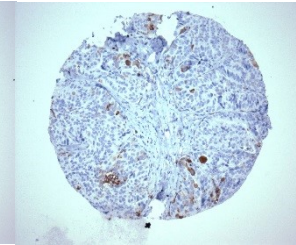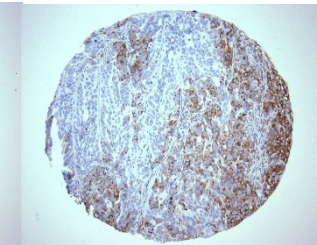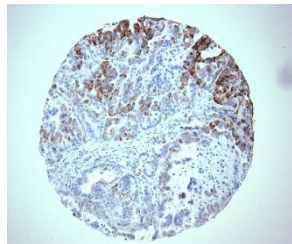
Day 29 PF-04691502

Day 46 PF-04691502

Day 4 Gedatolisib

Day 7 Gedatolisib

Day 29 Gedatolisib

Day 46 Gedatolisib

Day 29 Control

Supplementary Figure 4. Representative images of pS6 (Ser235/236) immunohistochemical staining in TMA cores at each time point. TMA cores were stained as described in Materials and Methods.

OV1002

Day 4 PF-04691502
Day 7 PF-04691502
Day 29 PF-04691502
Day 46 PF-04691502
Day 0 control
Day 29 Control
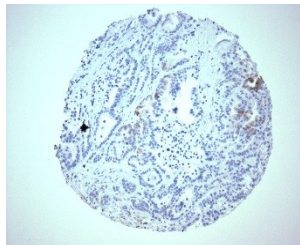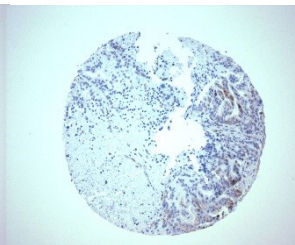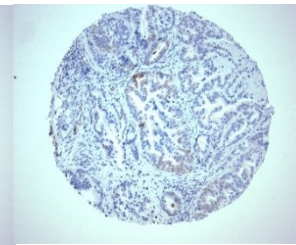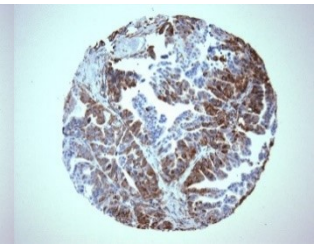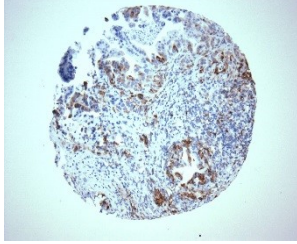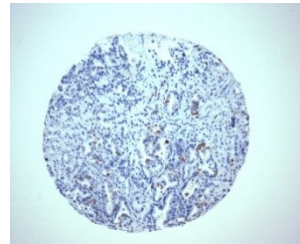Day 4 Gedatolisib
Day 7 Gedatolisib
Day 29 Gedatolisib
Day 46 Gedatolisib
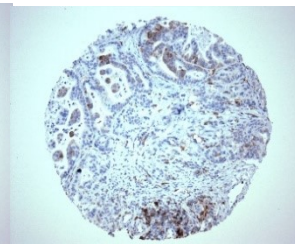
HOX424
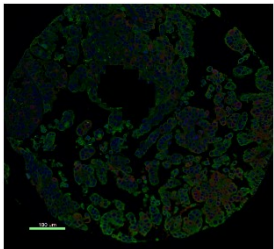
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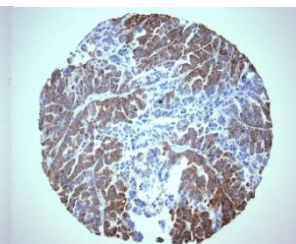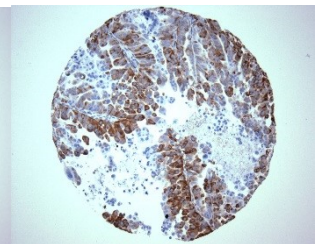Day 7 PF-04691502
Day 29 PF-04691502
Day 46 PF-04691502
Day 0 control
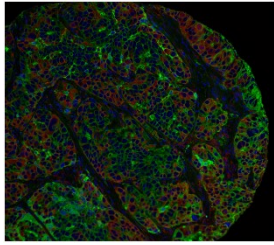Day 29 Control
Day 4 Gedatolisib
Day 7 Gedatolisib
Day 29 Gedatolisib
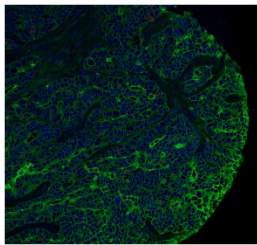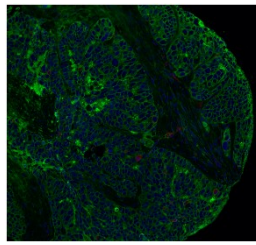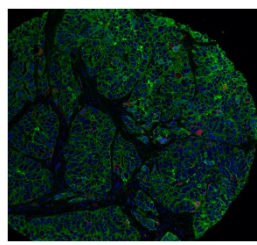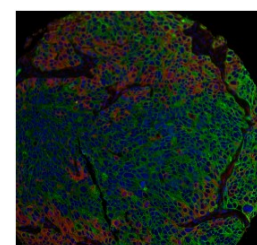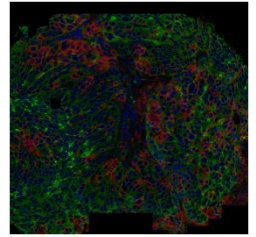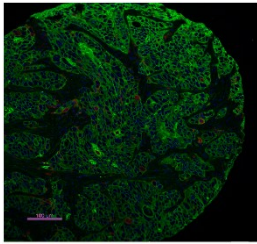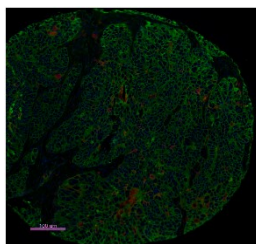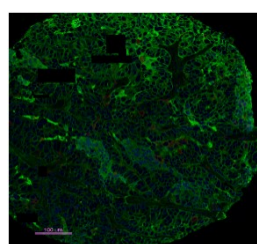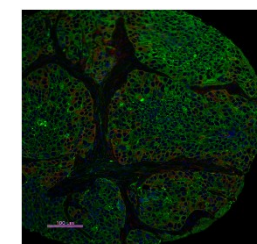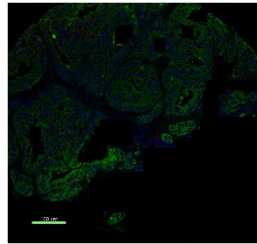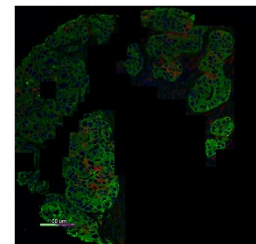Day 46 Gedatolisib

Supplementary Figure 5. Representative images of pS6 (Ser235/236) immunofluorescence staining in TMA cores at each time point. TMA cores were stained as described in Materials and Methods.
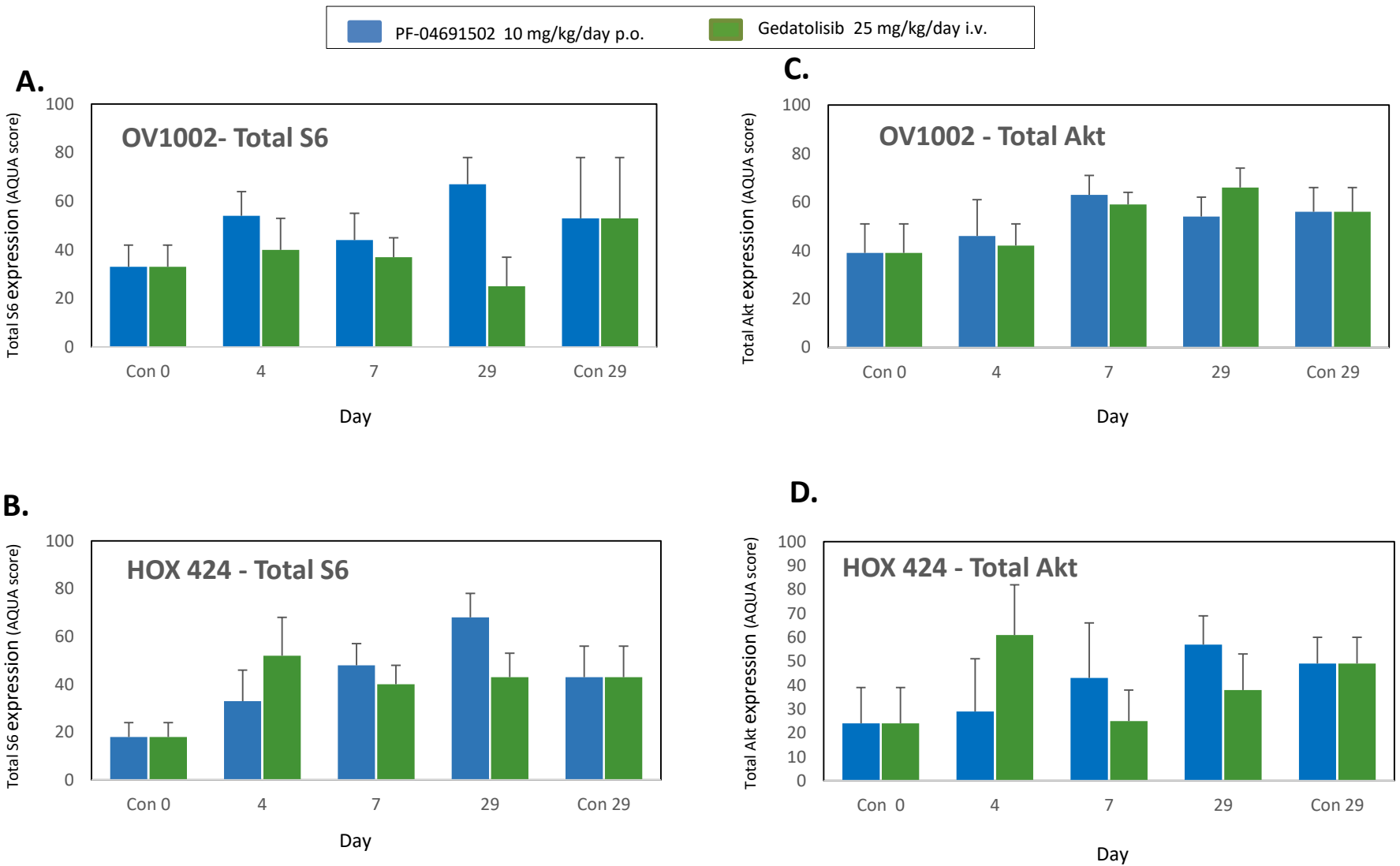
Supplementary Figure 6 Expression of total S6 and Akt in OV1002 and HOV424 xenografts after treatment with PF-04691502 and gedatolisib. A and B: Total S6 expression detected by immunofluorescence in OV1002 (A) and HOX 424 (B) xenograft sections. C and D: Total Akt expression detected by immunofluorescence in OV1002 (C) and HOX 424 (D) xenograft sections. Normalised AQUA scores are shown. Values shown are mean values +/- S.D. for each group of xenografts

Xenograft	pS6/Total S6 ratio	Mean treated tumour volume / mean control volume (Day 7)	Mean control Tumour doubling time (days)	Mean PF-04691502 Treated tumour regrowth rate on cessation of treatment (days)	Ratio of treated / control tumour doubling times
HOX 552	0.26	0.93	38	>79	> 2.1
OV 1002	0.5	0.57	28	21	0.75
HOX 493	0.28	0.76	42	42	1
HOX 424	0.65	0.67	19	10	0.53
HOX 299	0.3	0.68	29	24	1.27
HOX 516	0.2	0.77	21	29	1.4

Supplementary Table 1. Data used to test associations between pS6/total S6 expression and initial tumour response on Day 7 and also regrowth rate on cessation of treatment with PF-04691502. Associations are illustrated in Figures 5C and 5D. Doubling times were calculated by linear regression analysis using data shown in Figure 1. Control doubling time was taken from Day 0, while post-treatment doubling time was assessed from Day 28.