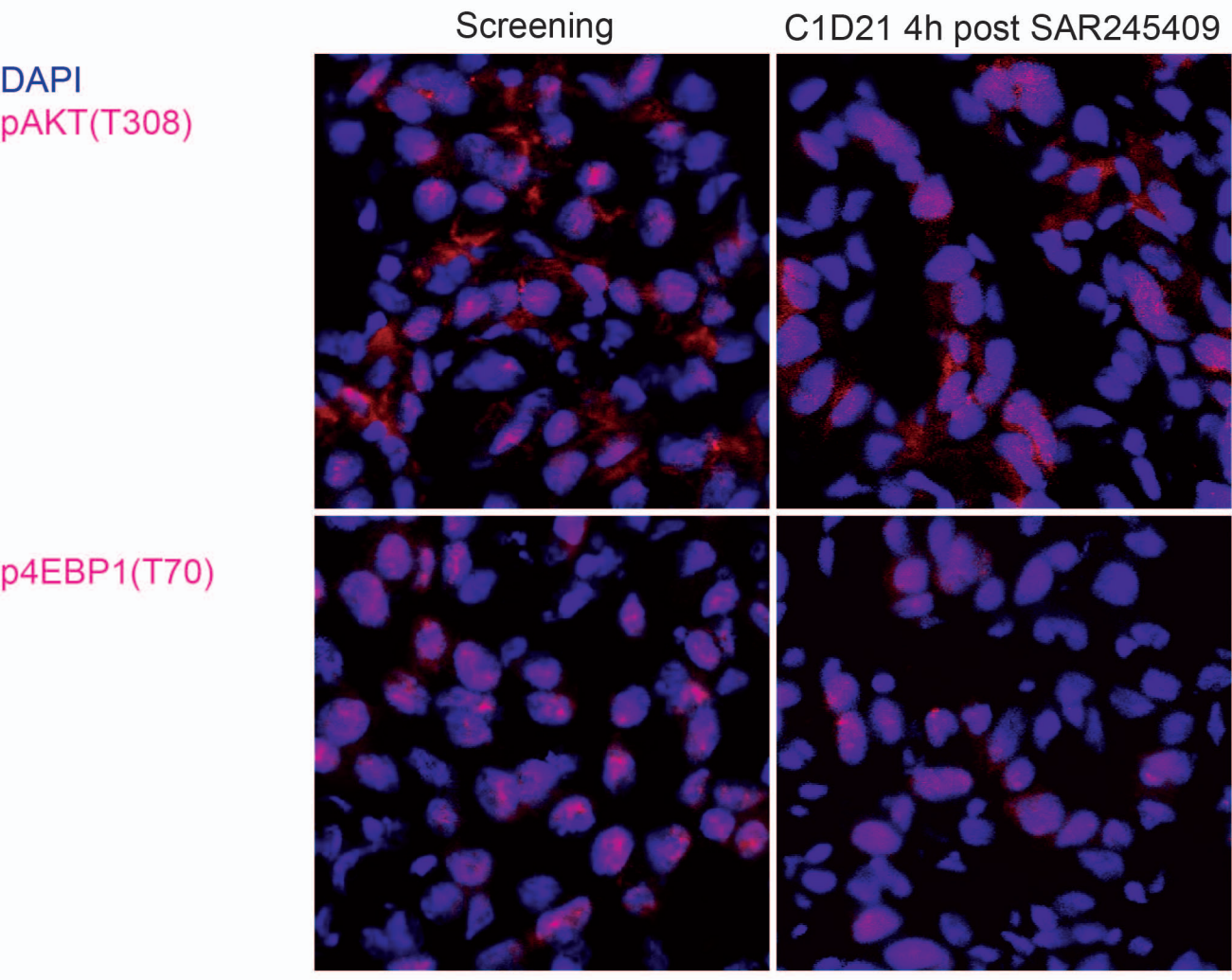
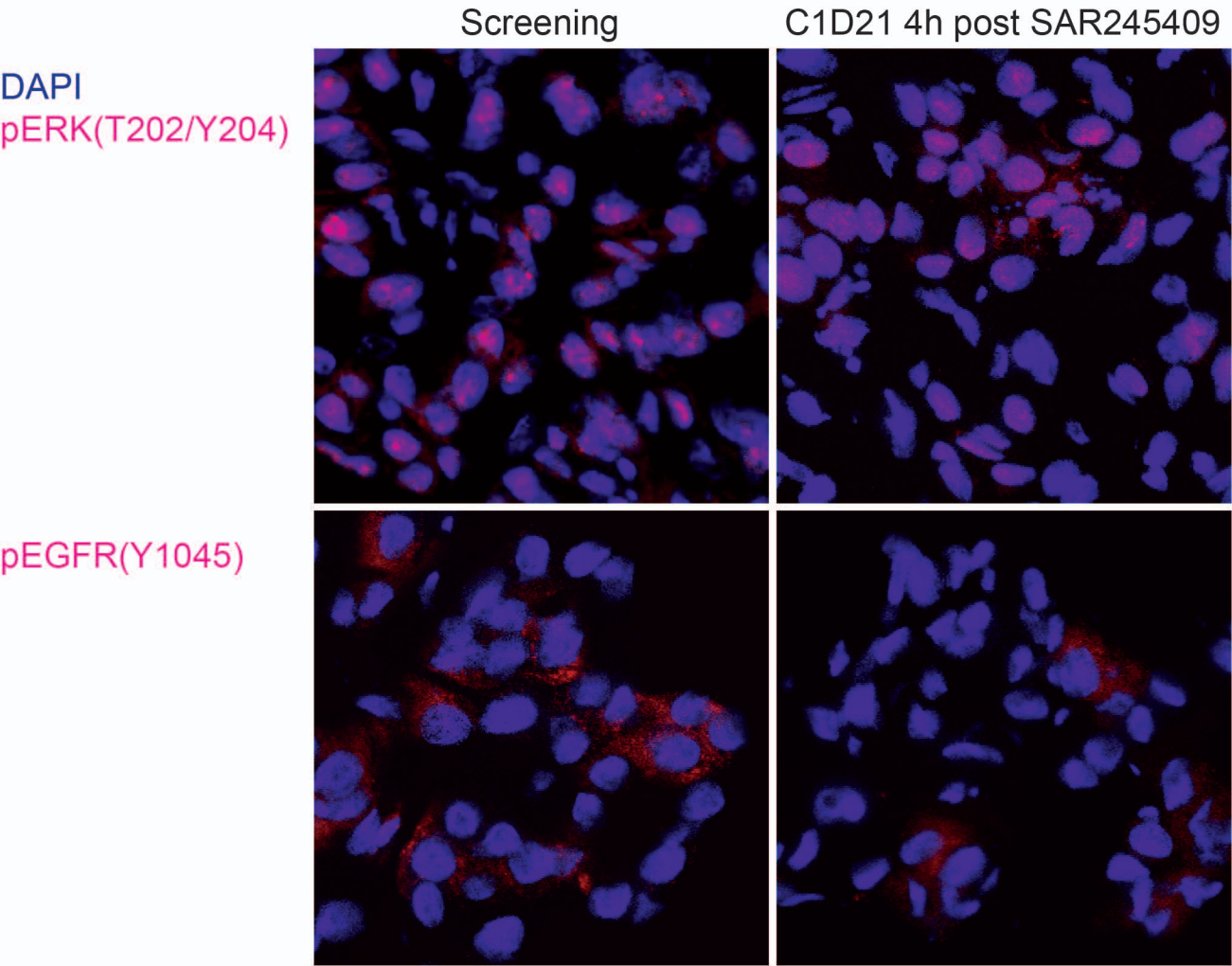
A


Screening
C1D21 4h post SAR245409
DAPI
pAKT(T308)
p4EBP1(T70)

B


Screening
C1D21 4h post SAR245409
DAPI
pERK(T202/Y204)
pEGFR(Y1045)

Supplemental Digital Content 5: Reduction of phosphatidylinositol-3-kinase (PI3K) and epidermal growth factor receptor (EGFR)/mitogen-activated protein kinase (MAPK) pathway signaling by SAR245409 in combination with erlotinib in paired tumor biopsies from a patient with NSCLC adenocarcinoma (patient 1)

A) Effect of SAR245409 in combination with erlotinib on the PI3K signaling pathway documented by immunofluorescence staining of $pAKT^{T308}$ and $p4EBP1^{T70}$ in cross-sections of tumor biopsies collected at baseline and Cycle 1, Day 21 4 hours post-dose from a patient administered erlotinib at 100 mg once daily (QD) and SAR245409 at 30 mg QD. Representative fields were captured per readout (red for $pAKT^{T308}$ or $p4EBP1^{T70}$, blue for 4',6-diamidino-2-phenylindole [DAPI]) at 400x magnification. Reductions in immunofluorescence of 57% ($pAKT^{T308}$) and 60% ($p4EBP1^{T70}$) were observed at Cycle1 Day 21 compared to baseline.

B) Effect of SAR245409 in combination with erlotinib on the PI3K signaling pathway documented by immunofluorescence staining of $pERK^{T202/Y204}$ and $pEGFR^{Y1045}$ in cross-sections of tumor biopsies collected at baseline and Cycle 1, Day 21 4 hours post-dose from a patient administered erlotinib at 100 mg once daily (QD) and SAR245409 at 30 mg QD. Representative fields were captured per readout (red for $pERK^{T202/Y204}$ or $pEGFR^{Y1045}$, blue for 4',6-diamidino-2-phenylindole [DAPI]) at 400x magnification. Reductions in immunofluorescence of 61% ($pERK^{T202/Y204}$) and 38% ($pEGFR^{Y1045}$) were observed at Cycle1 Day 21 compared to baseline.

AKT, serine/threonine-specific protein kinase; C, Cycle; D, Day; 4EBP1, 4E-binding protein 1; ERK, extracellular signal-regulated kinase.