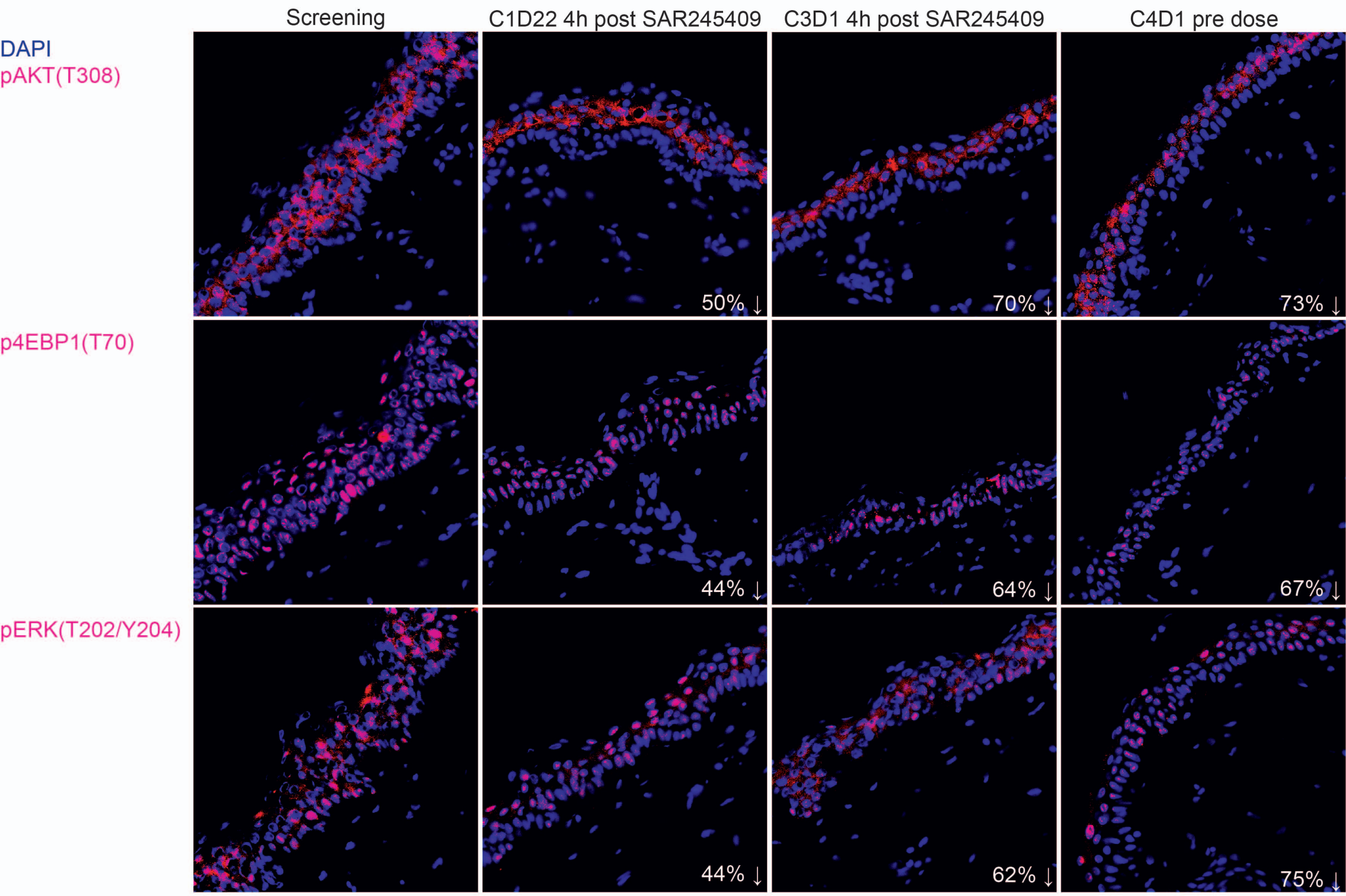
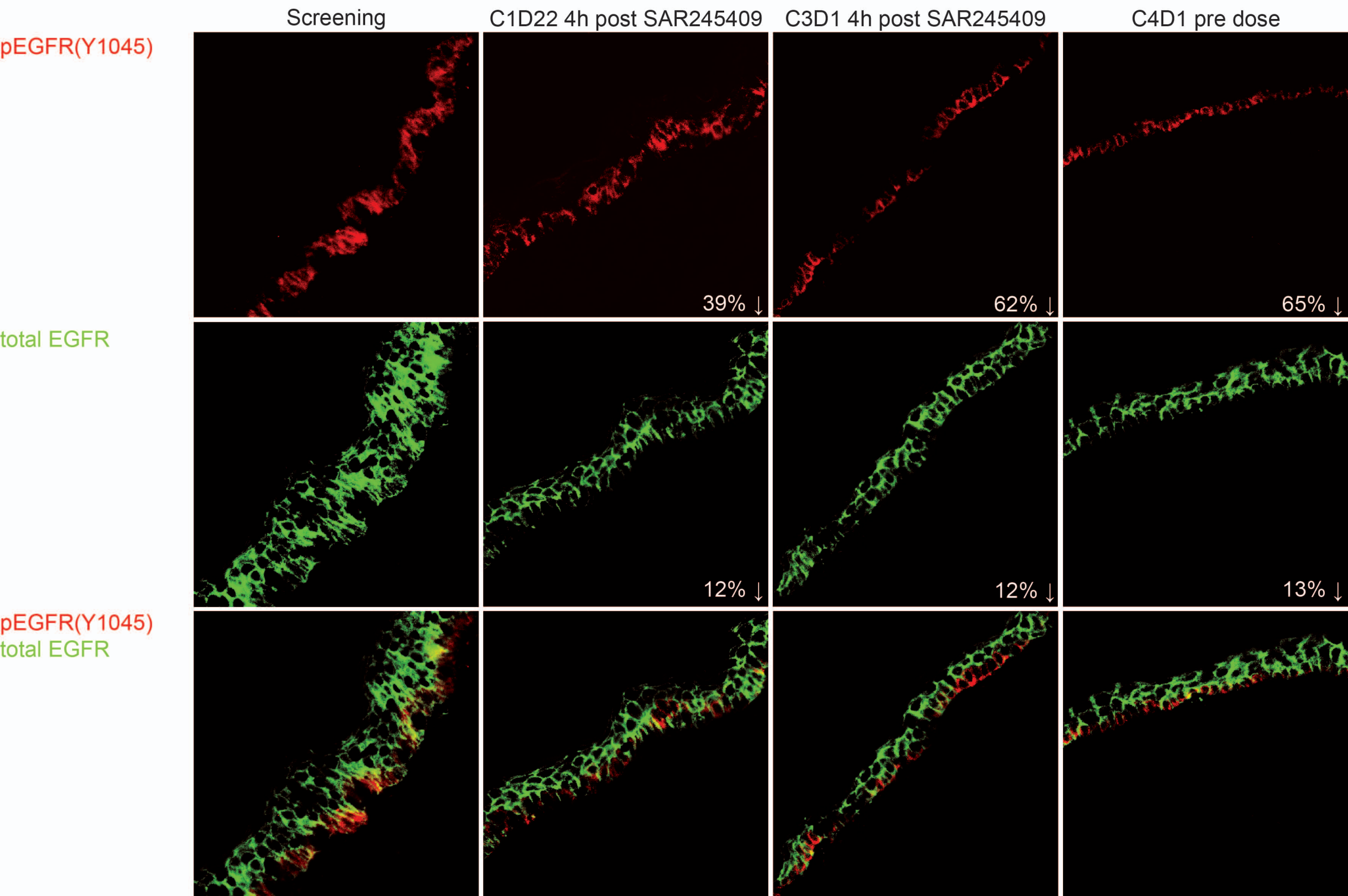
A


Screening
C1D22 4h post SAR245409
C3D1 4h post SAR245409
C4D1 pre dose
DAPI
pAKT(T308)
50% ↓
70% ↓
73% ↓
p4EBP1(T70)
44% ↓
64% ↓
67% ↓
pERK(T202/Y204)
44% ↓
62% ↓
75% ↓

B


Screening
C1D22 4h post SAR245409
C3D1 4h post SAR245409
C4D1 pre dose
pEGFR(Y1045)
39% ↓
62% ↓
65% ↓
total EGFR
12% ↓
12% ↓
13% ↓
pEGFR(Y1045)
total EGFR

Supplemental Digital Content 4. 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 serial skin samples from a patient with squamous cell lung carcinoma (patient 2)

A) Effect of SAR245409 in combination with erlotinib on the PI3K and MAPK signaling pathways documented by immunofluorescence staining of $pAKT^{T308}$, $p4EBP1^{T70}$ and $pERK^{T202/Y204}$ in cross-sections of skin biopsies collected at baseline and at 4 hours post-dose on Cycle 1, Day 22 and Cycles 3 and 4, Day 1 from a patient administered erlotinib at 100 mg once daily (QD) and SAR245409 at 50 mg QD. Representative fields were captured per readout (red for $pAKT^{T308}$, $p4EBP1^{T70}$, or $pERK^{T202/Y204}$, blue for 4',6-diamidino-2-phenylindole [DAPI]) at 400x magnification.

B) Effect of SAR245409 in combination with erlotinib on the EGFR signaling pathway documented by immunofluorescence staining of $pEGFR^{Y1045}$ and total EGFR in cross-sections of skin biopsies collected at baseline and at 4 hours post-dose on Cycle 1, Day 22 and Cycles 3 and 4, Day 1 from a patient administered erlotinib at 100 mg once daily (QD) and SAR245409 at 50 mg QD. Representative fields were captured per readout (red for $EGFR^{Y1045}$, green for total EGFR) at 400x magnification.

AKT, serine/threonine-specific protein kinase; C, Cycle; D, Day; 4EBP1, 4E-binding protein 1; EGFR, epidermal growth factor receptor.