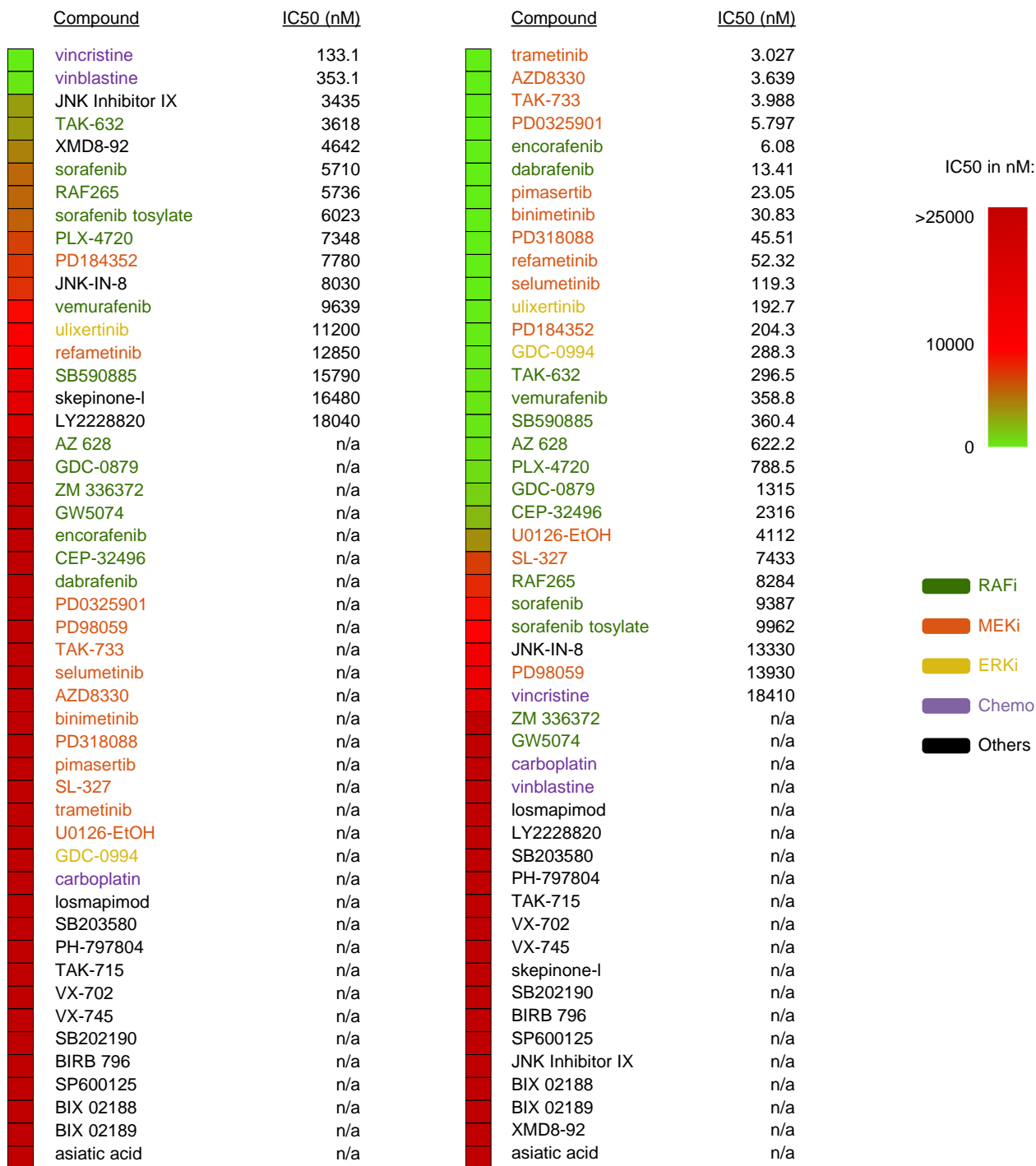


# Suppl. Figure S1

KIAA1549:BRAF fusion (DKFZ-BT66)

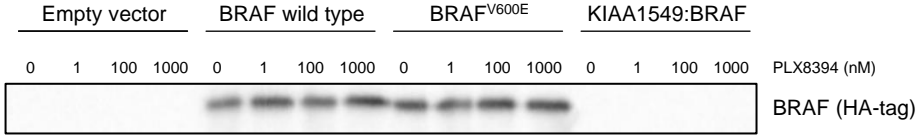
BRAF<sup>V600E</sup> mutation (BT-40)



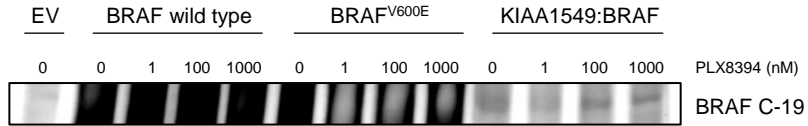
**Suppl. Figure S1: Initial MAPKi screen using metabolic activity as readout:** Heatmap of tested compounds ranked by the estimated IC50 values for DKFZ-BT66 and BT-40 cells determined by metabolic activity by CellTiter-Glo® One Solution assay. Cells were treated for 72 hours with indicated drugs in concentrations ranging from 0.0043 to 25000 nM.

# Suppl. Figure S2

A



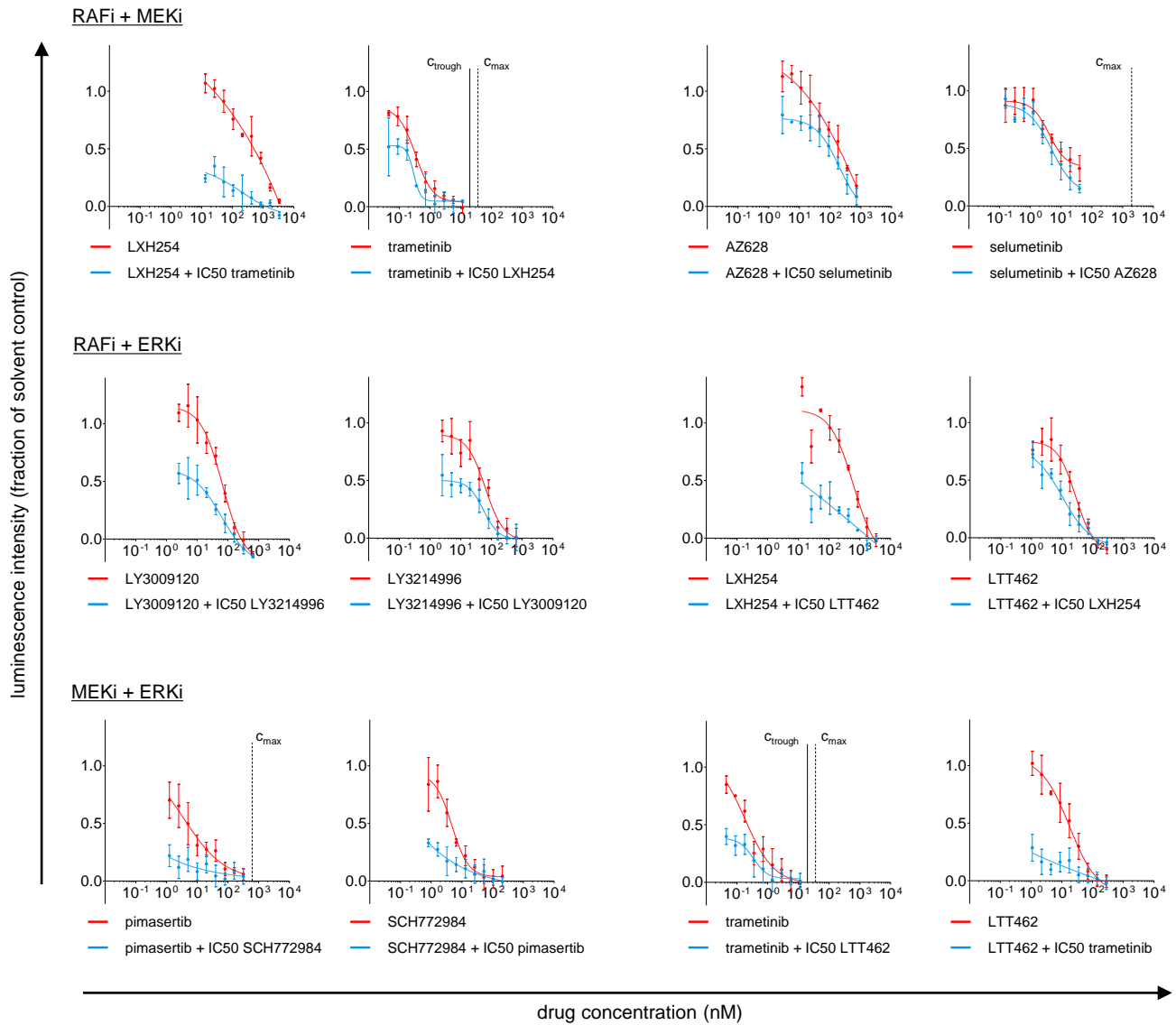
B



**Suppl. Figure S2: Western blot validation of MAPK pathway alterations in HEK293T cells:** Cells were transfected with different MAPK pathway alterations and subsequently treated with PLX8394 in the indicated concentrations for 24 hours. A) Expression of BRAF wild type and BRAF<sup>V600E</sup> was assessed by using an HA-tag antibody (Abcam). B) Expression of the *KIAA1549:BRAF* fusion was assessed using a BRAF C-19 antibody (Santa Cruz Biotechnology). EV: empty vector.

# Suppl. Figure S3

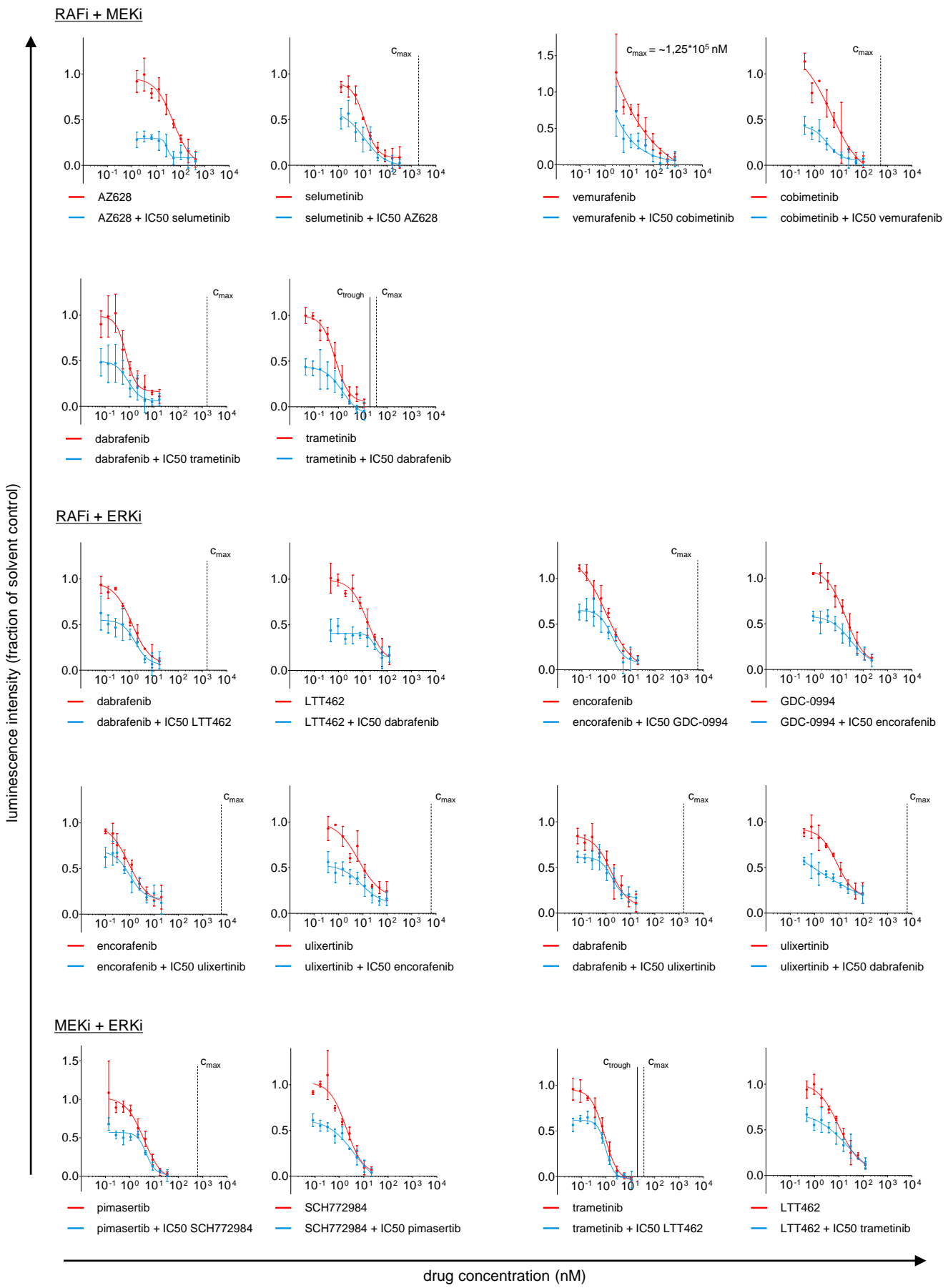
KIAA1549:BRAF fusion (DKFZ-BT66 pDIPZ-CMV)



**Suppl. Figure S3: Dose-response curves of MAPKi combination treatment in DKFZ-BT66 pDIPZ-CMV cells:** Assessment of luminescence intensity measured by luciferase assay (Steady-Glo® Luciferase Assay System). DKFZ-BT66 cells transduced with pDIPZ-CMV were treated for 24 hours with the indicated drugs as single or combination treatment in the indicated concentrations.  $C_{max}$  and  $C_{trough}$  were added if available and are listed in Suppl. Table S5. Depicted are mean +/- SD of three biological replicates.

# Suppl. Figure S4

## BRAF<sup>V600E</sup> mutation (BT-40 pDIPZ-CMV)

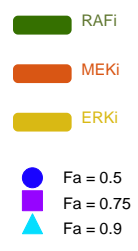


**Suppl. Figure S4: Dose-response curves of MAPKi combination treatment in BT40 pDIPZ-CMV cells:** Assessment of luminescence intensity measured by luciferase assay (Steady-Glo® Luciferase Assay System). BT-40 cells transduced with pDIPZ-CMV were treated for 24 hours with the indicated drugs as single or combination treatment in the indicated concentrations.  $C_{max}$  and  $C_{trough}$  were added if available and are listed in Suppl. Table S5. Depicted are mean  $\pm$  SD of three biological replicates.

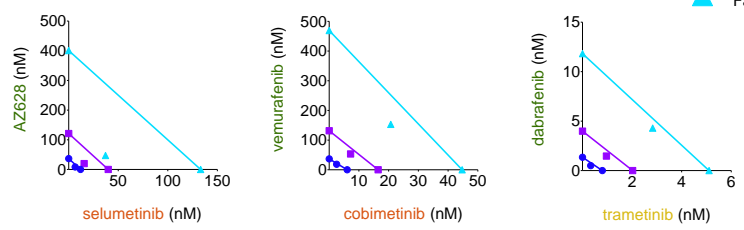
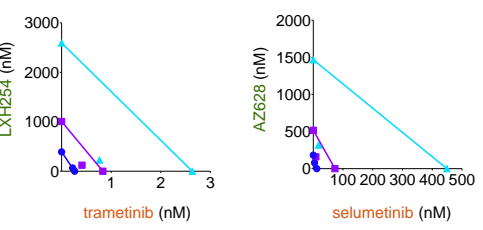
# Suppl. Figure S4

KIAA1549:BRAF fusion (DKFZ-BT66 pDIPZ-CMV)

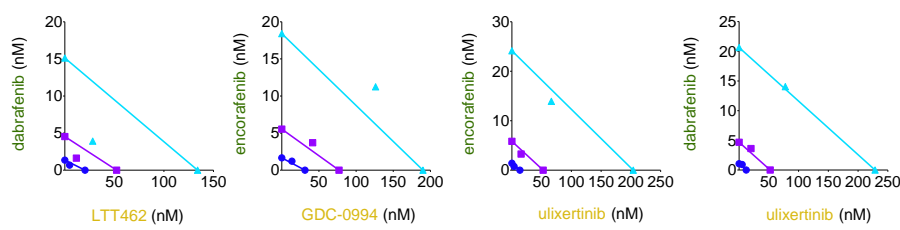
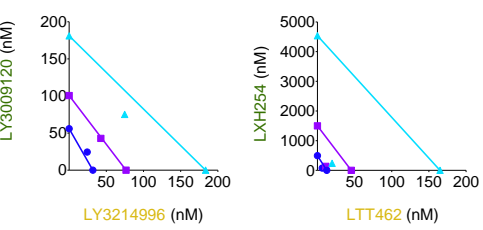
BRAF<sup>V600E</sup> mutation (BT-40 pDIPZ-CMV)



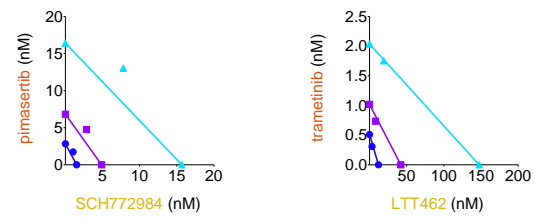
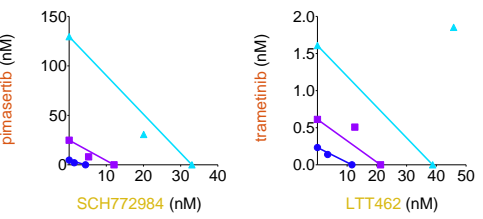
## RAFi + MEKi



## RAFi + ERKi



## MEKi + ERKi



**Suppl. Figure S5: Isobolograms of MAPKi combination treatment in DKFZ-BT66 pDIPZ-CMV and BT-40 pDIPZ-CMV cells:** Assessment of luminescence intensity measured by luciferase assay (Steady-Glo® Luciferase Assay System). DKFZ-BT66 and BT-40 cells transduced with pDIPZ-CMV were treated for 24 hours with the indicated drugs in the indicated concentrations. Isobolograms were calculated using CompuSyn. Diagonal lines represent the line of additivity. Actual experimental points are indicated as circle, square or triangle. Three biological replicates were used to calculate the coordinates of the isobolograms. Fa: fraction affected.