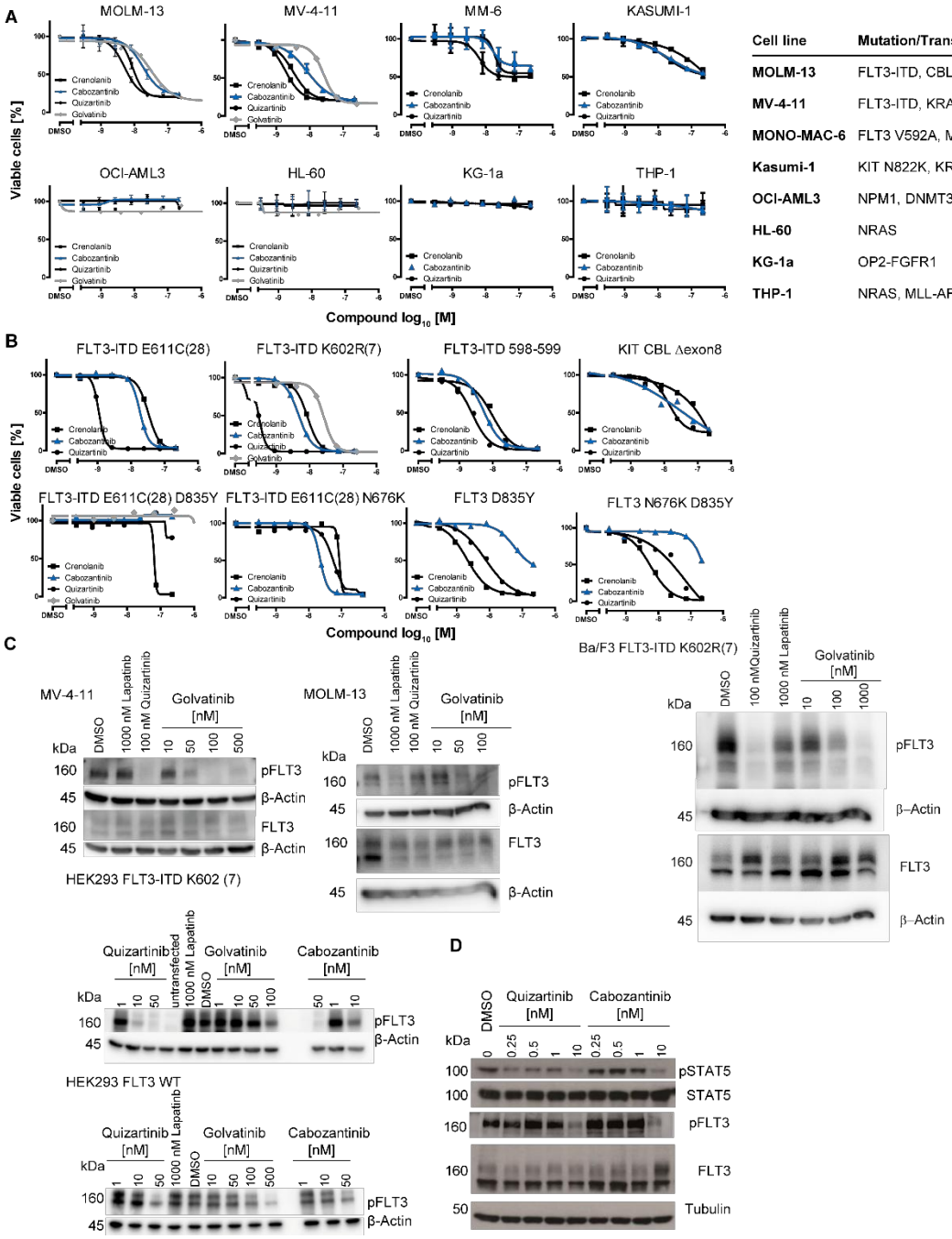
Fig. S10.



Cell line	Mutation/Translocation
MOLM-13	FLT3-ITD, CBL, MLL-AF9
MV-4-11	FLT3-ITD, KRAS, MLL-AF9
MONO-MAC-6	FLT3 V592A, MLL-AF9
Kasumi-1	KIT N822K, KRAS, AML-ETD
OCI-AML3	NPM1, DNMT3A
HL-60	NRAS
KG-1a	OP2-FGFR1
THP-1	NRAS, MLL-AFF9

Fig. S10 | Preclinical evaluation of Cabozantinib for treatment of AML. (A) Cell viability assays for Cabozantinib, Golvatinib, Quizartinib and Crenolanib in AML cell lines (standard deviation of technical triplicates). Mutations and translocations of the cell lines are provided in the table (right). FLT3-mutated cell lines were sensitive towards FLT3 inhibition. **(B)** Proliferation assays for Cabozantinib, Golvatinib, Quizartinib and Crenolanib in Ba/F3 cells harbouring different FLT3 mutations. **(C)** Immunoblot analysis in MV-4-11 cells and MOLM-13, FLT3-WT and FLT3-ITD transfected HEK293 cells, and Ba/F3 FLT3-ITD cells revealed FLT3 target engagement for Golvatinib and Cabozantinib. FLT-ITD dependent cells are more sensitive to inhibitor treatment. **(D)** Immunoblot analysis of STAT5 phosphorylation for increasing doses of Quizartinib and Cabozantinib showed that both drugs can abrogate aberrant FLT3 signaling.

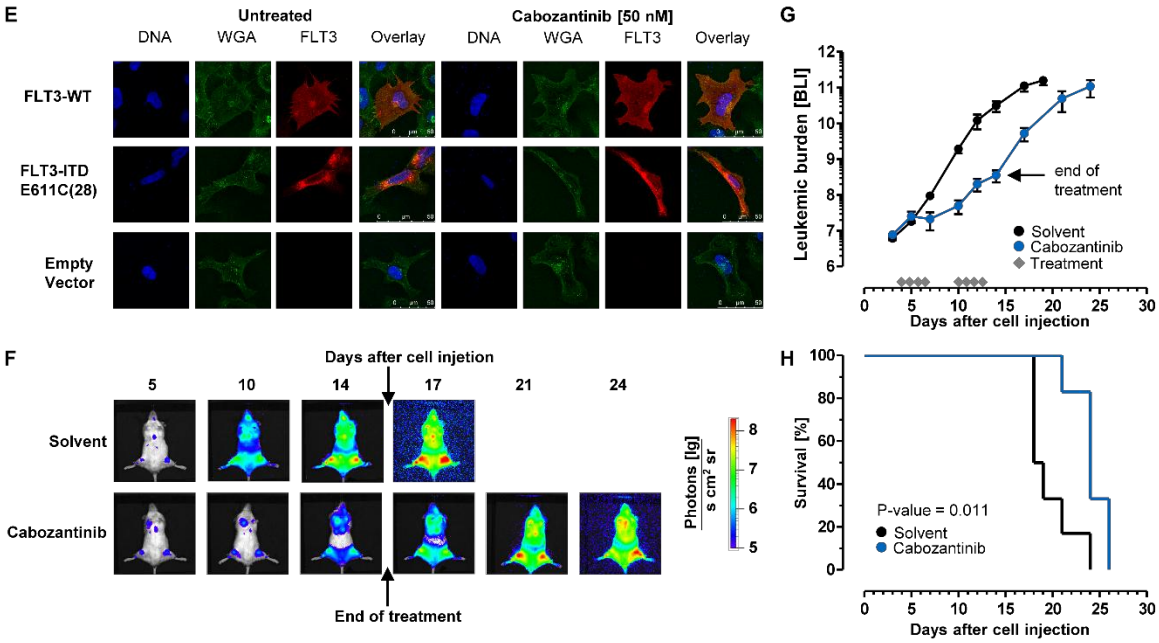


Fig. S10 continued | Preclinical evaluation of Cabozantinib for treatment of AML. (E) Immunofluorescence staining for FLT3-WT, FLT3-ITD 611C(28) or empty-vector transfected U-2 OS cells with no, or 6 h treatment with 50 nM Cabozantinib. Drug treatment restored membrane localization of FLT3-ITD analogous to WT. **(F-H)** NOD scid gamma mice were injected i.v. with MOLM13 cells. Three days post-injection, mice were treated with Cabozantinib (60 mg/kg) or left untreated. **(F)** Representative bioluminescence images of treated and control mice for up to 24 d after cell injection (MOLM-13). **(G)** BLI (bioluminescence in photons [lg]/(s*cm^2*sr) signals for Cabozantinib- (blue, n=6) or vehicle-treated animals (black, n=5). Error bars depict standard deviation; diamonds indicate treatment days. **(H)** Kaplan-Meier survival curves for Cabozantinib (blue, n=6) or vehicle-treated animals (black, n=5). P-values were obtained after log rank test.