Supplemental Tables and Figures

MRX-2843 Estimated Cellular Kinase Selectivity (IC_{90}'s)			
Kinase	nM	Kinase	nM
FLT3	8	PHKG1	329
MER	17	FGFR2	354
TRKA	48	KDR	383
AXL	47	PDGFRα[V561D]	407
LOK	68	DDR1	434
TRKC	136	CLK2	463
SLK	143	SIK	501
TYRO3	150	FGFR3	514
NuaK1	162	FGFR4[V550L]	570
KIT	182	PDGFRα	605
FLT4	206	PDGFRβ	708
MAP4K2	209	IRR	780
TRKB	222	CDK6 /CycD3	814
FLT1	232	KIT[T670I]	821
MELK	243	RSK1	867
FGFR1	244	RSK4	884
QIK	246	DDR2	929
KIT[V654]	262	AurB/INCENP	945

Table S1

Predicted concentration required for 90% inhibition of each reported kinase in cellular systems. Estimate takes into account the IC_{50} in an *in vitro* kinase assay, the K_m for ATP of each kinase and the cell permeability estimated from MERTK, AXL, TYRO3 and FLT3 cellular assays.

	MRX-2843		AC220	
	IC50 (nM)	SEM	IC50 (nM)	SEM
Parental BA/F3 + IL3	272.5	65.1	586.9	231.3
ITD	3.0	0.5	0.24	0.04
D835Y	1.3	0.3		
D835V	1.4	0.3		
ITD+D835Y	7.2	1.3	24.9	4.1
ITD+F691L	20.4	4.3	93.3	18.4
ITD+F691I	102.7	33.2		
ITD+Y842H	6.9	1.9		
ITD+Y842C	11.9	3.5		
ITD+D835F	9.2	1.8		
ITD+D835V	7.8	1.6		
MOLM-14	19.1	4.7		
MOLM-14:D835Y	21.7	4.3		
MOLM-14:F691L	34.8	7.9		

Table S2
MRX-2843 retains activity against quizartinib resistant FLT3 mutant proteins. IC_{50} values were generated from the data shown in Figure 6 and S3.

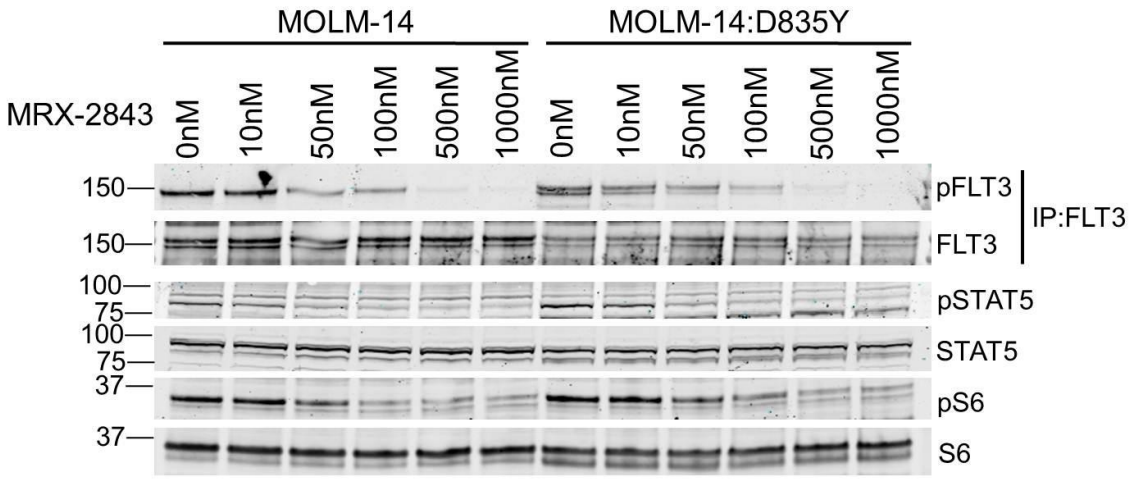

Figure S1

MRX-2843 inhibits activation of FLT3 and downstream effectors in the presence of human plasma. MOLM-14 parental and MOLM-14:D835Y cells were cultured for 2 hours in 100% human plasma with the indicated concentrations of MRX-2843. Lysates were prepared and phosphorylated and total proteins were detected by immunoblot.

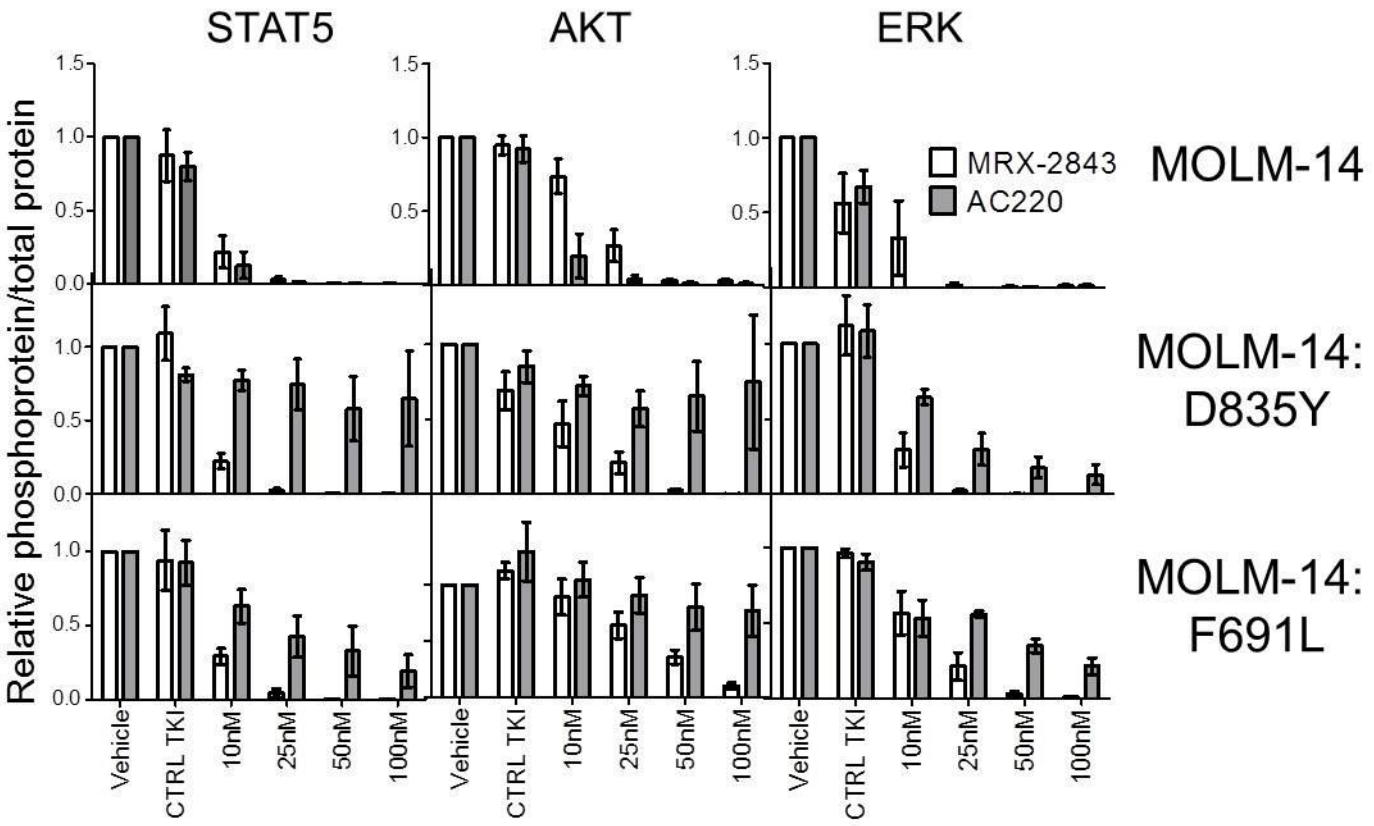

Figure S2

MRX-2843 abrogates activation of signaling through pathway components downstream of FLT3 in cell lines resistant to quizartinib. Phosphorylation of downstream effectors was analyzed by immunoblot as shown in Figure 6. Phosphorylated and total proteins were quantitated by densitometry and expression of phosphorylated protein relative to total protein was determined. Mean values and standard errors derived from 3 independent experiments are shown.

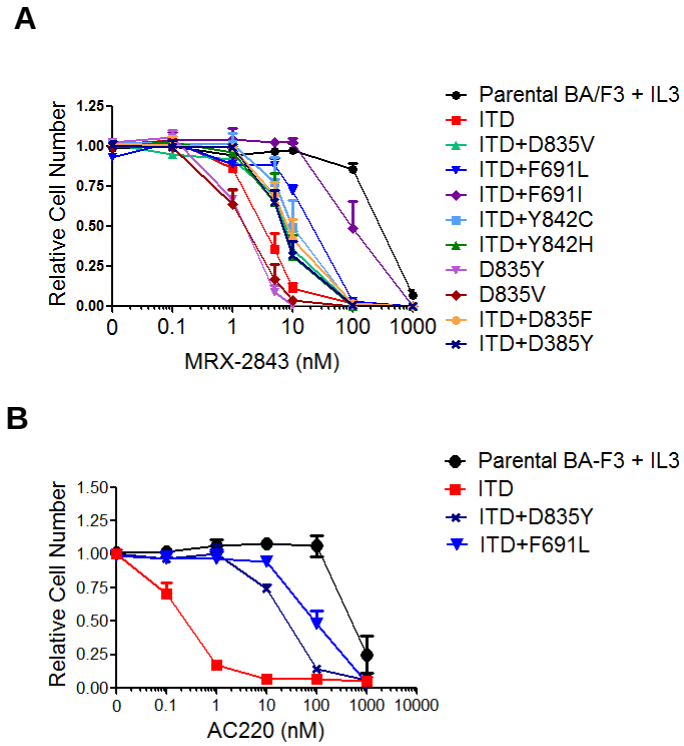

Figure S3

MRX-2843 retains activity against quizartinib-resistant FLT3-ITD mutant proteins identified by saturation mutagenesis screening. BA/F3 cells expressing FLT3-ITD or FLT3-ITD mutant protein were cultured for 48 hours in the absence of IL-3 and with the indicated concentrations of MRX-2843 (A) or quizartinib (B) and relative numbers of viable cells were determined as described in Figure 6A. Cultures grown in the presence of IL-3 are shown for reference (Parental BA/F3+IL3). Mean values and standard errors were derived from 3 independent experiments.