

**Supplementary Table S1: MRTX0902 Selectively Inhibits KRAS-MAPK Signaling and Cellular Viability in Cancer Cell Lines**

Cell Line	Genotype	Assay, IC <sub>50</sub> (nM)	
		pERK In-Cell Western <sup>1</sup> (nM)	3D Viability (CTG) <sup>2</sup> (nM)
NCI-H1975	<i>EGFR</i> L858R/T790M; <i>PIK3CA</i> G118D	39.8 ± 15.0	15.2 ± 8.0
SNU-C4	<i>SOS1</i> I429N; <i>PIK3CA</i> E545G; <i>TP53</i> G245S	20.1 ± 3.9	38.4 ± 10.7 (D7)
NCI-H358	<i>KRAS</i> G12C	21.5 ± 3.6	113.6 ± 5.0
LN229	<i>PTPN11</i> A72S; <i>ERBB2</i> L755S	38.9 ± 19.3	65.0 ± 18.2
NCI-H1838	<i>NF1</i> N184Qfs*17; <i>TP53</i> R273L	101.2 ± 14.5	50.1 ± 24.9
PC9	<i>EGFR</i> ex19del; <i>TP53</i> R248Q	218.3 ± 22.4	140.5 ± 17.2
NCI-H508	class III <i>BRAF</i> G596R; <i>PIK3CA</i> E545K	22.5 ± 19.3	98.5 ± 29.0
A549	<i>KRAS</i> G12S; <i>KEAP1</i> G333C	80.1 ± 8.1	135.2 ± 57.8
DLD-1	<i>KRAS</i> G13D	23.3 ± 14.6	196.7 ± 156.4
NCI-H1666	class III <i>BRAF</i> G466V	24.7 ± 12.0	152.0 ± 95.4
HCC1438	<i>NF1</i> S2040F	46.8 ± 15.4	176.2 ± 141.3
HOP92	<i>SOS1</i> N233Y; <i>RASA1</i> C1002*; <i>TP53</i> R175L; <i>NF1</i> M799fs*22	35.4 ± 6.6	220.4 ± 0.35

Cell Line	Genotype	Assay, IC <sub>50</sub> (nM)	
		pERK In-Cell Western <sup>1</sup> (nM)	3D Viability (CTG) <sup>2</sup> (nM)
HT115	<i>SOS1</i> R660C; <i>PTPN11</i> Q510H; <i>NF1</i> R1241*; <i>NF1</i> E595*; <i>PIK3CA</i> R88Q; <i>SMAD2</i> R321Q; <i>FBXW7</i> R465C;	10 ± 2.8	>1000 (D7)
OCI-AML5	<i>SOS1</i> N233Y; <i>PTPN11</i> R265Q; <i>NF1</i> X244_splice	106.7 ± 33.7	89.3 ± 0.07 (D7)
NCI-H1435	<i>NF1</i> K615N; <i>TP53</i> C141W	89.3 ± 6.5	>1000
MKN74	<i>NF1</i> X547_splice; <i>TP53</i> I251L	12.8 ± 6.6	>1000
NCI-H211	<i>PTPN11</i> E76G; <i>TP53</i> R248Q	55.0 ± 7.1	>1000
MKN1	wild-type <i>KRAS</i> , amplified; <i>PIK3CA</i> E545K; <i>TP53</i> V143A; <i>FBXW7</i> R465C;	39.6 ± 7.8	>1000 (D7)
RERF-LC-Ad1	<i>KRAS</i> G12A; <i>TP53</i> P278F	79.9 ± 58.7	>1000
AsPC-1	<i>KRAS</i> G12D; <i>SMAD4</i> R100T; <i>FBXW7</i> R465C	>1000	>1000

Abbreviations: 3D = three-dimensional; CTG = CellTiter-Glo®; pERK = phosphorylated extracellular signal regulated kinase 1/2

<sup>1</sup> An In-Cell Western assay was used to evaluate modulation of pERK by MRTX0902 in cell lines grown in standard tissue culture conditions. Data is representative of biological duplicate or triplicate repeats.

<sup>2</sup> A CellTiter-Glo® (CTG) assay to evaluate cell viability was performed in cell lines grown in 3D tissue culture conditions in a 14-day assay (7-day assay data for SNU-C4, HT115, OCI-AML5, and MKN1 cell lines). Data is representative of biological duplicate or triplicate repeats.