

RET-related *In Vivo* Models



WuXi AppTec Research Service Division, Oncology & Immunology Unit



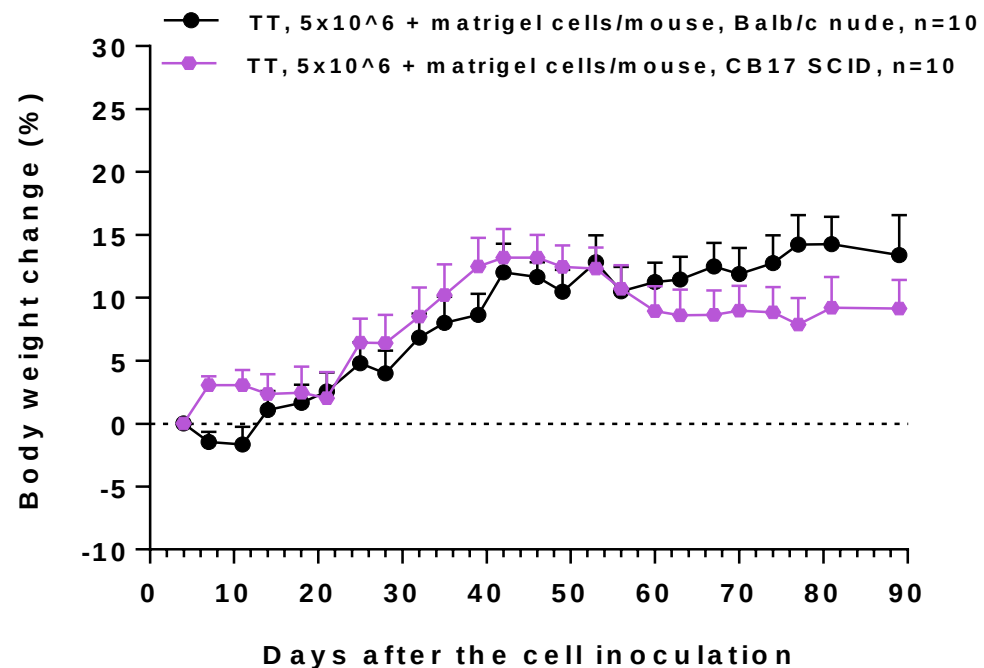
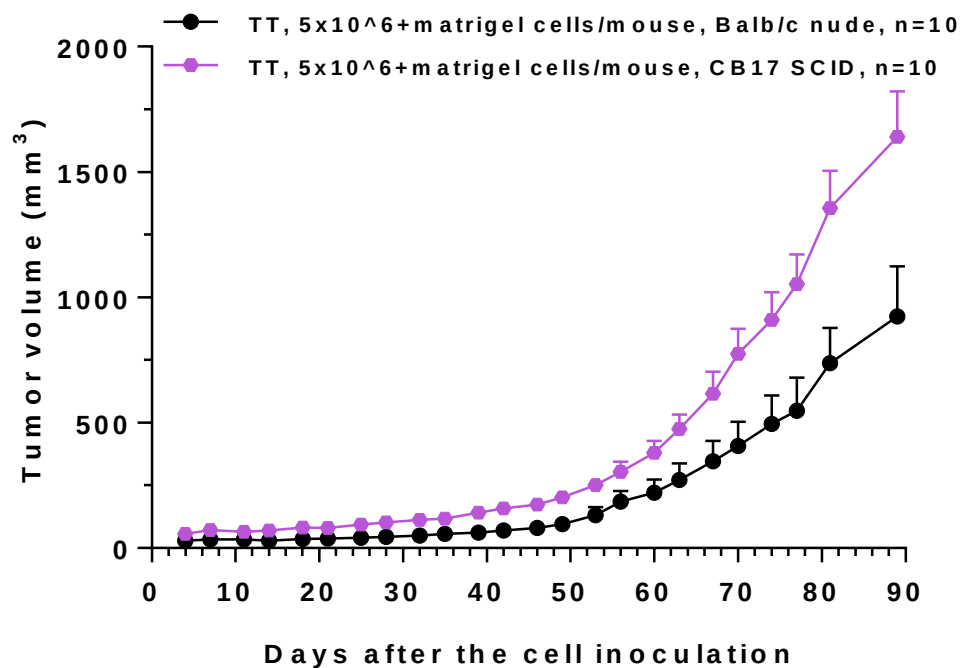
2021.10

- RET-related CDX models
- Ba/F3 engineered cell lines for RET fusions and case studies

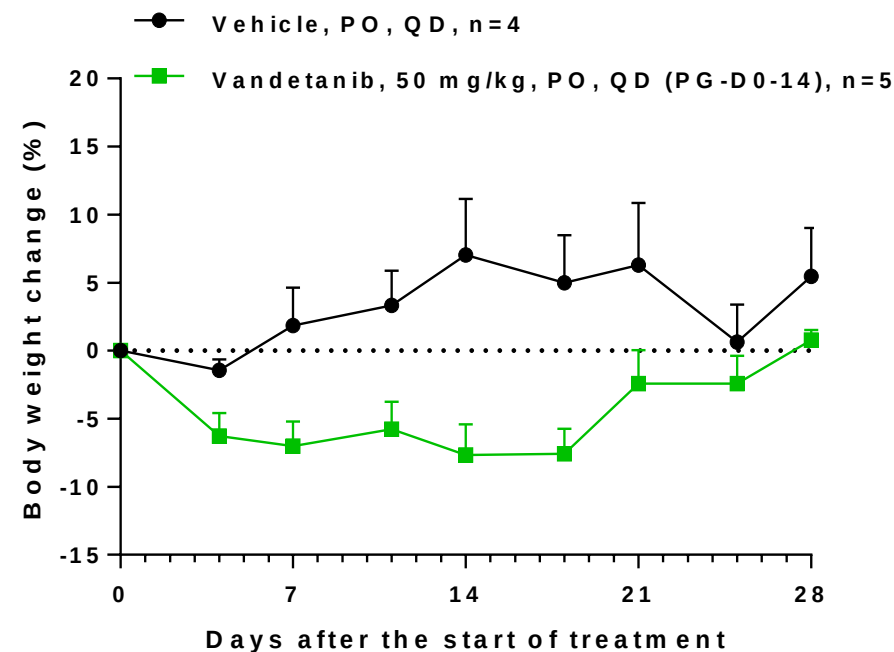
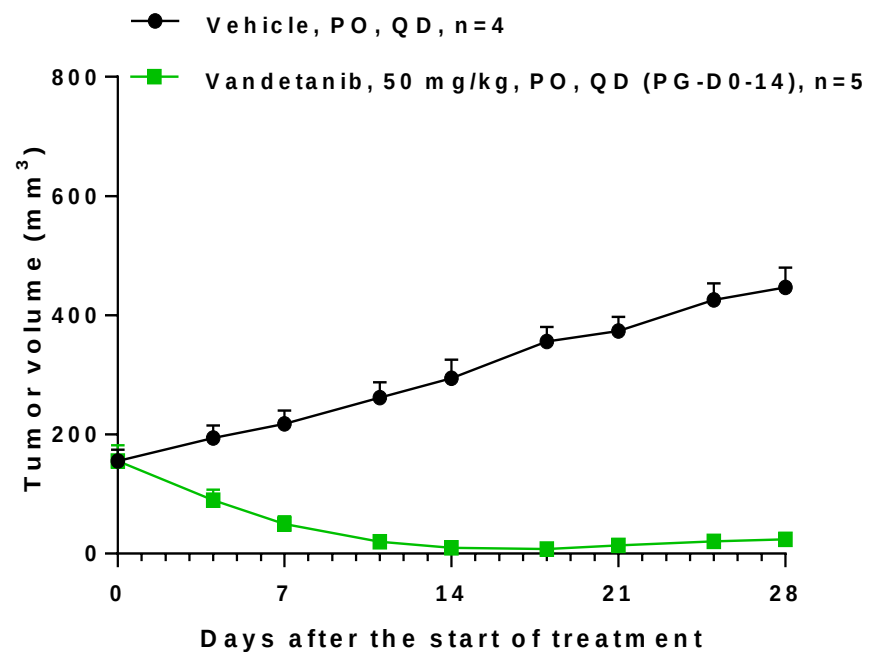
RET-related CDX models

Cancer type	Cell line	Model genetics	Model growth curve
Thyroid	TT	RET C634W	Yes
Lung	LC-2/ad	CCDC6-RET fusion	Yes

TT thyroid cancer CDX model



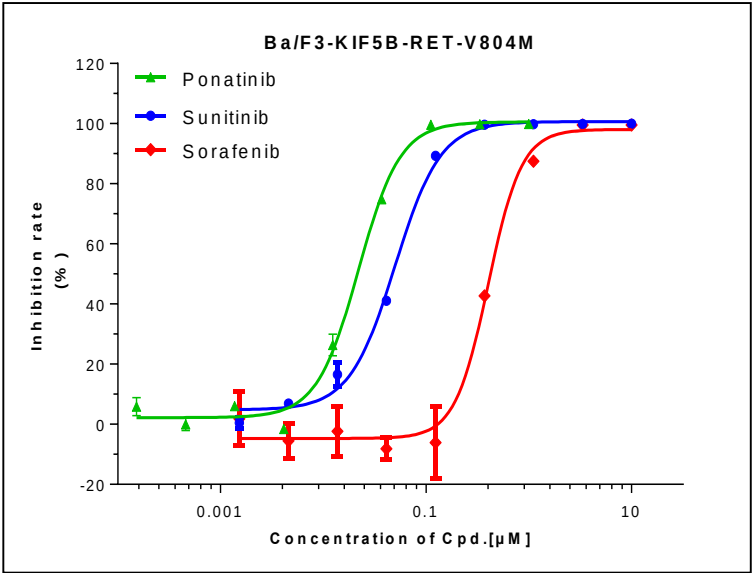
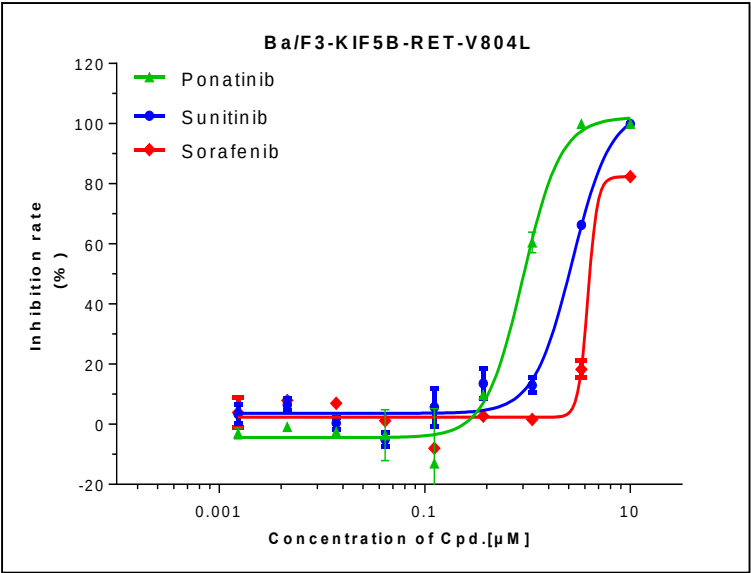
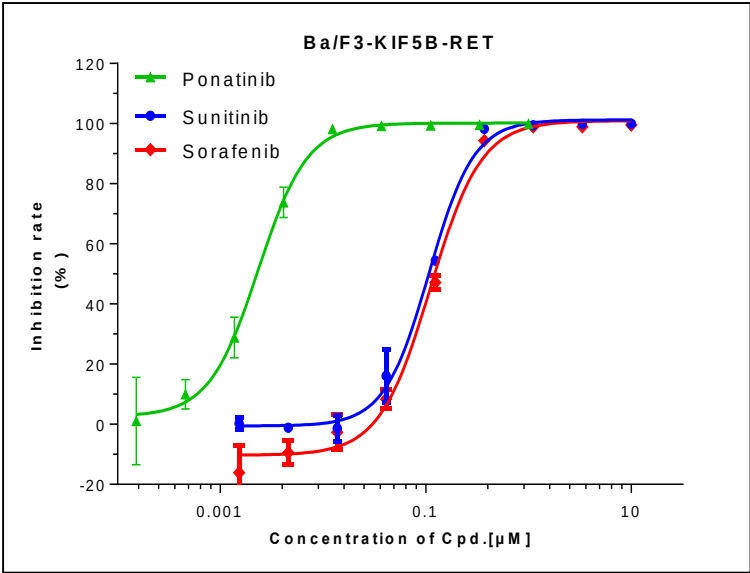
LC-2/ad lung cancer CDX model



RET-related genetically engineered Ba/F3 cell lines

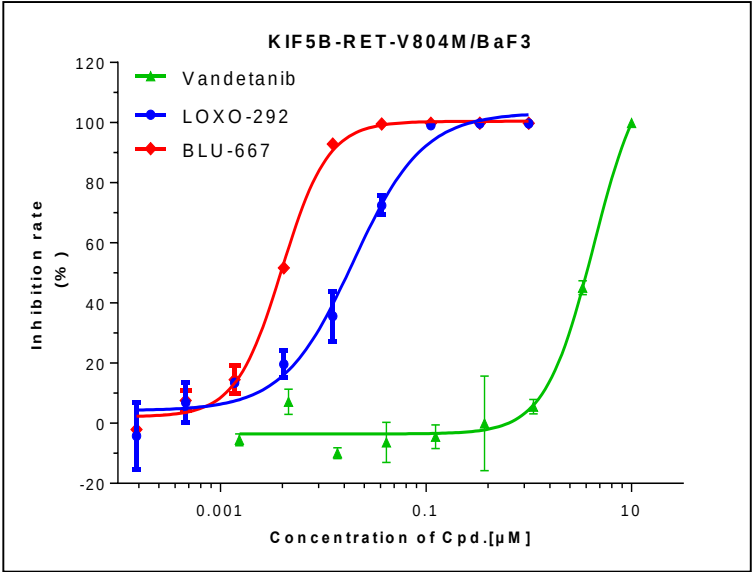
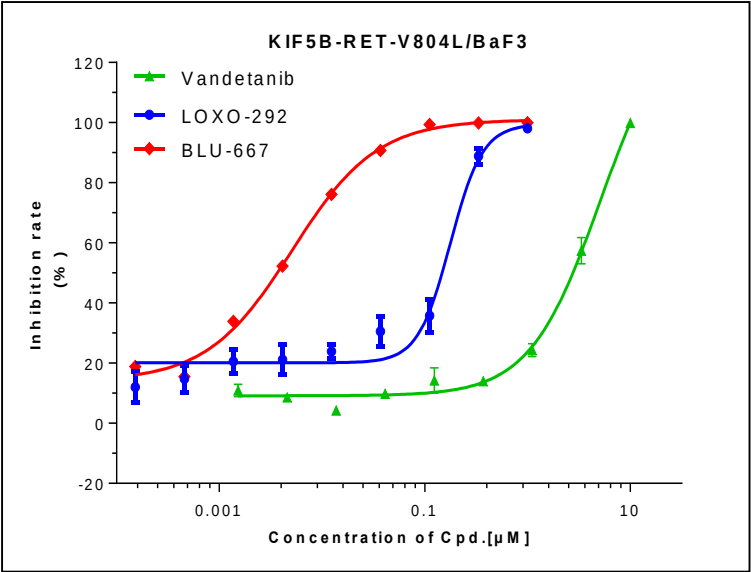
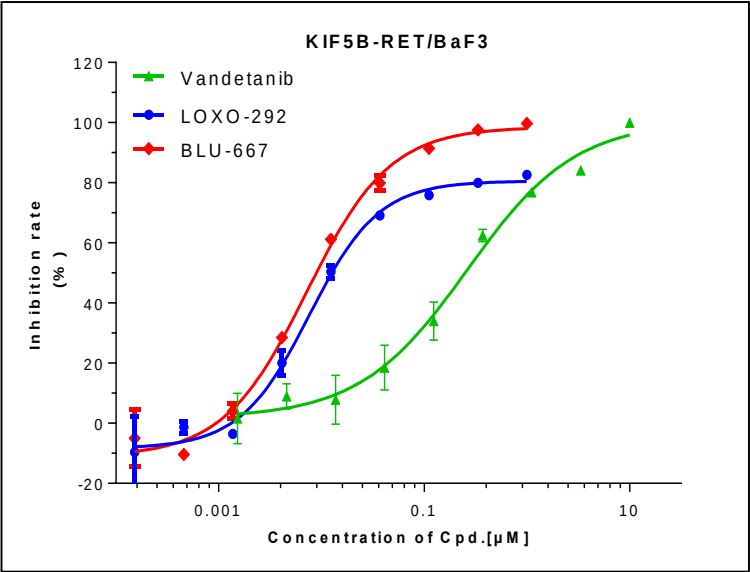
Cell type	Cell line	<i>In vitro</i> test	Model growth curve
Pro-B cells	BaF3-KIF5B-RET-WT	Ready	Ongoing
	BaF3-KIF5B-RET-V804L	Ready	Ongoing
	BaF3-KIF5B-RET-V804M	Ready	Ready
	BaF3-KIF5B-RET-G810S	Ready	Ready
	BaF3-KIF5B-RET-G810R	Ready	Ready
	BaF3-CCDC6-RET-WT	Ready	Ready
	BaF3-CCDC6-RET-V804M	Ready	Ready
	BaF3-CCDC6-RET-V804L	Ready	Ready

Relative IC₅₀ of RET inhibitors in Ba/F3 KIF5B-RET cell lines



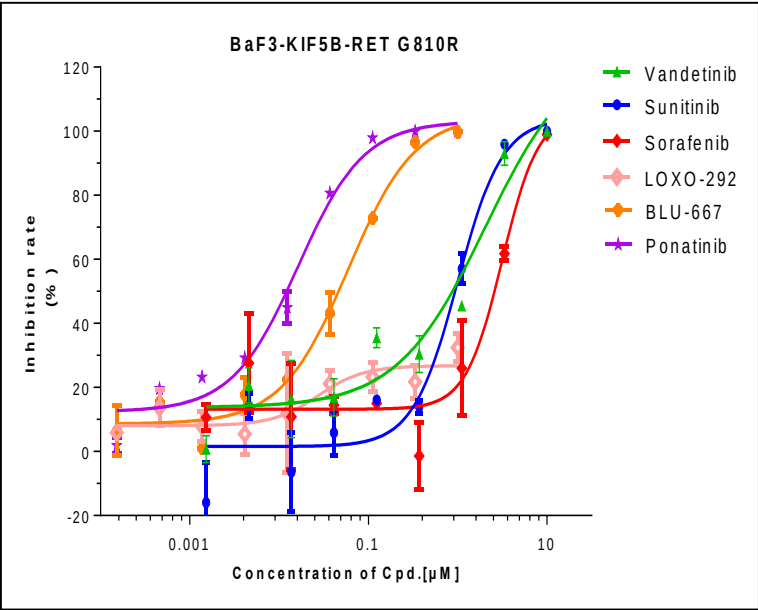
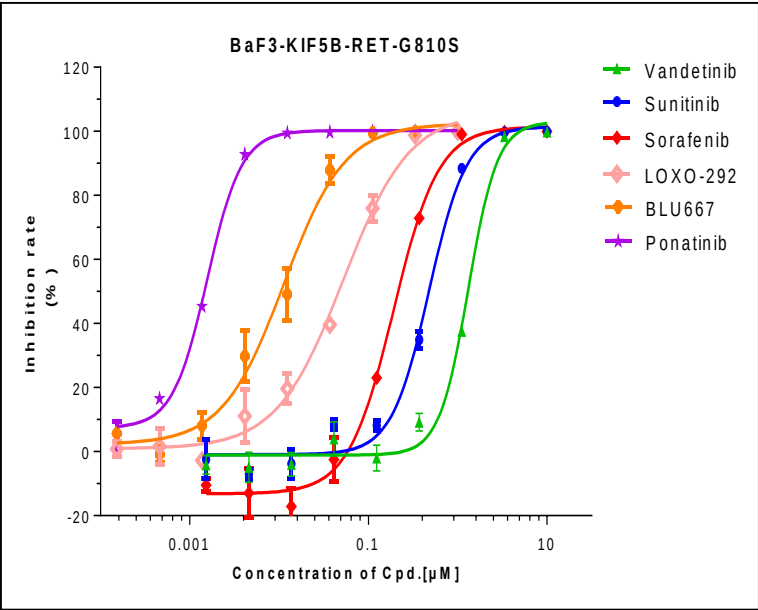
Cell Name	Compound	RelIC ₅₀ (μM)
Ba/F3-KIF5B-RET-WT	Ponatinib	0.0023
	Sunitinib	0.1075
	Sorafenib	0.1107
Ba/F3-KIF5B-RET-V804L	Ponatinib	0.9040
	Sunitinib	2.722
	Sorafenib	~3.864
Ba/F3-KIF5B-RET-V804M	Ponatinib	0.0222
	Sunitinib	0.0499
	Sorafenib	0.4032

Relative IC₅₀ of RET inhibitors in Ba/F3 KIF5B-RET cell lines



Cell Name	Compound	RelIC ₅₀ (μM)
BaF3-KIF5B-RET-WT	Vandetanib	0.2635
	LOXO-292	0.0076
	BLU-667	0.0072
BaF3-KIF5B-RET-V804L	Vandetanib	5.0810
	LOXO-292	0.1770
	BLU-667	0.0051
BaF3-KIF5B-RET-V804M	Vandetanib	4.2580
	LOXO-292	0.0196
	BLU-667	0.0040

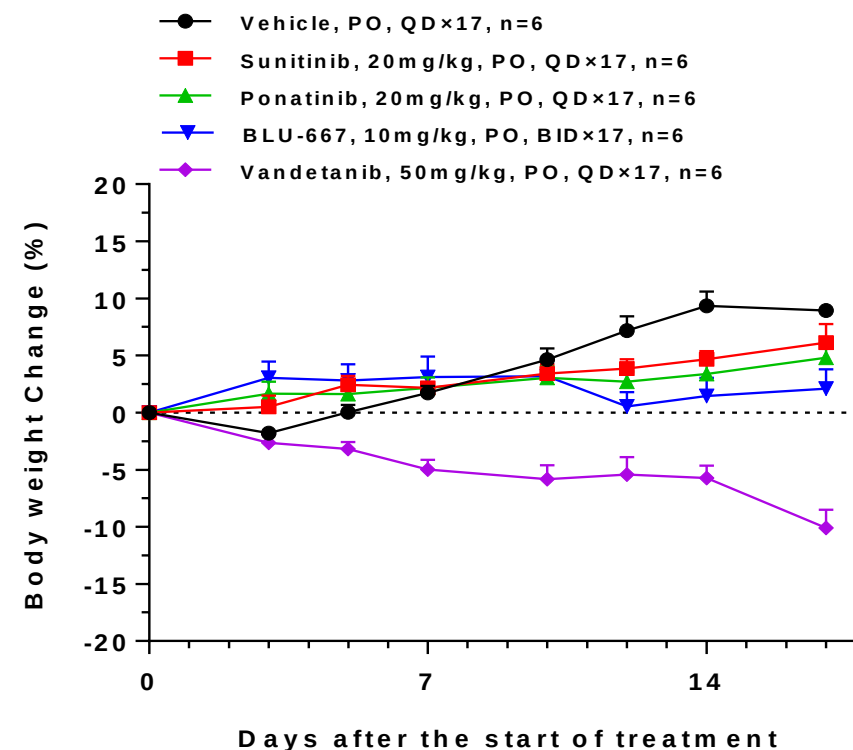
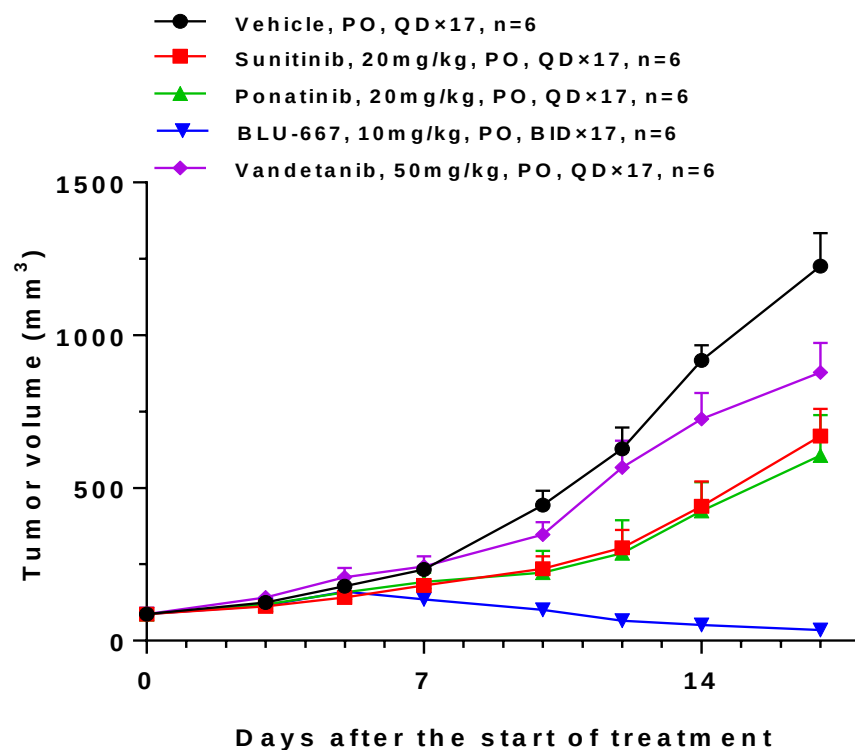
Relative IC₅₀ of RET inhibitors in Ba/F3 KIF5B-RET cell lines



Cell Name	Compound	RelIC ₅₀ (μM)
BaF3-KIF5B-RET-G810S	Vandetanib	1.315
	Sunitinib	0.478
	Sorafenib	0.191
	LOXO-292	0.052
	BLU-667	0.011
	Ponatinib	0.002
BaF3-KIF5B-RET-G810R	Vandetanib	2.030
	Sunitinib	0.995
	Sorafenib	3.139
	LOXO-292	NA
	BLU-667	0.059
	Ponatinib	0.016

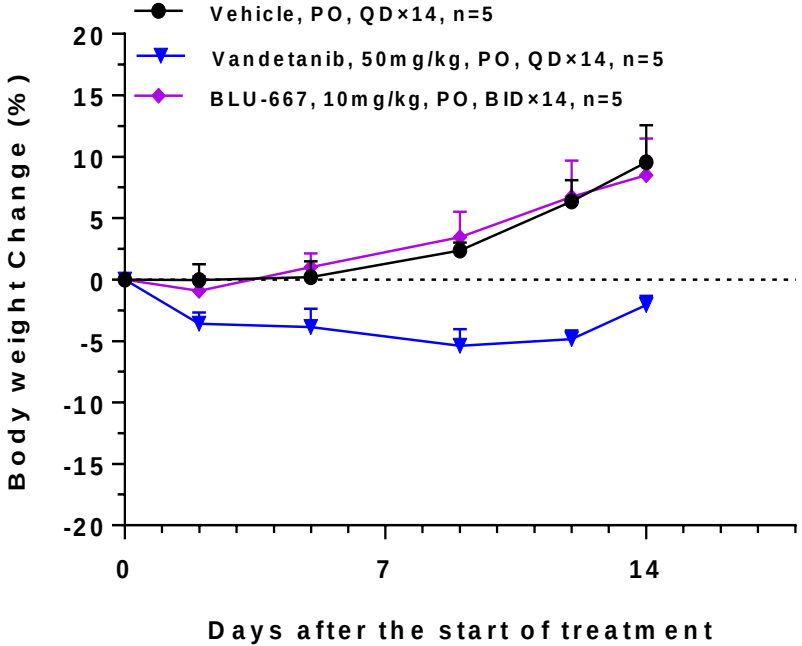
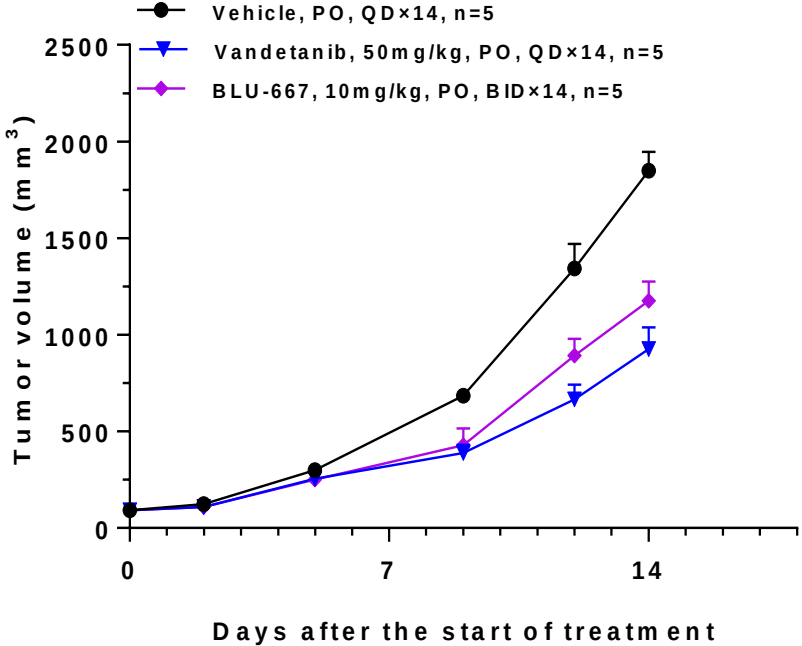
Sunitinib, Ponatinib, BLU-667, and Vandetanib in Ba/F3 KIF5B-RET-V804M model

Cell line	Model ID	Drugs tested	Dosage	TGI (%)	Model genetics
RET engineering murine pro-B cell line	Ba/F3 KIF5B-RET-V804M	Sunitinib Ponatinib BLU-667 Vandetanib	20 mpk, QD 20 mpk, QD 10 mpk, BID 50 mpk, QD	48.86 54.45 104.65 30.60	KIF5B-RET-V804M



BLU-667 and Vandetanib in Ba/F3 KIF5B-RET-G810R model

Cell line	Model ID	Drugs tested	Dosage	TGI (%)	Model genetics
RET engineering murine pro-B cell line	Ba/F3 KIF5B-RET-G810R	BLU-667 Vandetanib	10 mpk, BID 50 mpk, QD	38.38 52.55	KIF5B-RET-G810R



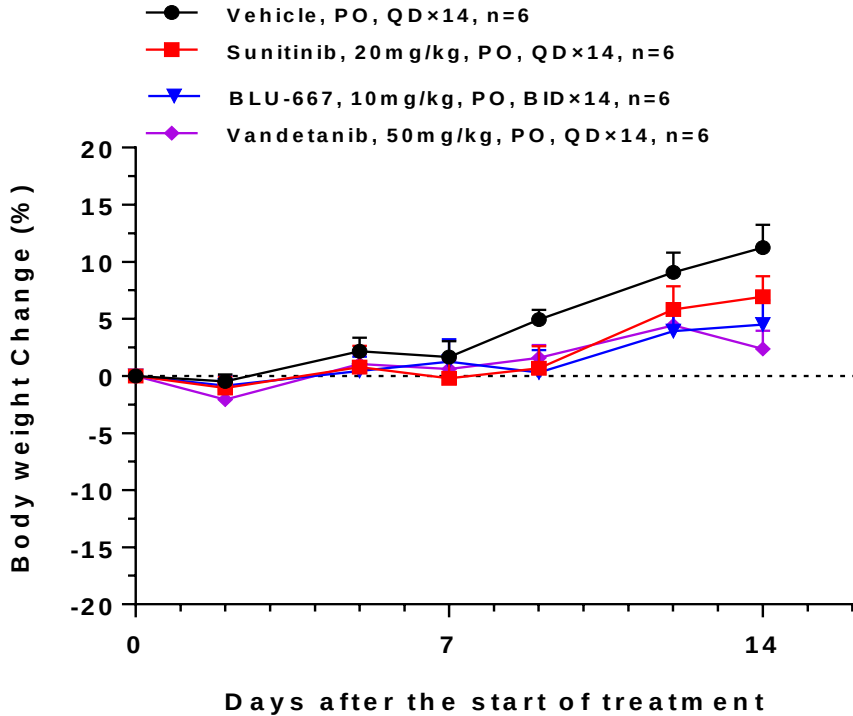
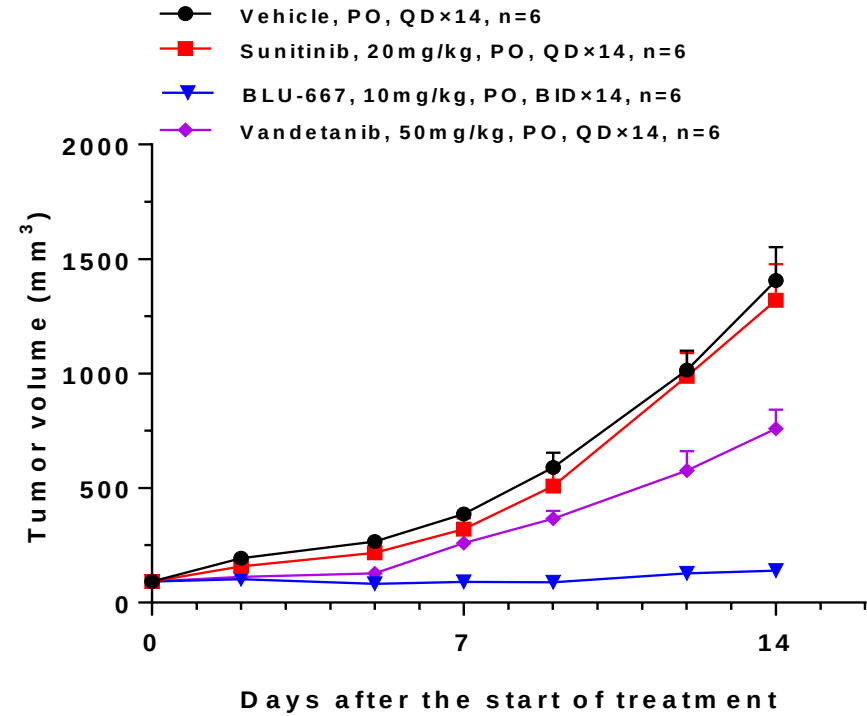
Relative IC₅₀ of RET inhibitors in Ba/F3 CCDC6-RET cell lines

Cell Name	Compound	Re IC ₅₀ (μM) Ave±SD
Ba/F3-CCDC6-RET-WT	Cabozatinib (XL 184)	0.454 ± 0.078
	Vandetanib (ZD6474)	0.470 ± 0.045
	Lenvatinib (E7080)	0.190 ± 0.021
	Sunitinib	0.394 ± 0.049
	Regorafenib (BAY 73-45)	0.210 ± 0.026
	Pralsetinib (BLU-667)	0.016 ± 0.003
Ba/F3-CCDC6-RET-V804M	Cabozatinib (XL 184)	3.028 ± 0.535
	Vandetanib (ZD6474)	4.752 ± 0.212
	Lenvatinib (E7080)	2.005 ± 0.774
	Sunitinib	0.263 ± 0.040
	Regorafenib (BAY 73-45)	1.577 ± 0.264
	Pralsetinib (BLU-667)	0.016 ± 0.009
Ba/F3-CCDC6-RET-V804L	Cabozatinib (XL 184)	2.825 ± 0.268
	Vandetanib (ZD6474)	4.285 ± 0.178
	Lenvatinib (E7080)	3.542 ± 0.717
	Sunitinib	0.494 ± 0.052
	Regorafenib (BAY 73-45)	2.124 ± 0.368
	Pralsetinib (BLU-667)	0.01 ± 0.005

RET inhibitors	Note
Cabozatinib (XL 184)	1 st generation
Vandetanib (ZD6474)	1 st generation
Lenvatinib (E7080)	1 st generation
Sunitinib	1 st generation
Regorafenib (BAY 73-45)	1 st generation
Pralsetinib (BLU-667)	2 nd generation

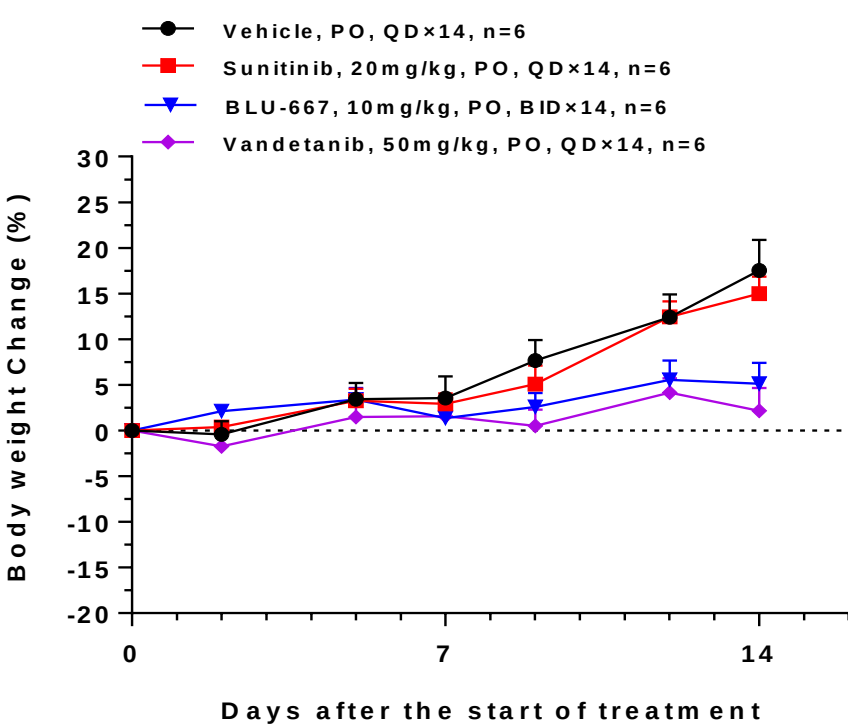
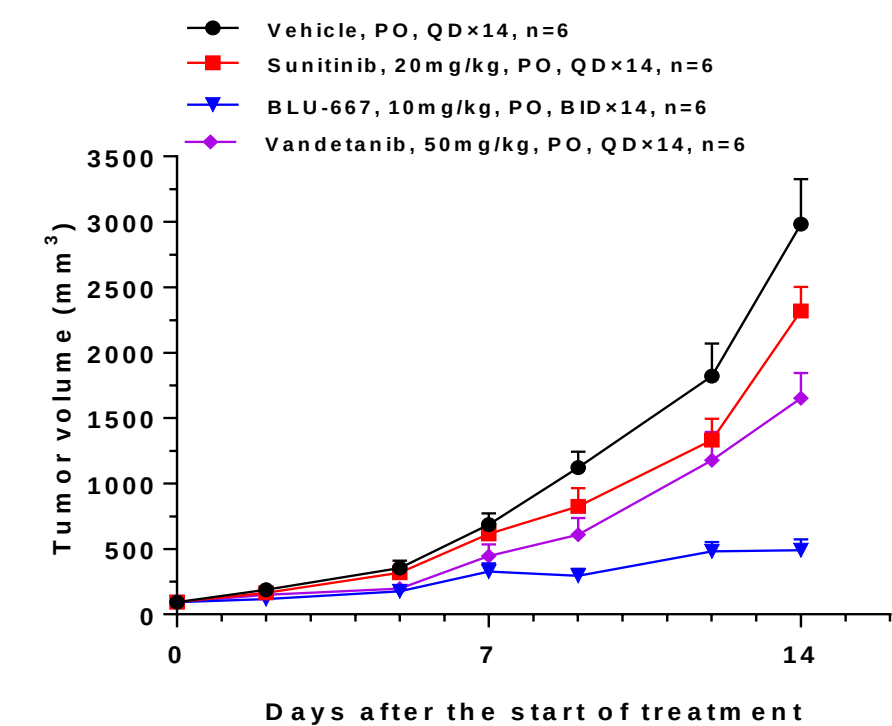
Sunitinib, BLU-667 and Vandetanib in Ba/F3 CCDC6-RET model

Cell line	Model ID	Drugs tested	Dosage	TGI (%)	Model genetics
RET engineering murine pro-B cell line	Ba/F3 CCDC6-RET	Sunitinib BLU-667 Vandetanib	20 mpk, QD 10 mpk, BID 50 mpk, QD	6.57 96.38 49.13	CCDC6-RET



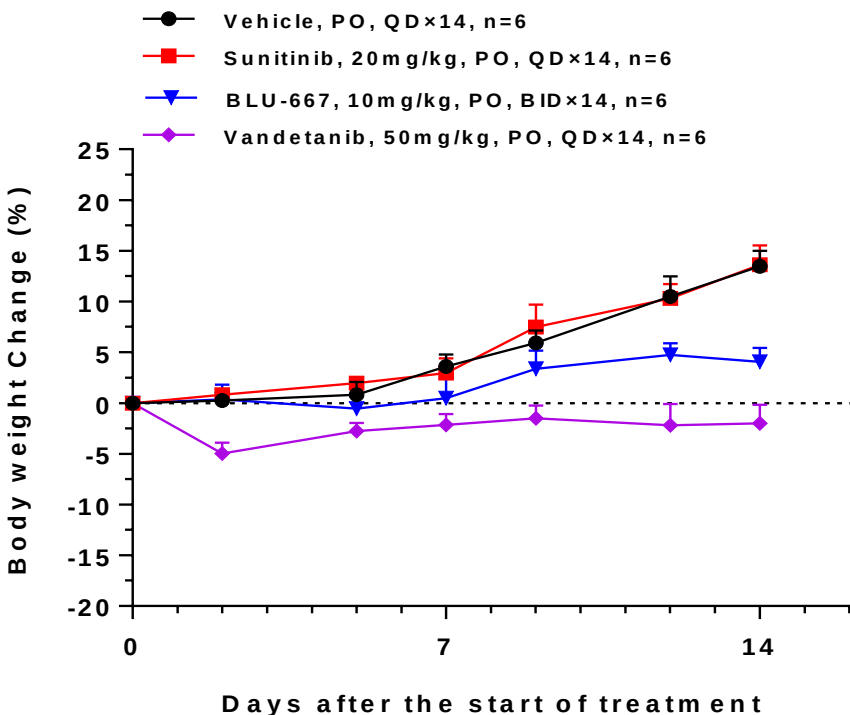
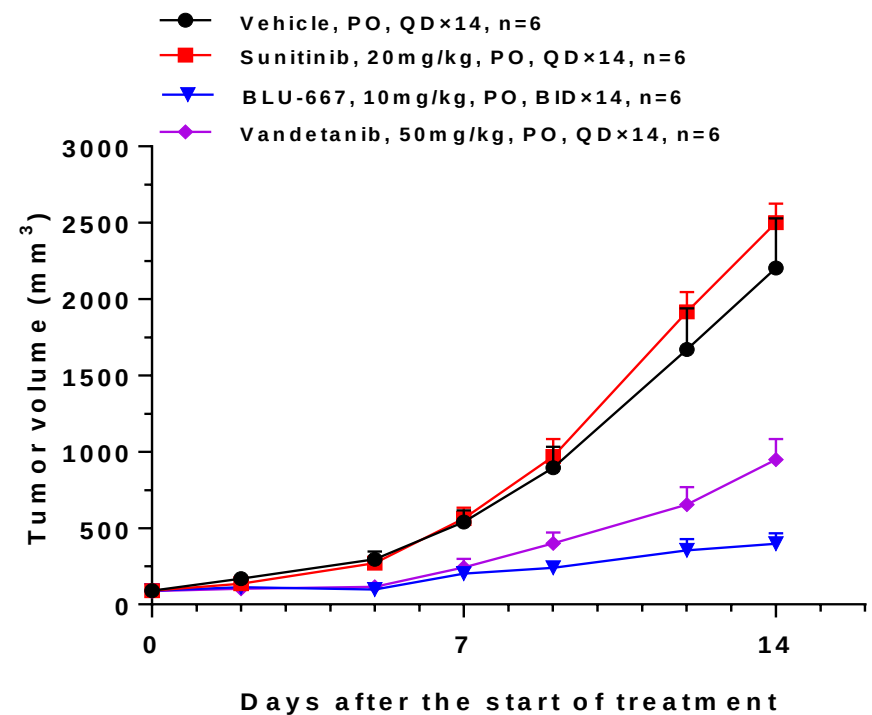
Sunitinib, BLU-667 and Vandetanib in Ba/F3 CCDC6-RET-V804M model

Cell line	Model ID	Drugs tested	Dosage	TGI (%)	Model genetics
RET engineering murine pro-B cell line	Ba/F3 CCDC6-RET-V804M	Sunitinib BLU-667 Vandetanib	20 mpk, QD 10 mpk, BID 50 mpk, QD	22.96 86.29 46.03	CCDC6-RET-V804M



Sunitinib, BLU-667 and Vandetanib in Ba/F3 CCDC6-RET-V804L model

Cell line	Model ID	Drugs tested	Dosage	TGI (%)	Model genetics
RET engineering murine pro-B cell line	Ba/F3 CCDC6-RET-V804L	Sunitinib BLU-667 Vandetanib	20 mpk, QD 10 mpk, BID 50 mpk, QD	-14.9 85.45 59.37	CCDC6-RET-V804L





OUR COMMITMENT

Improving Health. Making a Difference.

For questions and requests, please email to info_onco@wuxiapptec.com



<https://onco.wuxiapptec.com>



Mobile App