

# Clinical Drug Resistant Patient-derived Xenograft (PDX) Models

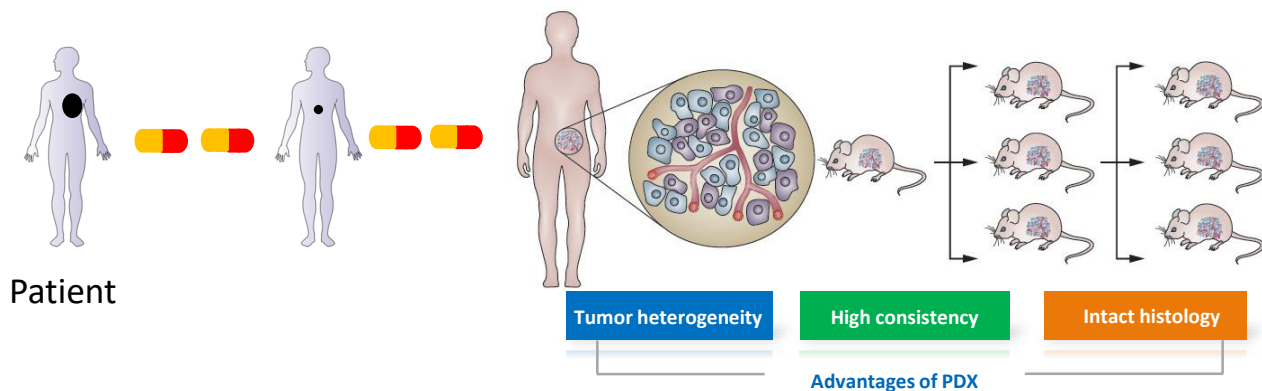


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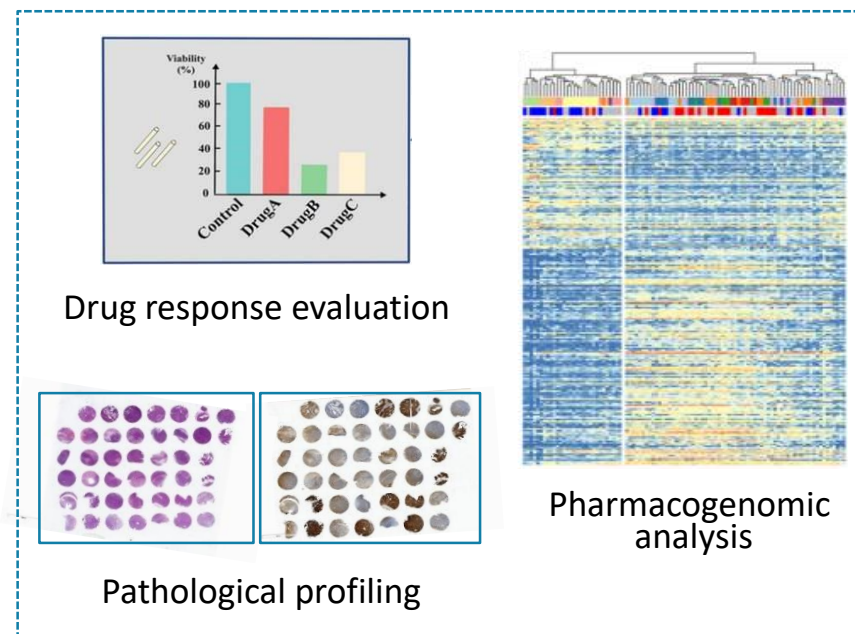
OncoWuXi Newsletter

# Introduction of clinical drug resistant PDX models

- Drug resistance has been a major clinical challenge, and the mechanisms that cause drug resistance are diverse. The development of pre-clinical animal models for drug resistance research is urgently needed. WuXi AppTec has a number of unique clinical resistance models derived from patients who have relapsed or developed resistance to currently prevalent therapeutic regimens resulting in therapeutic failure, which can provide you with more clinically relevant models to test your next-generation drug.



*Tentler et al., Nat Rev Clin Oncol 2012*



# Clinical drug resistant PDX models

Target	Drug resistant PDX models derived from clinical resistance patients			
	Model ID	Cancer type	Clinical treatment	Model genetics
<b>EGFR (8)</b>	LU-01-1157	NSCLC	1 <sup>st</sup> EGFR TKI	EGFR exon19del
	LU-01-1649	NSCLC	Gefitinib, Osimertinib, Crizotinib	EGFR L858R, MET amplification
	LU-01-1004	NSCLC	Osimertinib	EGFR L858R, T790M, V834L
	LU-01-1017	NSCLC	Osimertinib	EGFR L858R
	LU-01-1178	NSCLC	Osimertinib	EGFR L858R, MET amplification
	LU-01-1623	NSCLC	Osimertinib	EGFR exon19del
	LU-01-1031	SCLC	Osimertinib	EGFR L858R
	LU-01-1377	SCLC	Osimertinib	EGFR L858R
<b>PARP (1)</b>	OV-10-0076	Ovarian cancer	TP chemotherapy, Topotecan, Olaparib	HRD positive
<b>MET (3)</b>	LU-01-0751	NSCLC	Crizotinib	MET N375S, D1228N
	LU-01-1616	NSCLC	Osimertinib	MET exon 14 skipping
	LU-01-1476	NSCLC	Crizotinib	MET exon 14 skipping, EGFR overexpression
<b>ALK (1)</b>	LU-01-1651	NSCLC	Alectinib	EML4-ALK, MET expression:278
<b>Chemotherapy (4)</b>	BR-05-0567	TNBC	Paclitaxel + AC	-
	HN-13-0001	Head and Neck cancer	Chemotherapy	-
	LU-01-1388	Lung cancer	EC	-
	OV-10-0060	Ovarian cancer	Ovarian cancer surgery, docetaxel+carboplatin	-

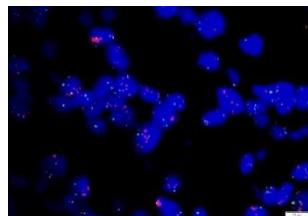
# Clinical drug resistant PDX models

Showcase of EGFR inhibitor resistant PDX models

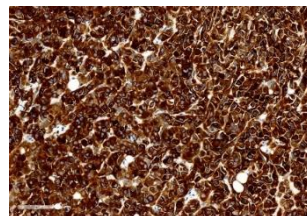
Model ID	Cancer type	Origin	Presurgery treatment	Model genetics
LU-01-1649	Lung Cancer (Adenocarcinoma)	Recurrent	Gefitinib, Osimertinib, Crizotinib	EGFR L858R, MET amplification (CNV:5)
LU-01-1178	Lung Cancer (Adenocarcinoma)	Recurrent	Osimertinib	EGFR L858R, MET amplification (CNV:6)

## LU-01-1649

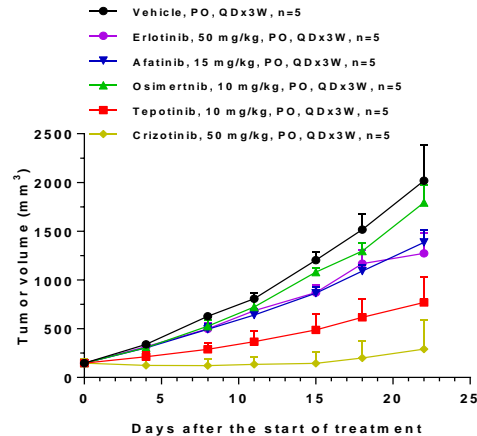
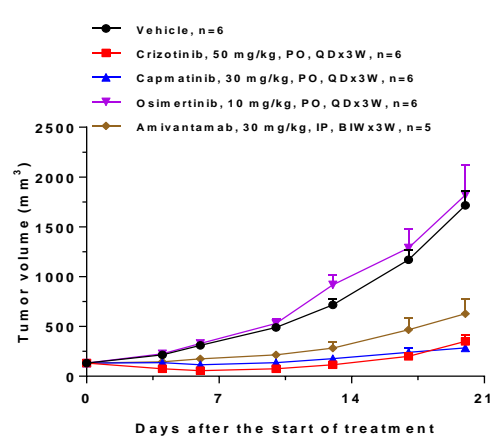
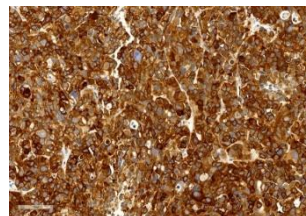
MET FISH (CNV:5)



MET (IHC, H-score 268)

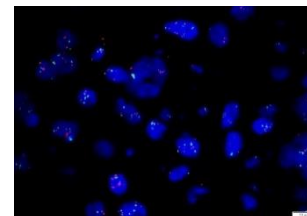


EGFR (IHC, H-score 234)

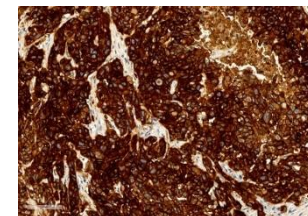


## LU-01-1178

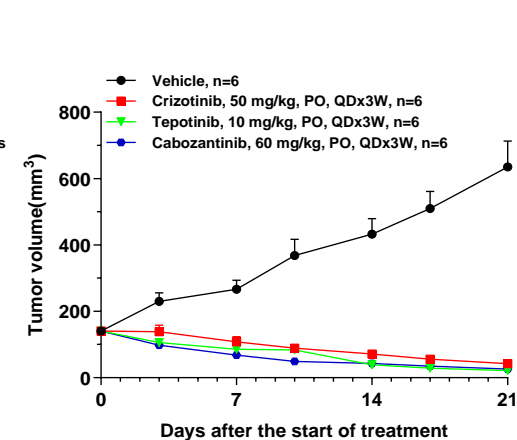
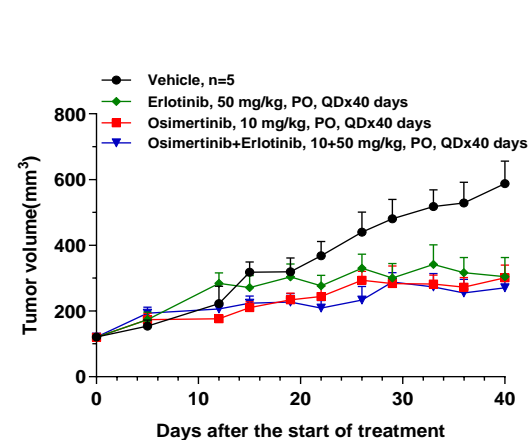
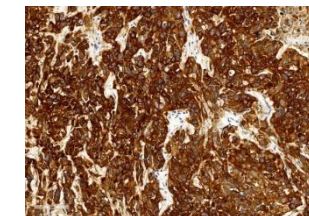
MET FISH (CNV:6)



MET (IHC, H-score 268)



EGFR (IHC, H-score 262)



# Clinical drug resistant PDX models

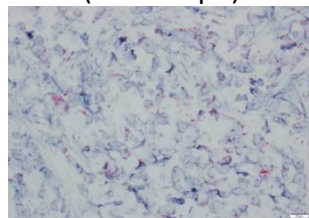
Showcase of MET inhibitor responsive and resistant PDX models

Model ID	Cancer type	Origin	Presurgery treatment	Model genetics
LU-01-1375	Lung Cancer (Adenocarcinoma)	Primary	NO	MET exon 14 skipping
LU-01-1476*	Lung Cancer (Squamous cell carcinoma)	Recurrent	Crizotinib	MET exon 14 skipping, EGFR overexpression
LU-01-1616	Lung Cancer (Adenocarcinoma)	Recurrent	Osimertinib	MET exon 14 skipping

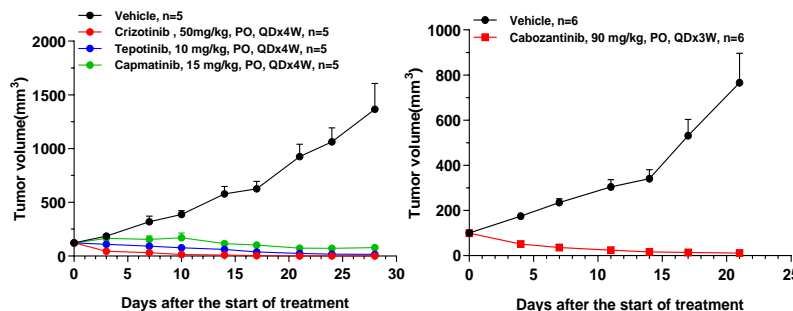
\* LU-01-1375 and LU-01-1476 are from the same patient

## LU-01-1375

MET exon 14 skipping (BaseScope)

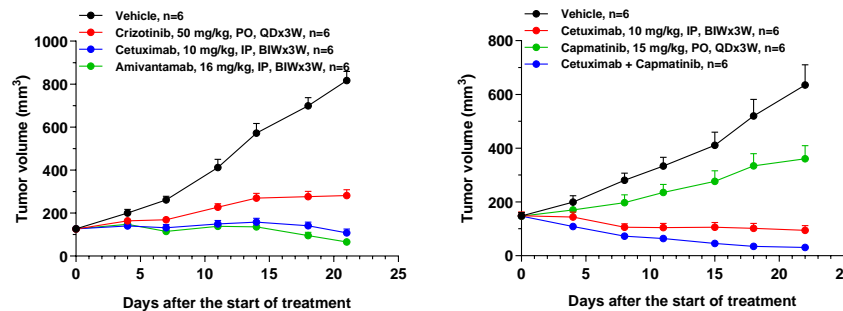
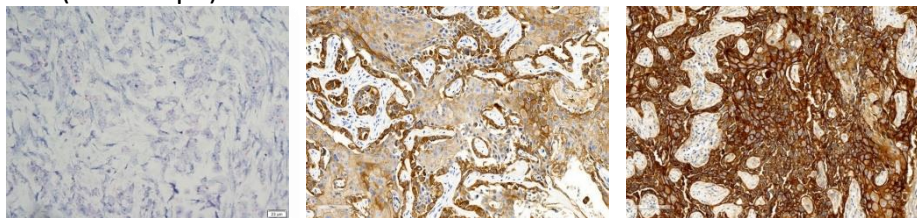


Note: Expression of MET $\Delta$ 14 in PDX tumor tissue was detected by the probe for exon junction 13/15.



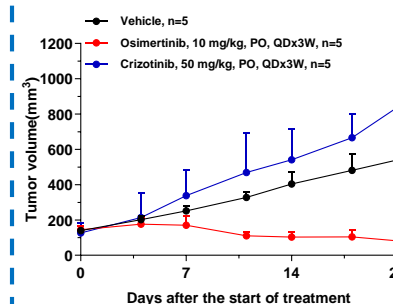
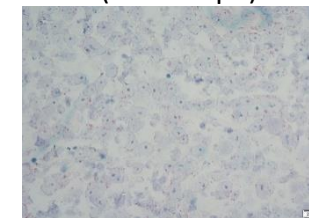
## LU-01-1476

MET exon 14 skipping (BaseScope) MET (IHC, H-score 133) EGFR (IHC, H-score 234)



## LU-01-1616

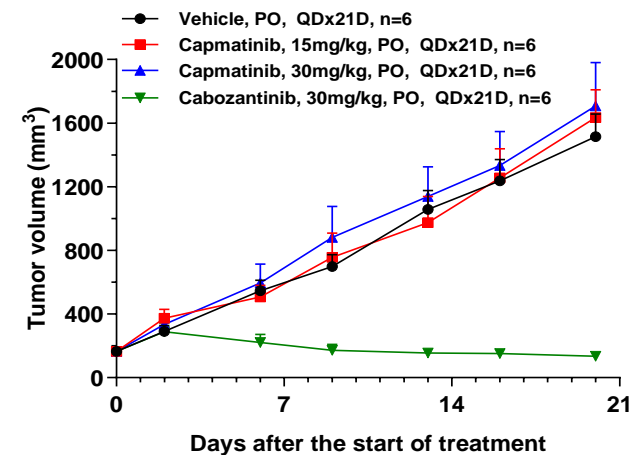
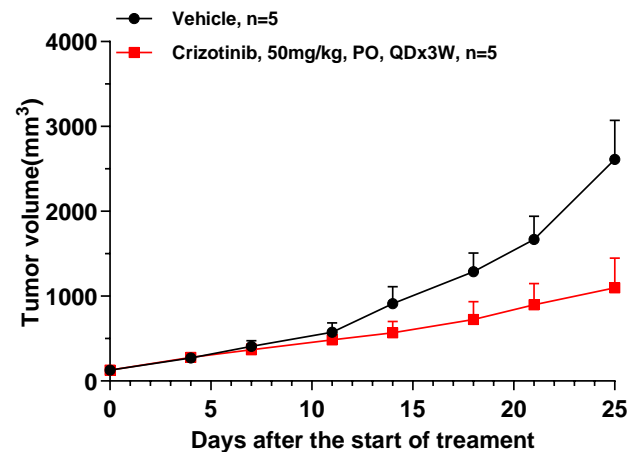
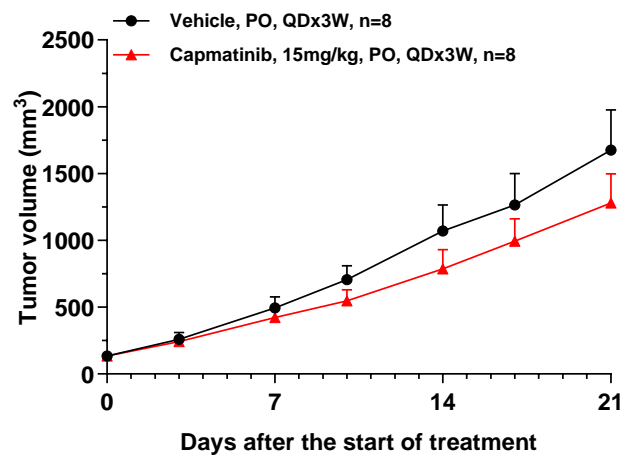
MET exon 14 skipping (BaseScope)



# Clinical drug resistant PDX models

Showcase of MET inhibitor resistant PDX models

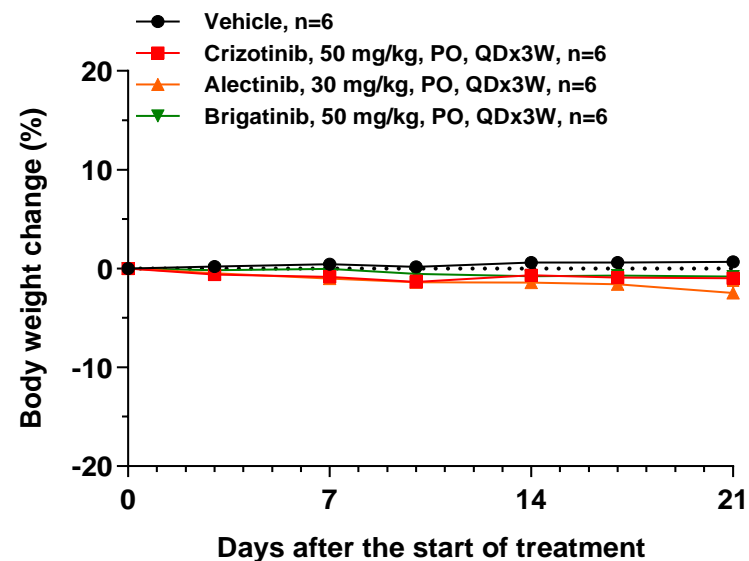
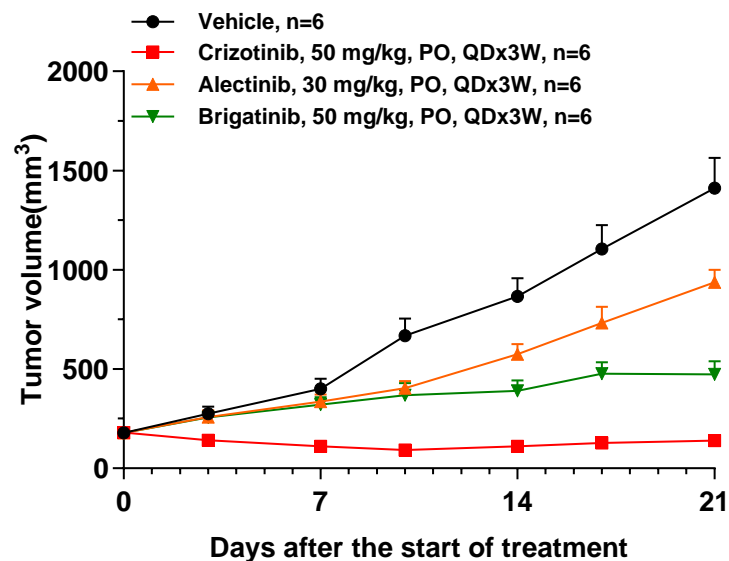
Model ID	Cancer type	Origin	Presurgery treatment	Model genetics
LU-01-0751	Lung Cancer (Adenocarcinoma)	Recurrent	NA	MET: N375S, D1228N



# Clinical drug resistant PDX models

Showcase of ALK inhibitor resistant PDX models

Model ID	Cancer type	Origin	Presurgery treatment	Model genetics
LU-01-1651	Lung Cancer (Adenocarcinoma)	Lymph node	Alectinib	EML4-ALK, MET expression:278 MYC (CNV:11) TP53 Q185X





# OUR COMMITMENT

*Improving Health. Making a Difference.*

For questions and requests, please email to [Pharmacology-BD-Translation@wuxiapptec.com](mailto:Pharmacology-BD-Translation@wuxiapptec.com)



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