

1/8

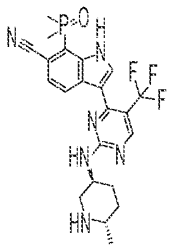
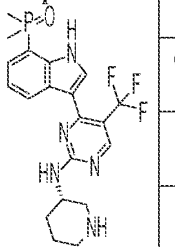
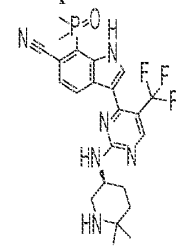
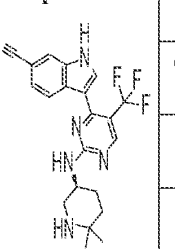
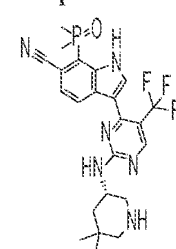
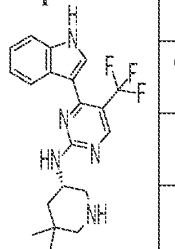
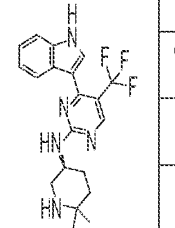
Compound 100 	CDK7 K_D (nM) = 0.057		Comparator 1 	CDK7 K_D (nM) = 0.18	
	CDK12 K_i (nM) 230	$(K_i/K_D \text{ CDK7})$ 4100		CDK12 K_i (nM) 51	$(K_i/K_D \text{ CDK7})$ 280
	CDK2 K_i (nM) 1500	$(K_i/K_D \text{ CDK7})$ 26000		CDK2 K_i (nM) 210	$(K_i/K_D \text{ CDK7})$ 1100
	CDK9 K_i (nM) 800	$(K_i/K_D \text{ CDK7})$ 14000		CDK9 K_i (nM) 140	$(K_i/K_D \text{ CDK7})$ 790
Compound 101 	CDK7 K_D (nM) = 0.065		Comparator 2 	CDK7 K_D (nM) = 0.45	
	CDK12 K_i (nM) 870	$(K_i/K_D \text{ CDK7})$ 13000		CDK12 K_i (nM) 140	$(K_i/K_D \text{ CDK7})$ 320
	CDK2 K_i (nM) 2600	$(K_i/K_D \text{ CDK7})$ 40000		CDK2 K_i (nM) 810	$(K_i/K_D \text{ CDK7})$ 1800
	CDK9 K_i (nM) 960	$(K_i/K_D \text{ CDK7})$ 15000		CDK9 K_i (nM) 130	$(K_i/K_D \text{ CDK7})$ 280
Compound 102 	CDK7 K_D (nM) = 0.059		Comparator 3 	CDK7 K_D (nM) = 0.21	
	CDK12 K_i (nM) 78	$(K_i/K_D \text{ CDK7})$ 1300		CDK12 K_i (nM) 18	$(K_i/K_D \text{ CDK7})$ 89
	CDK2 K_i (nM) 390	$(K_i/K_D \text{ CDK7})$ 6800		CDK2 K_i (nM) 26	$(K_i/K_D \text{ CDK7})$ 130
	CDK9 K_i (nM) 290	$(K_i/K_D \text{ CDK7})$ 4900		CDK9 K_i (nM) 20	$(K_i/K_D \text{ CDK7})$ 99
			Comparator 4 	CDK7 K_D (nM) = 0.34	
				CDK12 K_i (nM) 48	$(K_i/K_D \text{ CDK7})$ 140
				CDK2 K_i (nM) 64	$(K_i/K_D \text{ CDK7})$ 190
				CDK9 K_i (nM) 36	$(K_i/K_D \text{ CDK7})$ 100

FIG. 1

SUBSTITUTE SHEET (RULE 26)

2/8

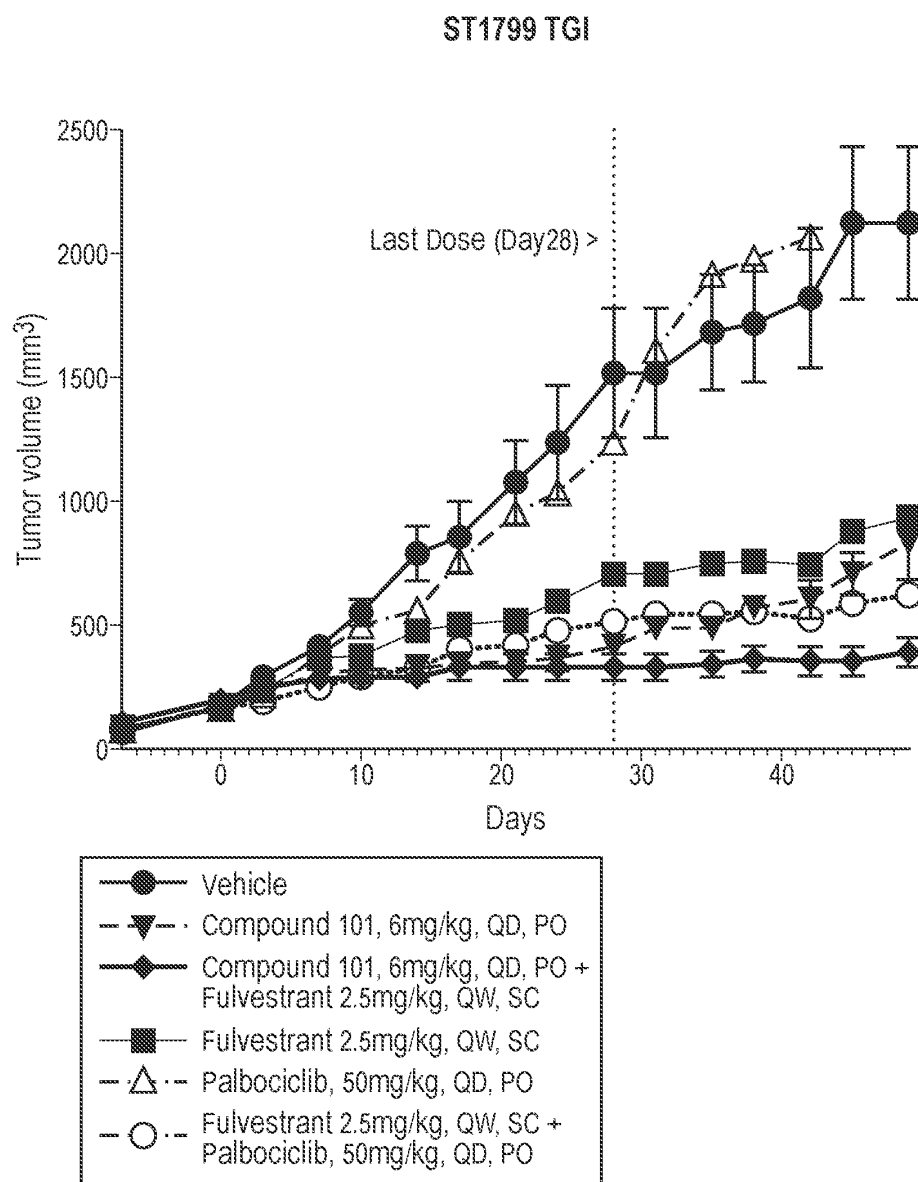


FIG. 2

3/8

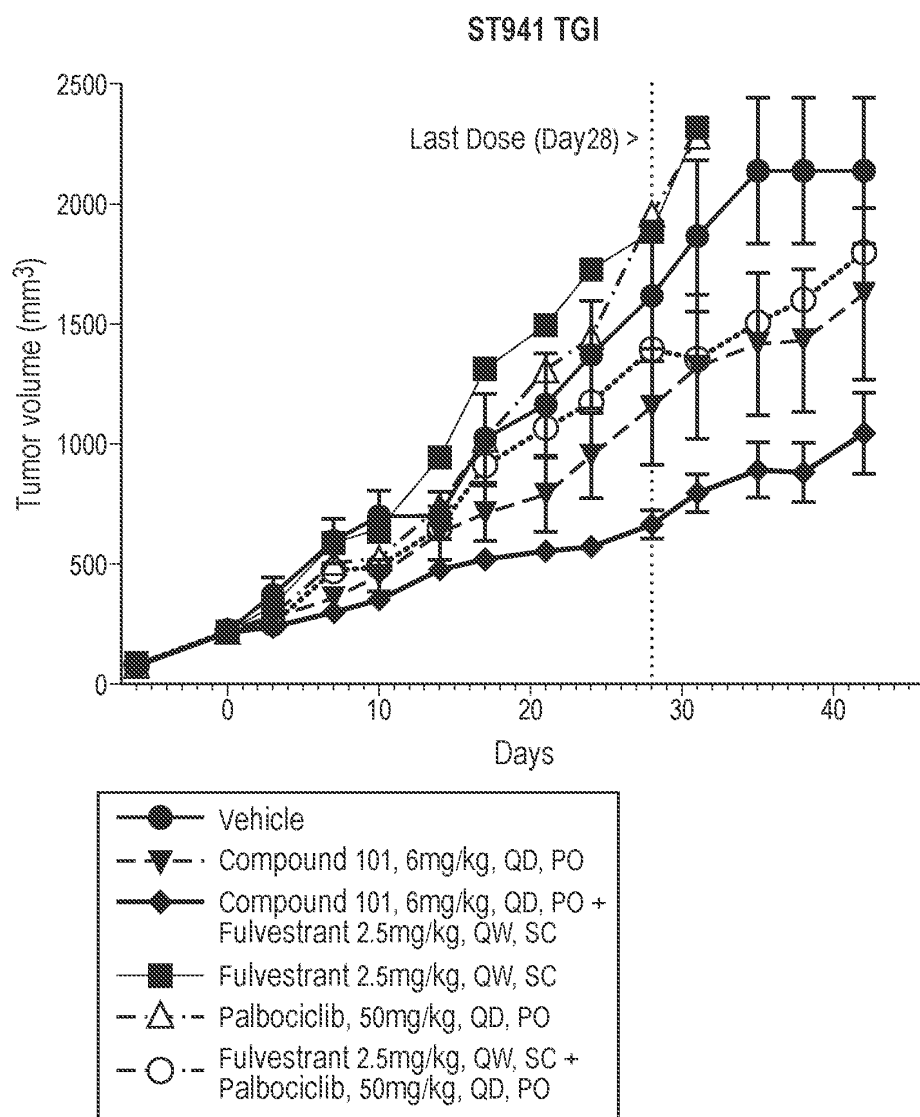


FIG. 3

SUBSTITUTE SHEET (RULE 26)

4/8

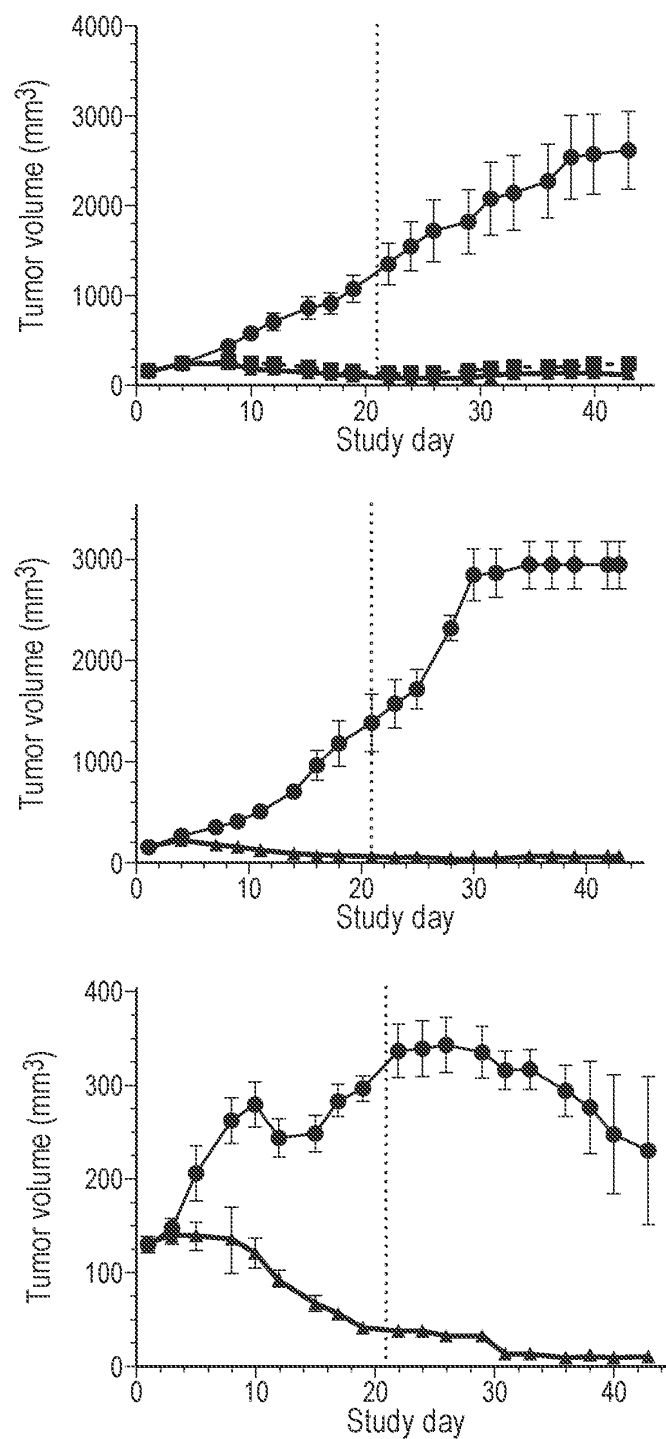


FIG. 4

SUBSTITUTE SHEET (RULE 26)

5/8

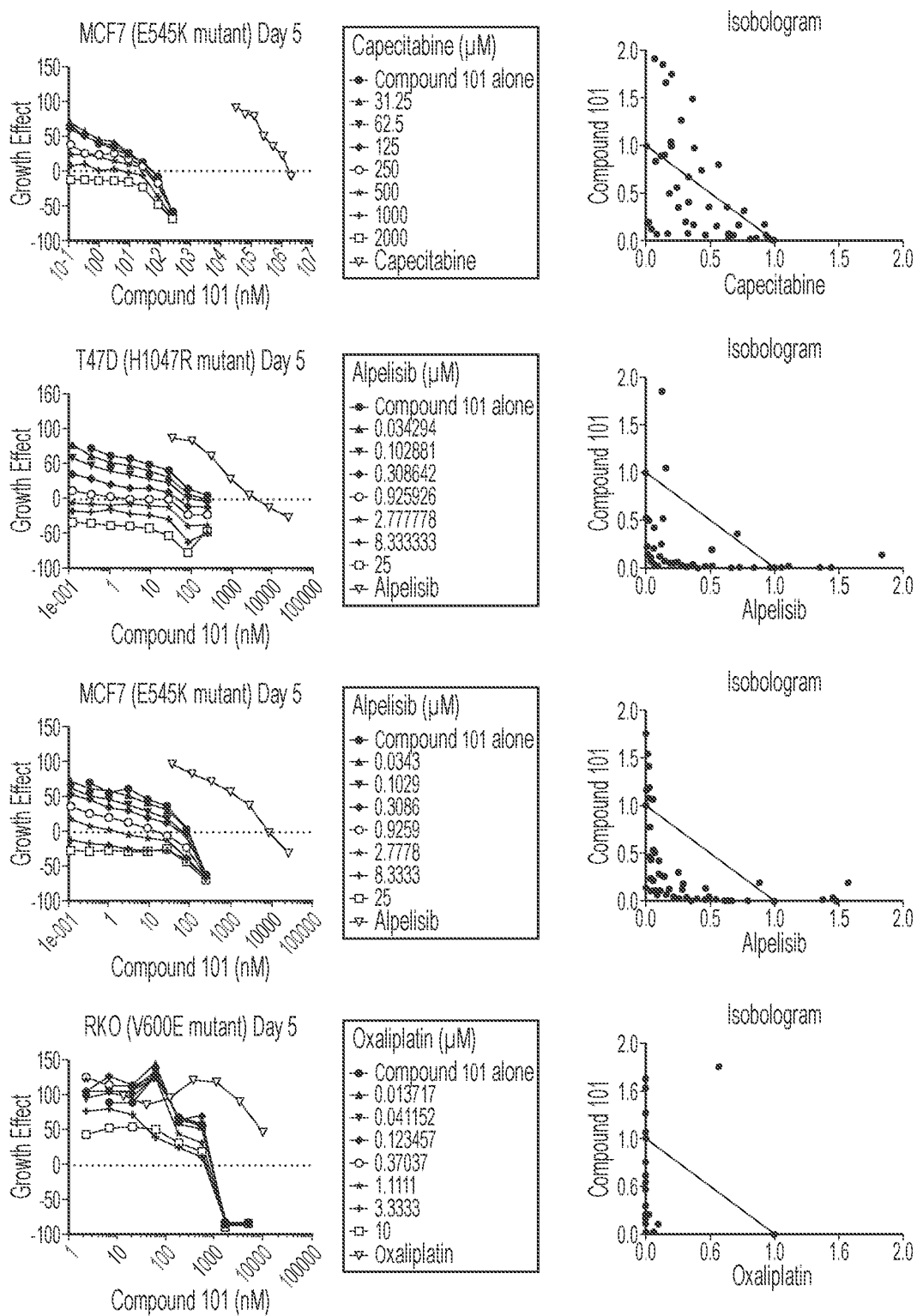
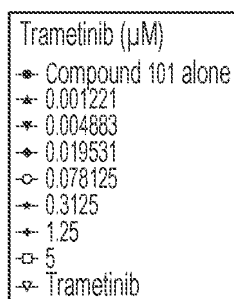
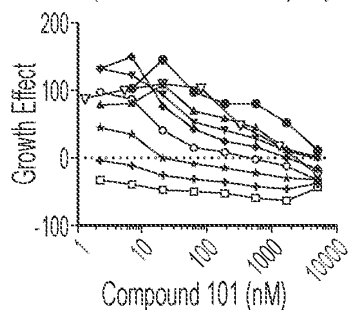


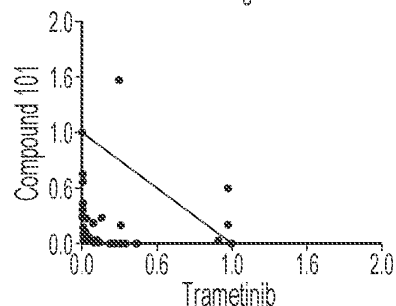
FIG. 5
SUBSTITUTE SHEET (RULE 26)

6/8

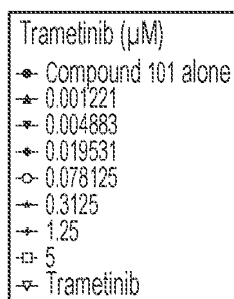
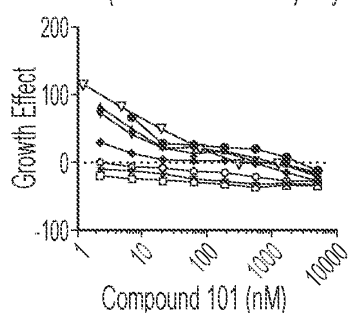
RKO (BRAF V600E mutant) Day5



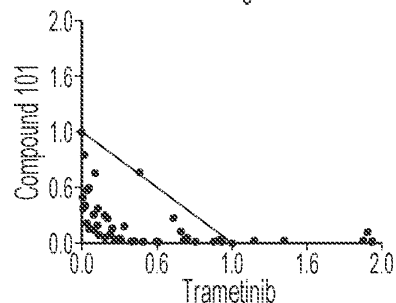
Isobologram



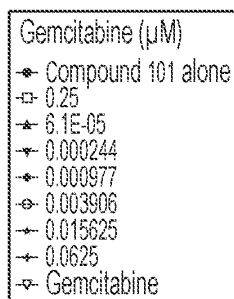
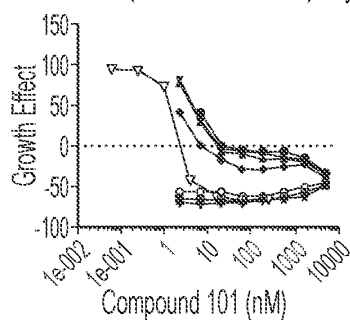
SW480 (KRAS G12V mutant) Day5



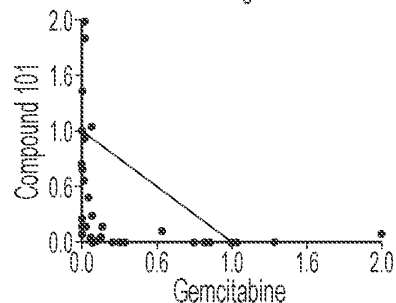
Isobologram



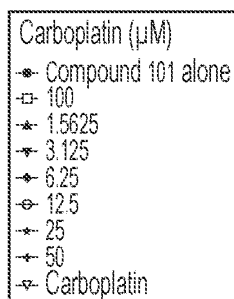
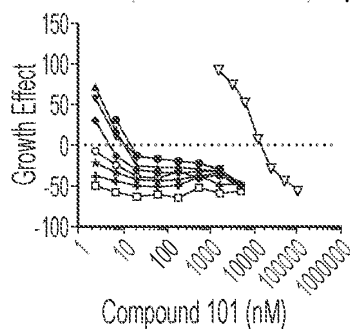
NCI-H1048 (RB mutant/deletion) Day5



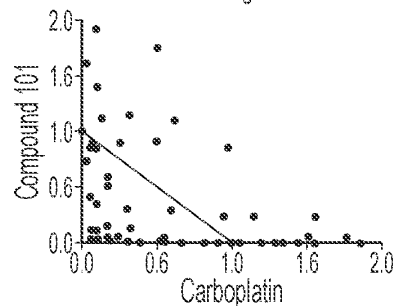
Isobologram



NCI-H1048 (RB mutant/deletion) Day5



Isobologram

FIG. 5 (cont.)
SUBSTITUTE SHEET (RULE 26)

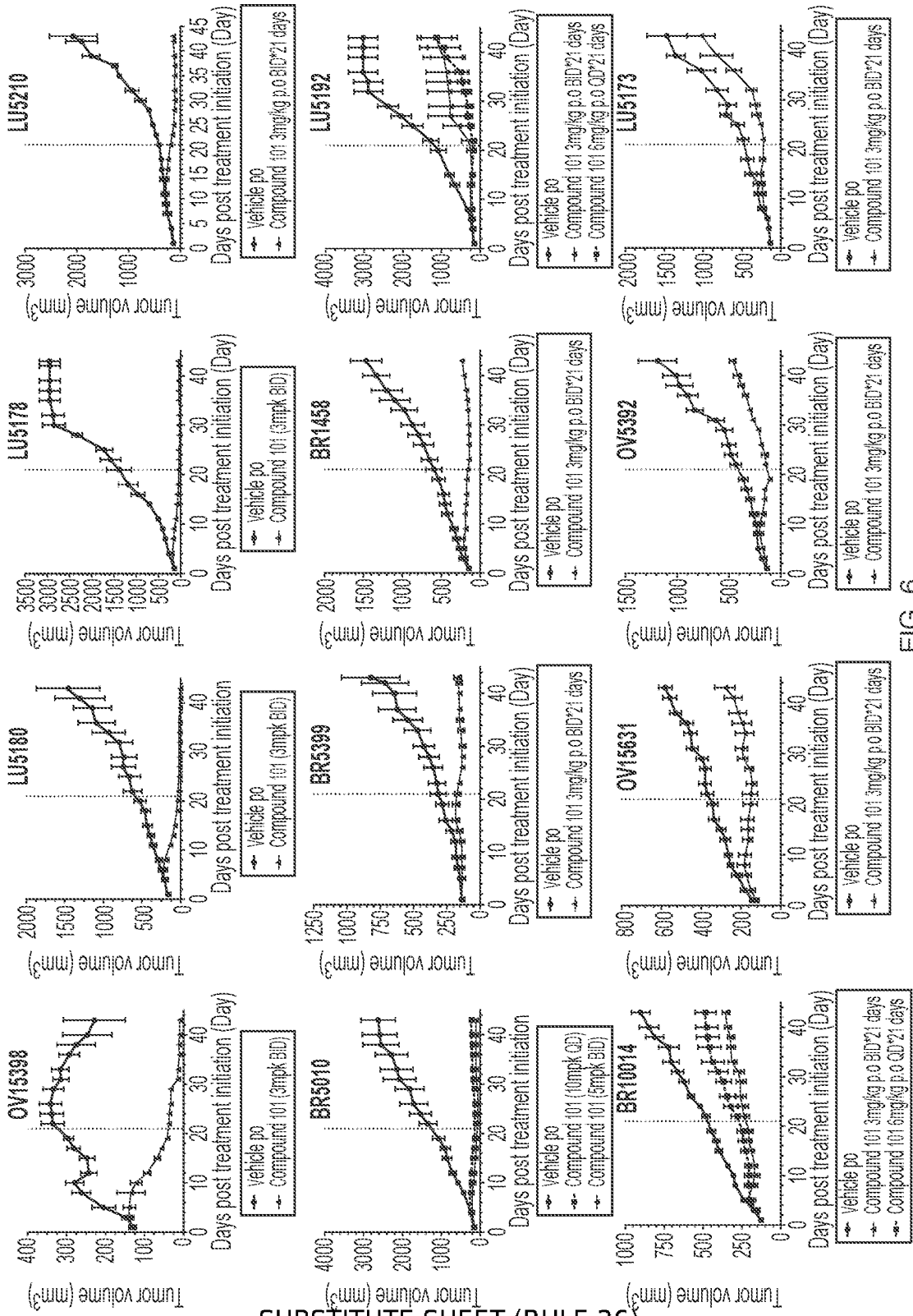


FIG. 6

PDX model	End of Treatment Day 21		Post-treatment Day 42		RB pathway genetics
	% TGI	% Regression	% TGI	% Regression	
OV15398	>100	80	>100	98	RB1 (CN=1, p.Q637*)
LU5180	>100	72	>100	93	CDKN2A (CN=1)
LU5178	>100	64	>100	73	RB1 (CN=0)
BR5010	>100	55	>100	27	CCNE1 (CN=21)
LU5210	82	0	>100	8	RB1 (p.L343SfsTer3)
BR1458	90	0	95	0	CDKN2A (CN=0)
					RB1 (CN=1, p.Y155C)
BR5399	82	0	95	0	RB1 (CN=1)
LU5192	94	0	69	0	None
BR10014	91	0	67	0	None
OV5392	92	0	64	0	None
OV15631	70	0	71	0	None
LU5173	74	0	33	0	None

FIG. 7