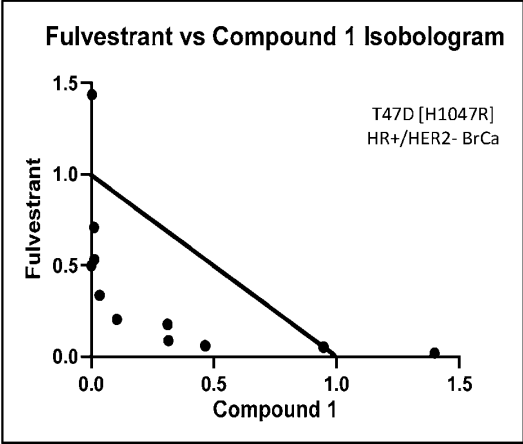


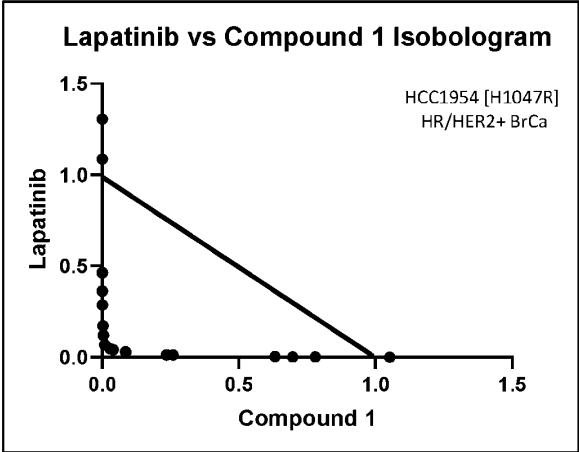
Hormone Tx



N=1

FIG. 1A

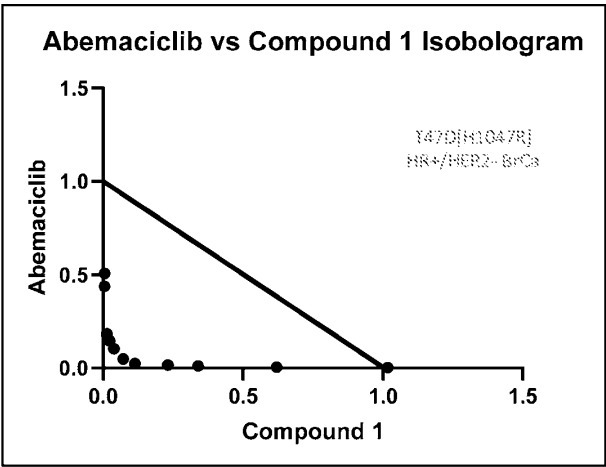
HER2 Inhibitor



N=2

FIG. 1B

CDK4/6 Inhibitor



N=2

FIG. 1C

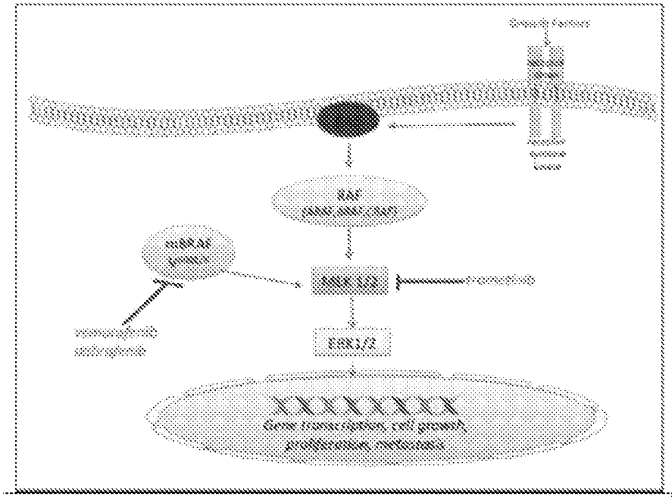


FIG. 1D

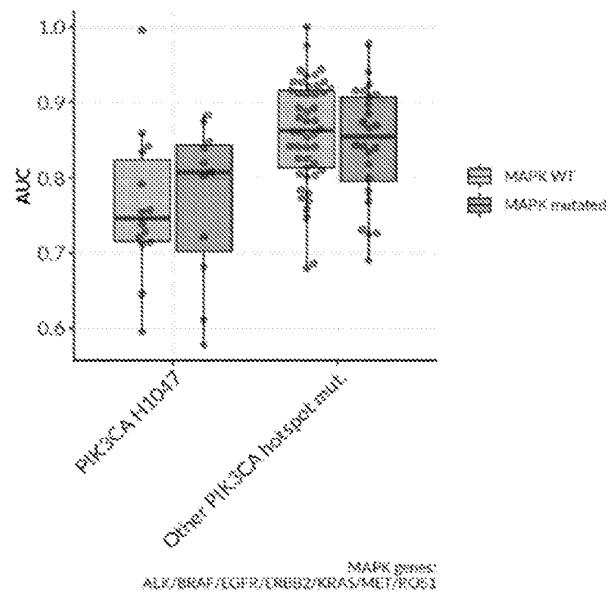


FIG. 1E

MEK1/2 inhibitor

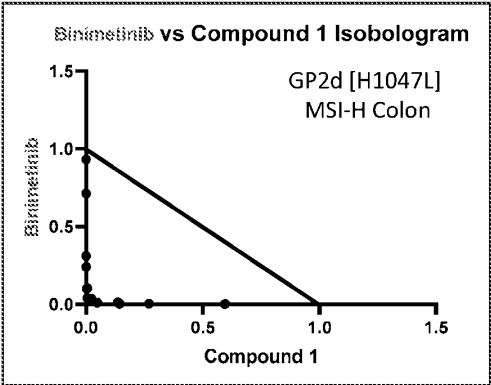


FIG. 1F

Compound 1 + Binimetinib
72 hr viability in HCT116

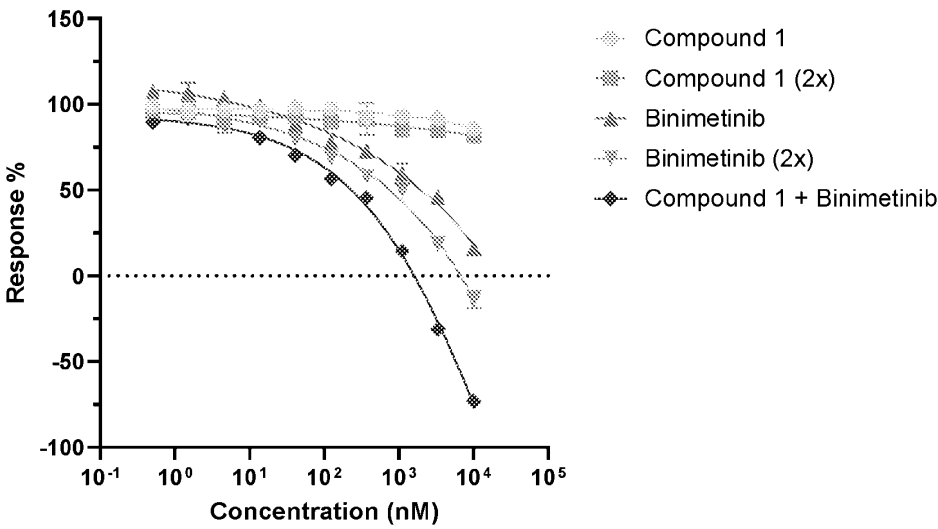


FIG. 1G

PDX Model 1: PIK3CA [H1047R], ER+

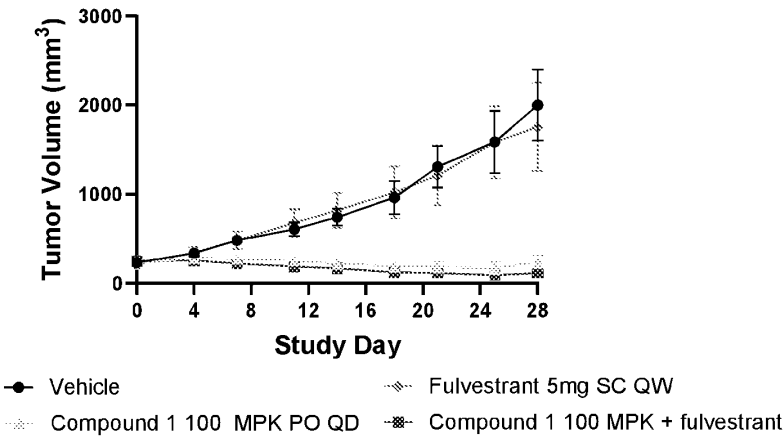


FIG. 2A

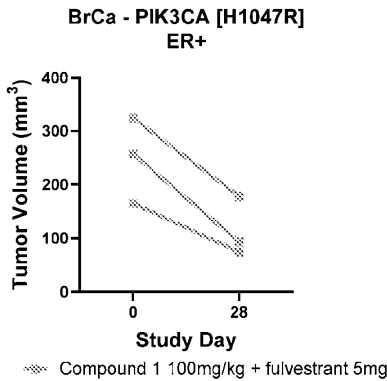


FIG. 2B

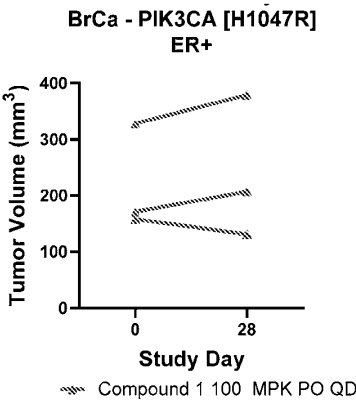


FIG. 2C

PDX Model 2: PIK3CA [H1047R/R108H] ER+/HER2+

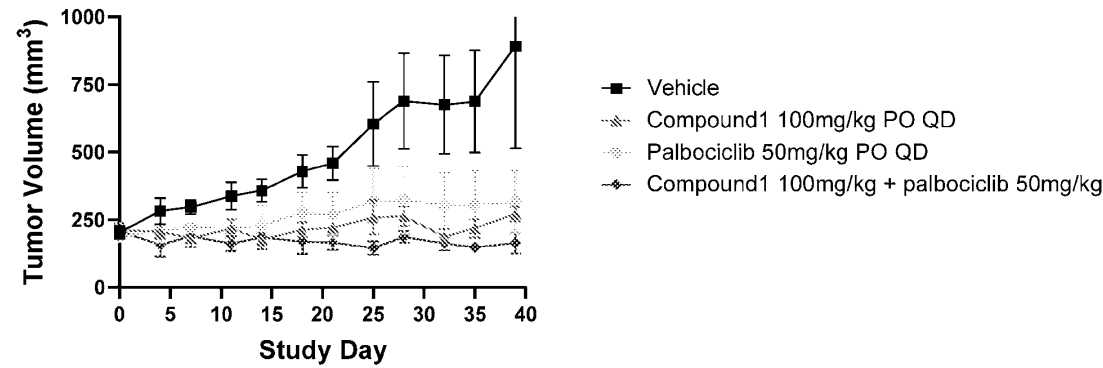


FIG. 3A

PDX Model 3: PIK3CA [H1047R] ER+/HER2+

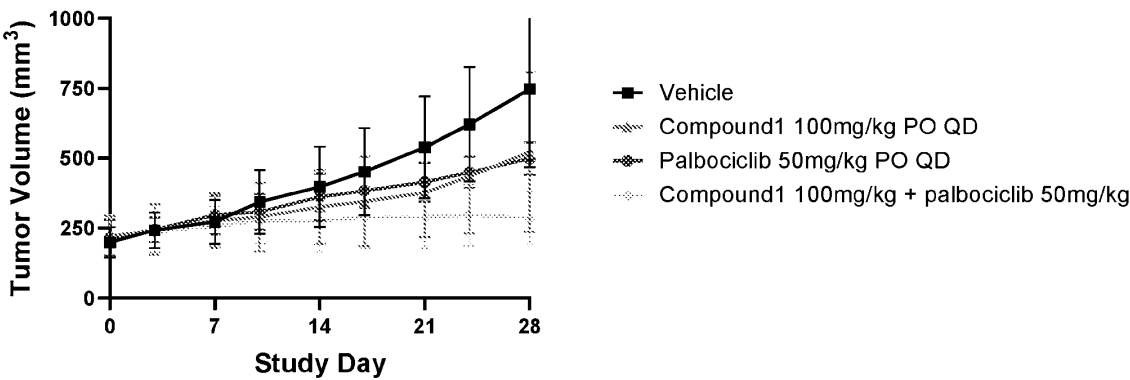


FIG. 3B

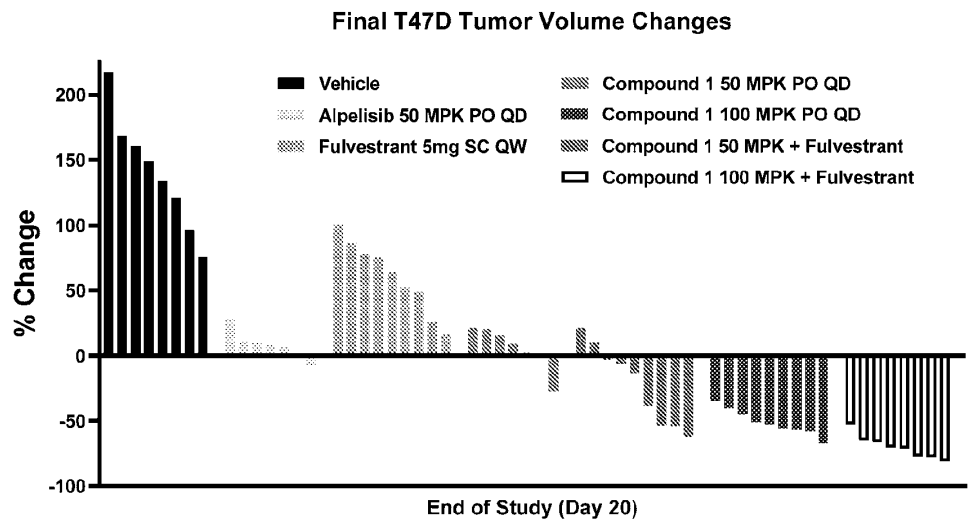


Fig. 4A

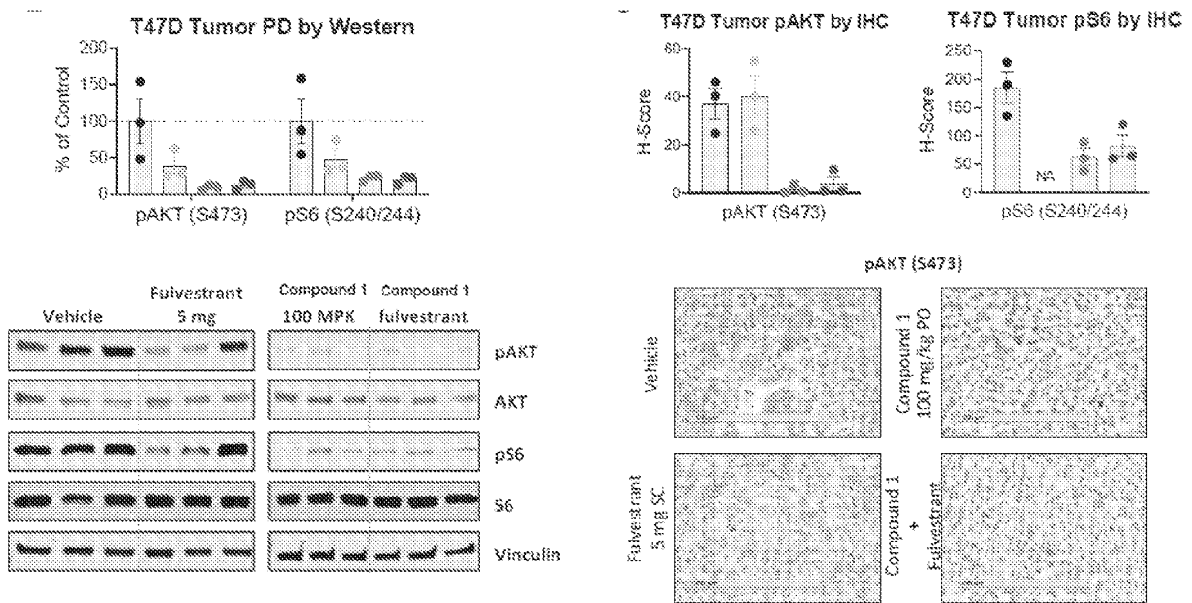


Fig. 4B

Fig. 4C

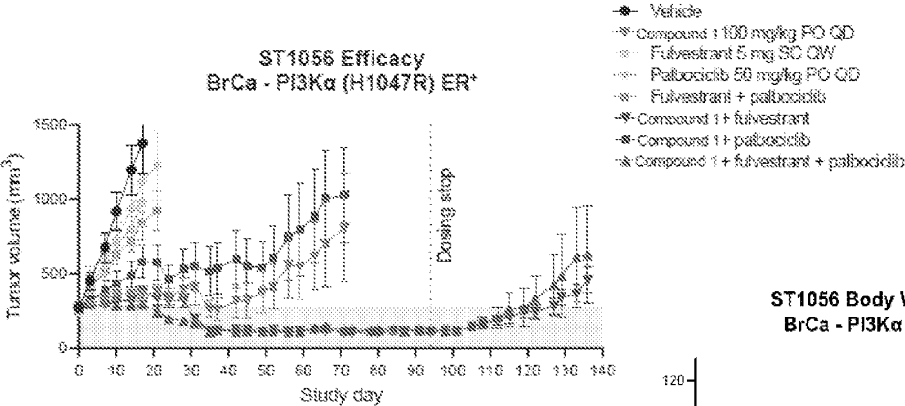


Fig. 4D

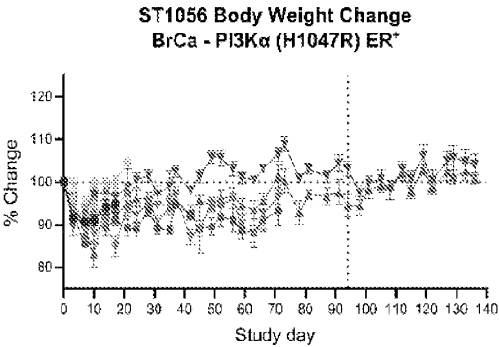


Fig. 4E

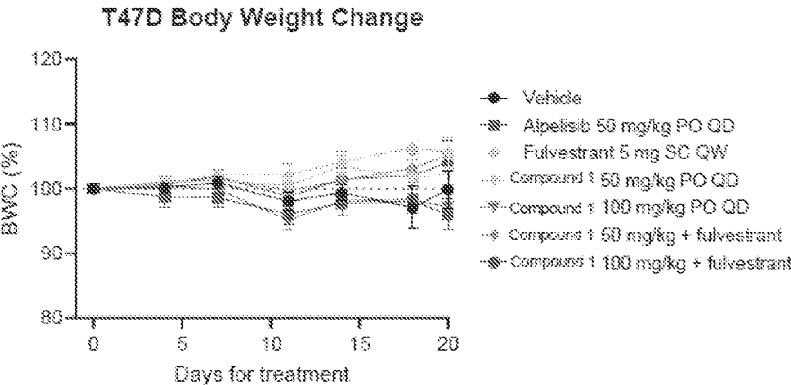


Fig. 4F

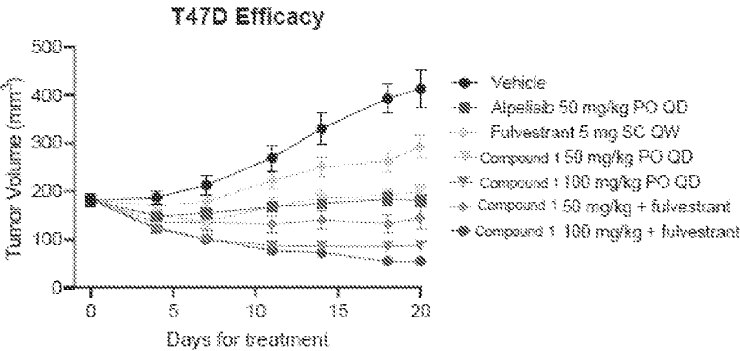


Fig. 4G

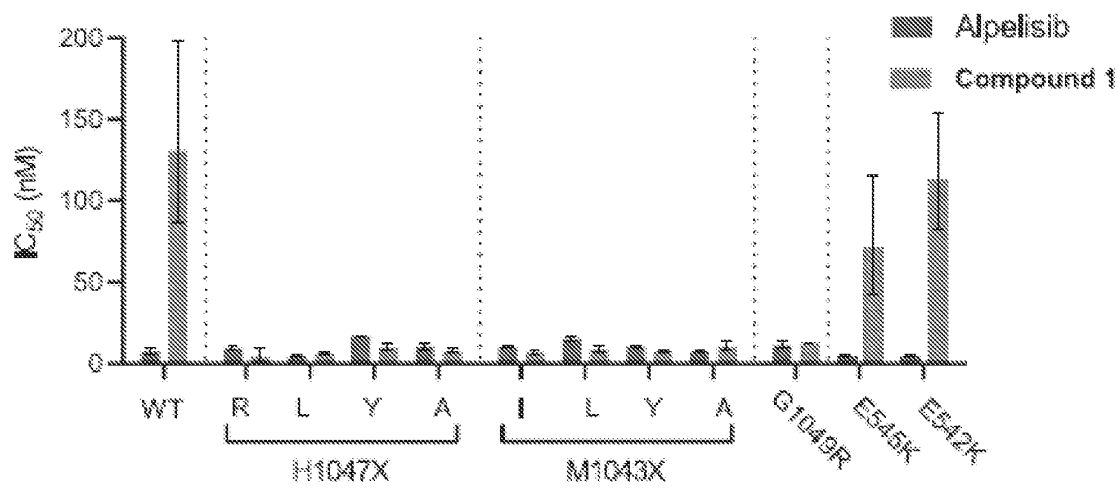
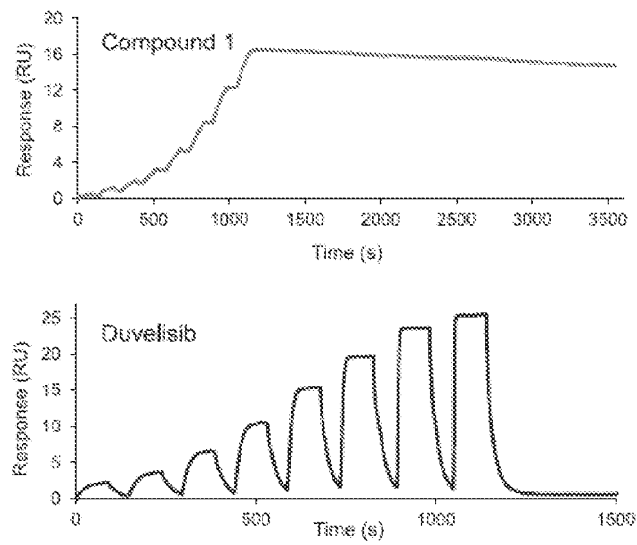


Fig. 5A



	Compound 1 (top)			Duvelisib (bottom)		
	K_D (nM)	k_{on} ($M^{-1}s^{-1}$) $\times 10^{-3}$	k_{off} (s^{-1}) $\times 10^{-3}$	K_D (nM)	k_{on} ($M^{-1}s^{-1}$) $\times 10^{-3}$	k_{off} (s^{-1}) $\times 10^{-3}$
WT PI3K α	70	1.7	1.2	30	1.7	5.1
PI3K α^{H1047R}	4.7	11	0.49	44	1.9	8.1
PI3K α^{E545K}	47	3.7	1.7	41	1.7	7.2

Fig. 5B

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Fig. 5C

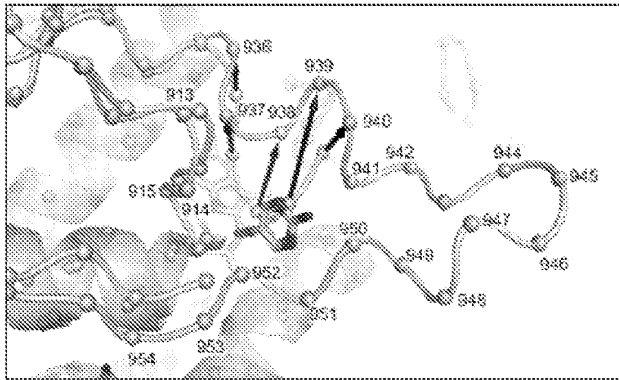


Fig. 5D

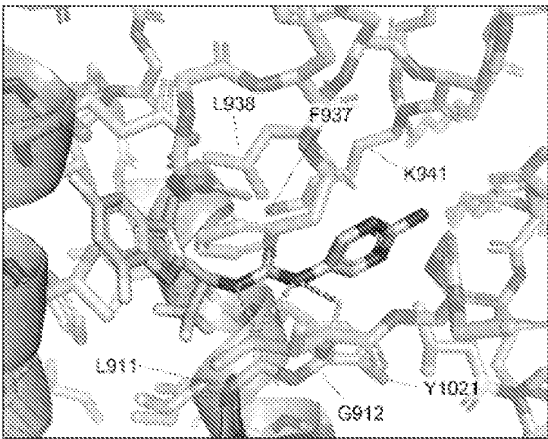
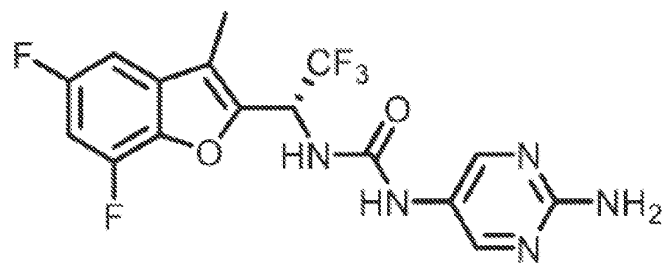


Fig. 5E

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Compound 1
H1047R PI3Kα K_D = 2.9 nM

Fig. 5F

Kinase	Alpelisib IC ₅₀ (nM)	STX-478 IC ₅₀ (nM)
PI3Kβ	>1000	50,000
PI3Kγ	250	>100,000
PI3Kδ	290	9700
Kinome profiling	11/254 kinases <10,000	1/373 kinases* <10,000

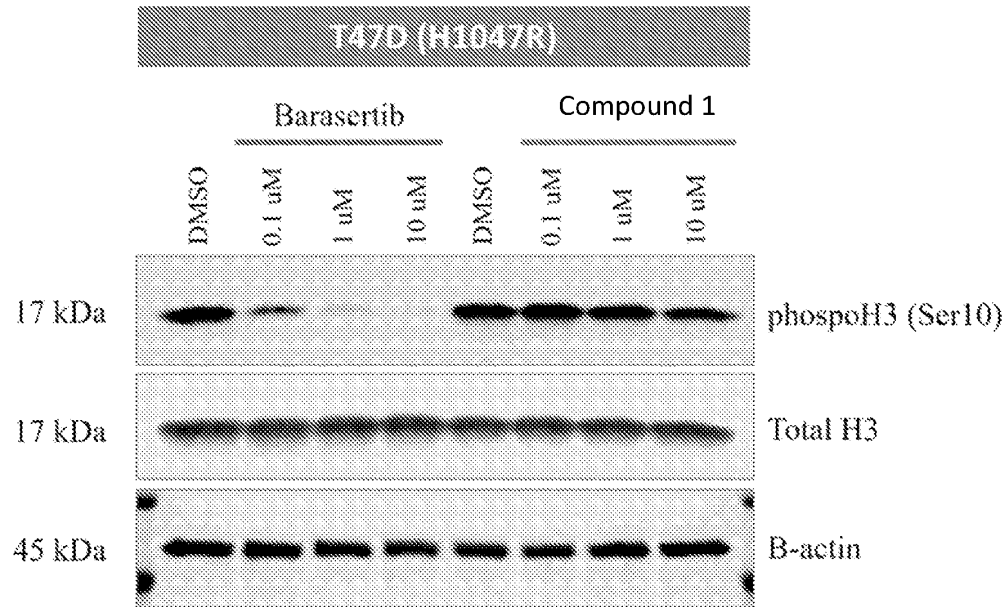


Fig. 5G

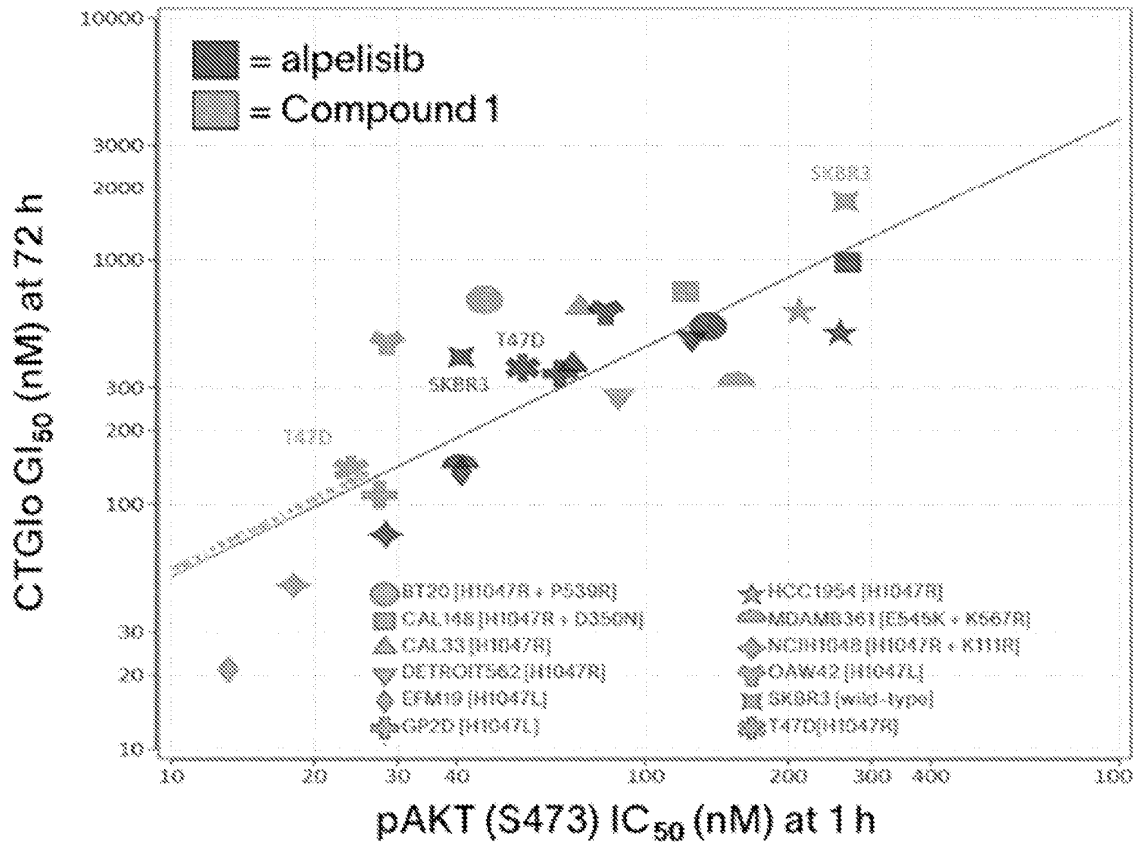


Fig. 6A

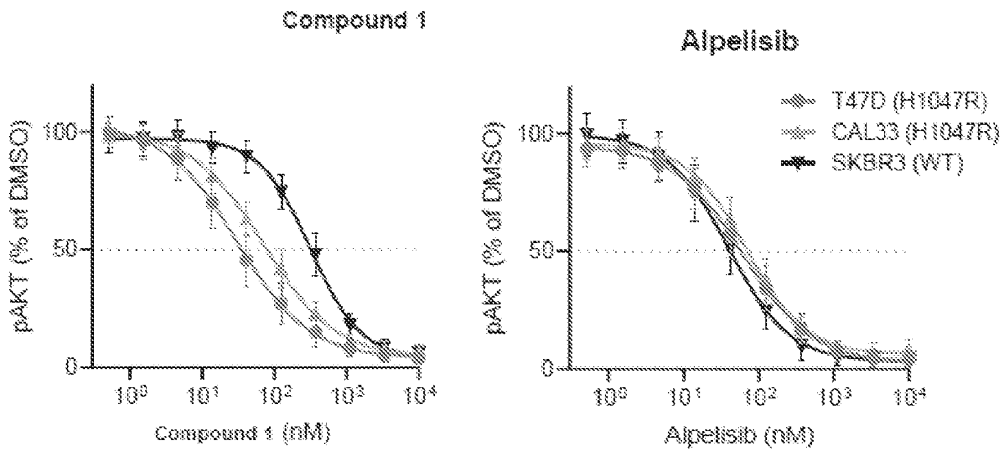


Fig. 6B

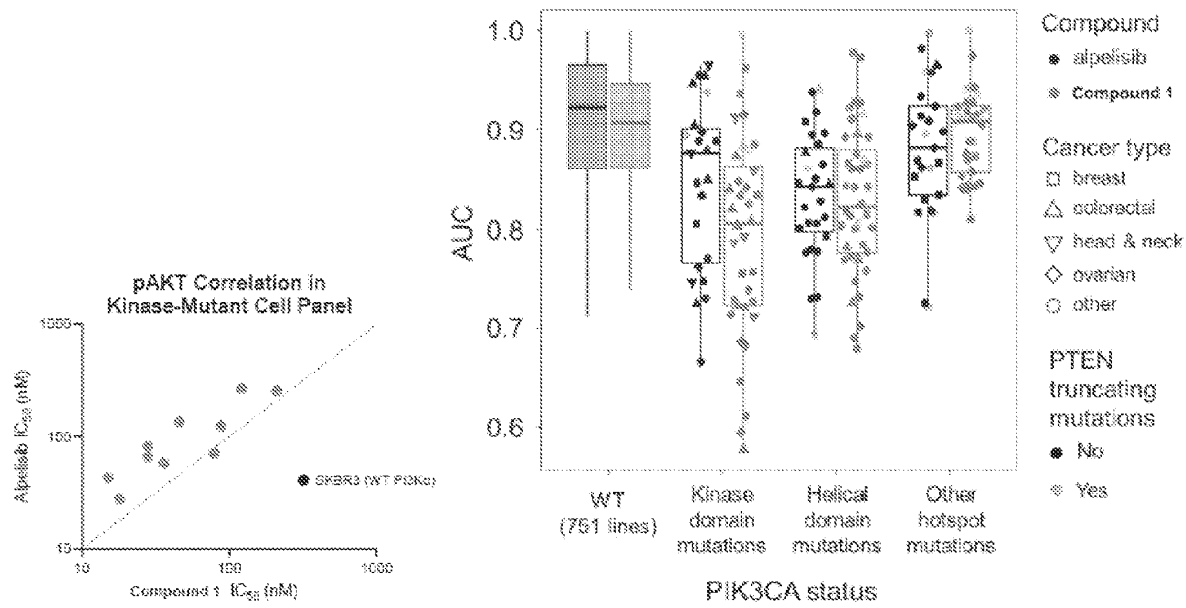


Fig. 6C

Fig. 6D

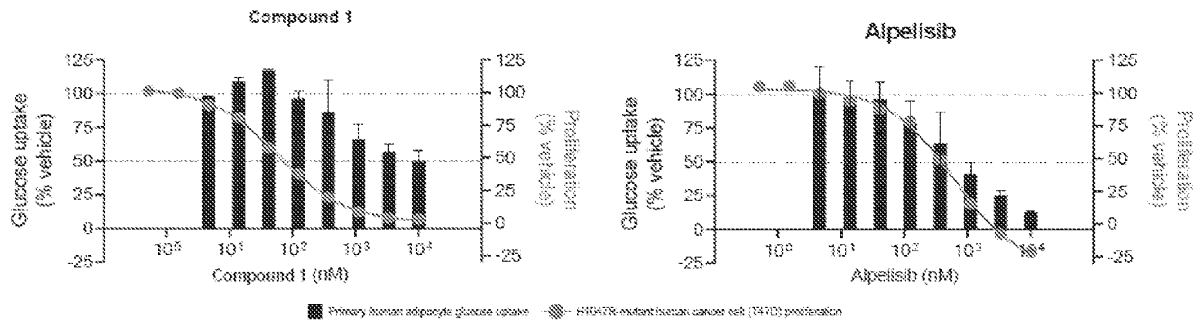


Fig. 6E

Fig. 6F

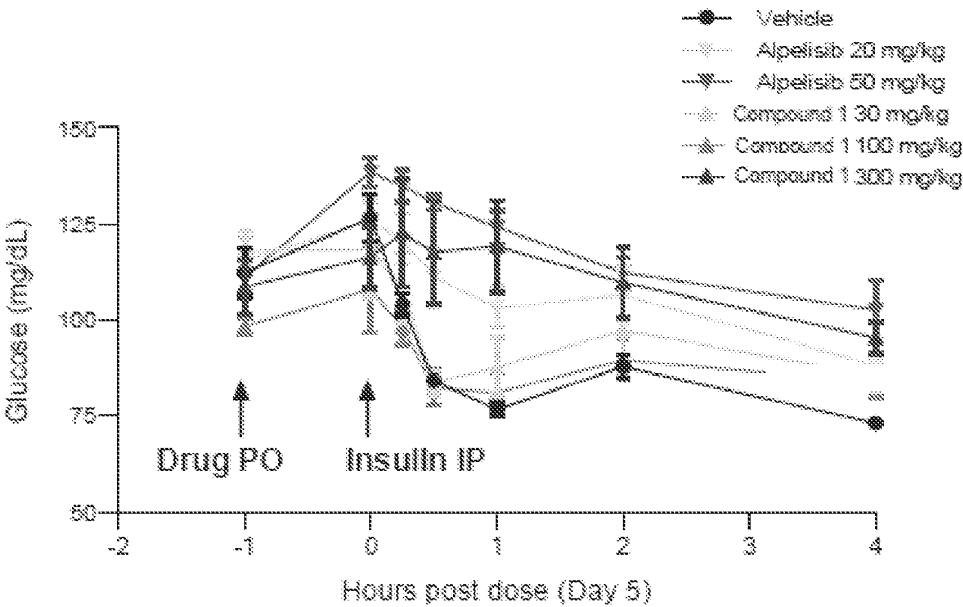


Fig. 7A

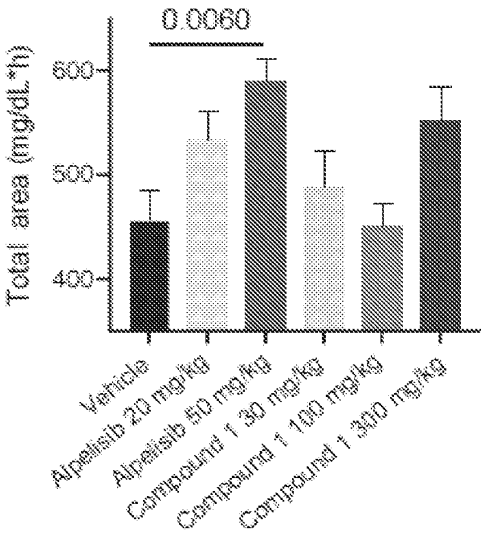


Fig. 7B

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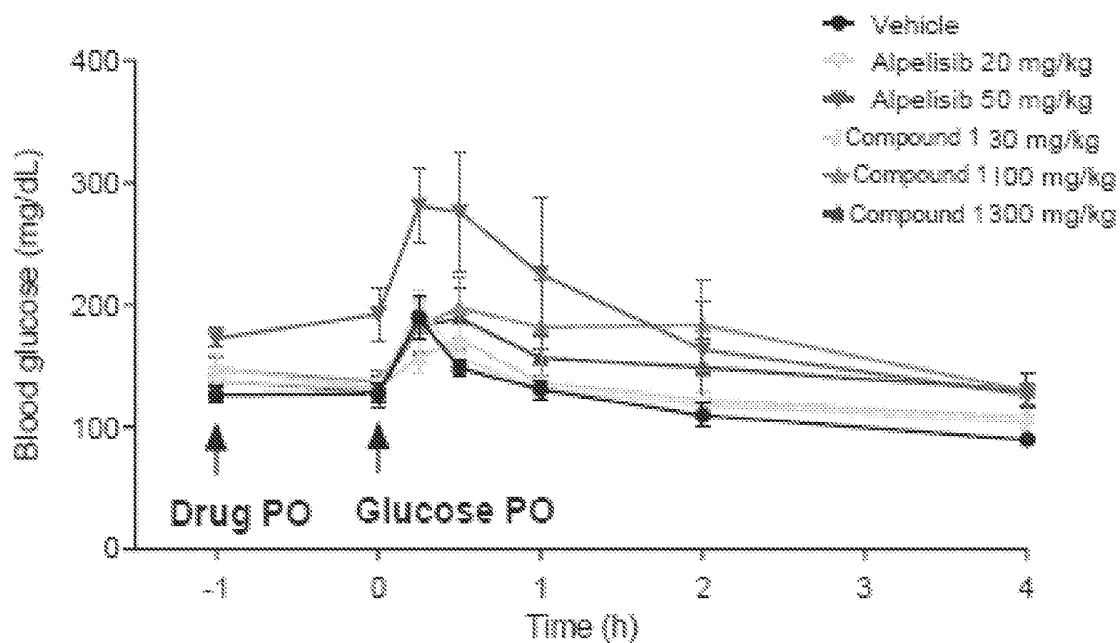


Fig. 7C

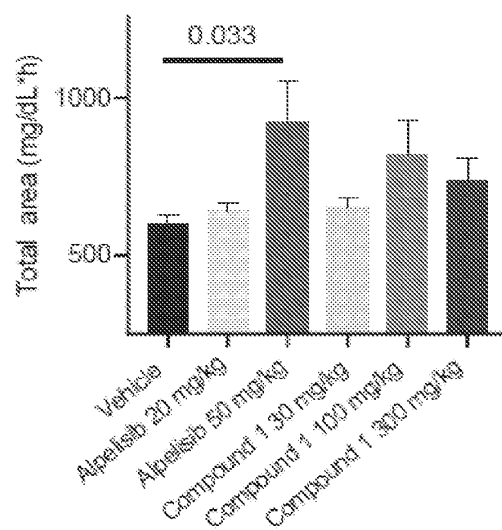


Fig. 7D

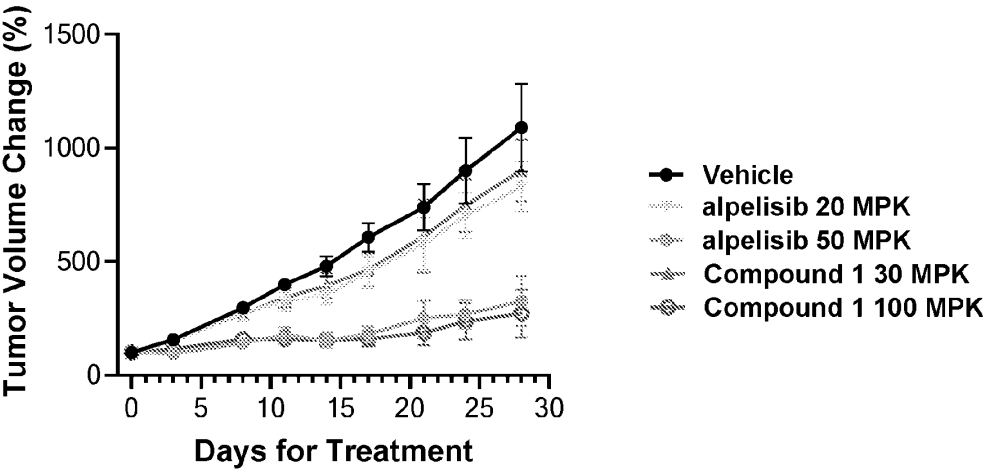


Fig. 8A

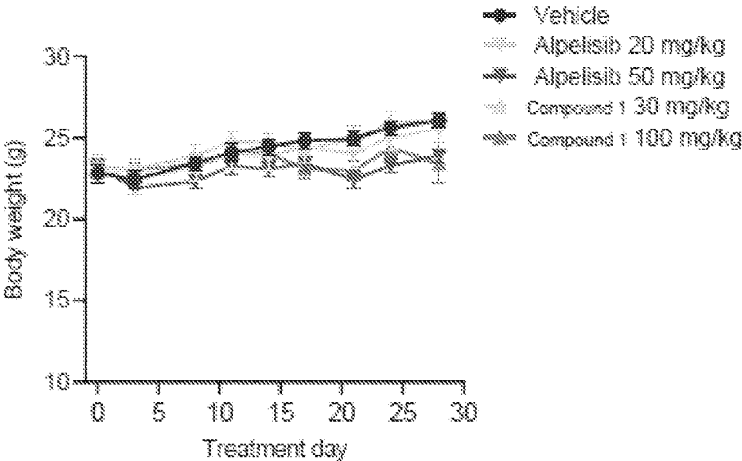


Fig. 8B

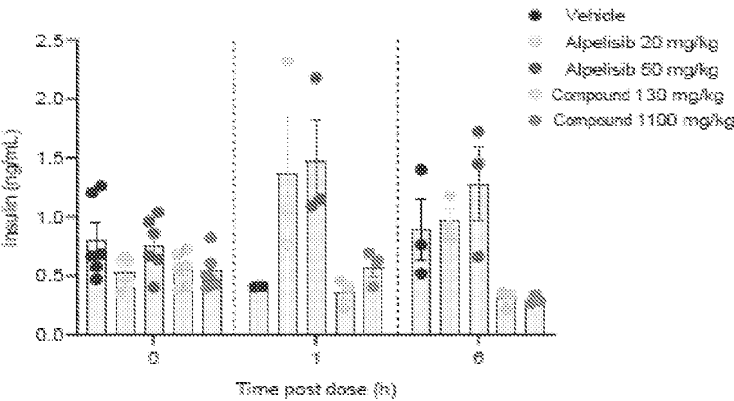


Fig. 8C

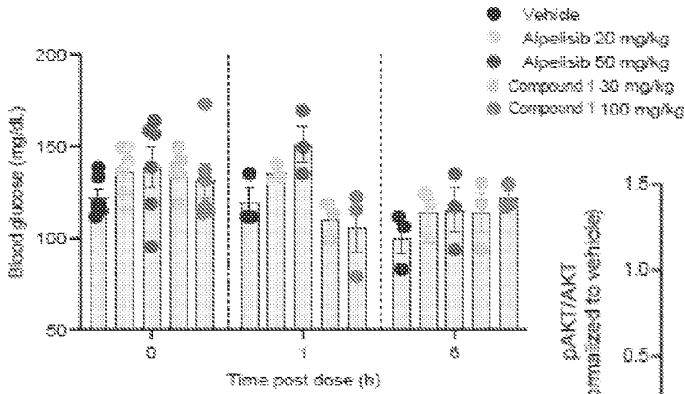


Fig. 8D

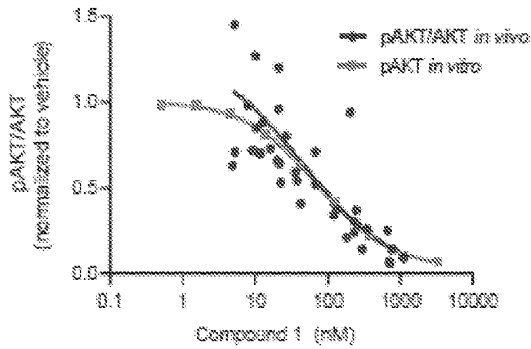


Fig. 8E

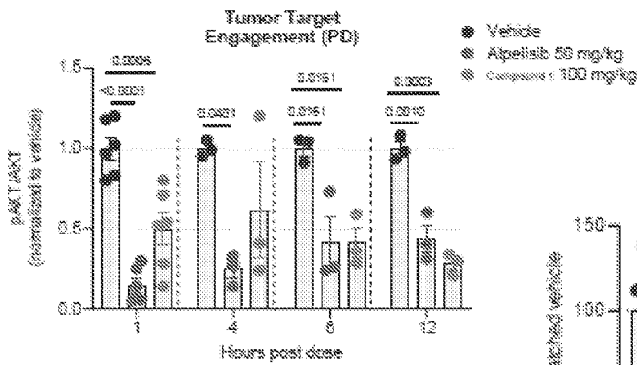


Fig. 8F

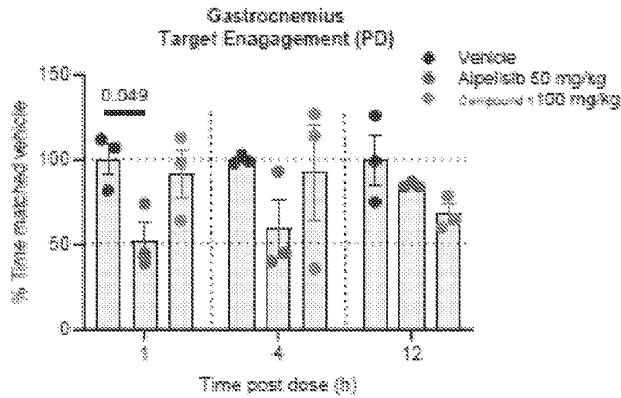


Fig. 8G

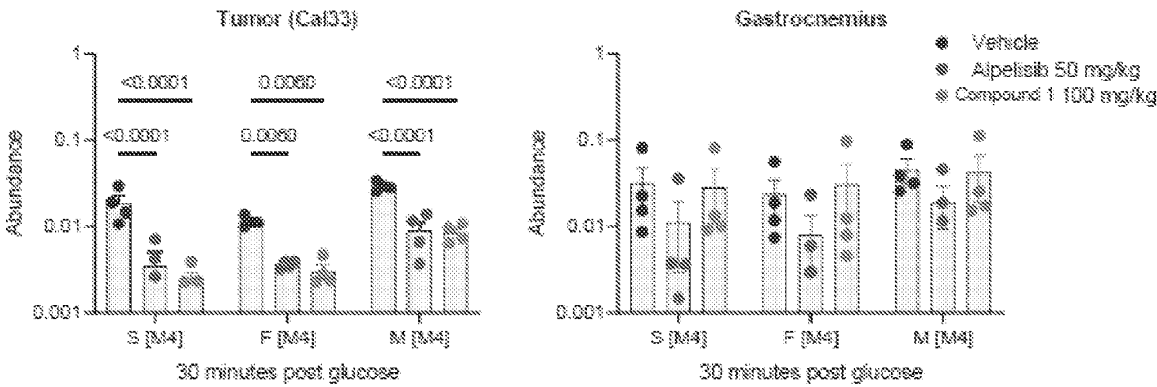


Fig. 8H

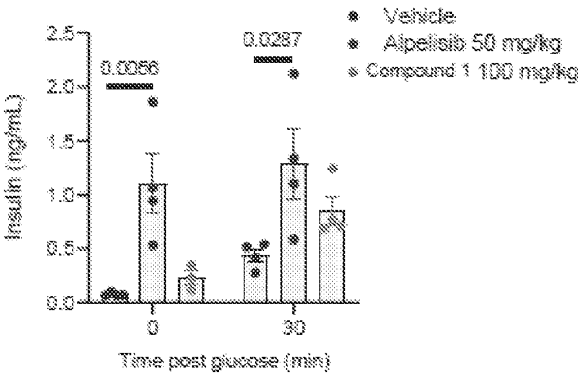


Fig. 8I

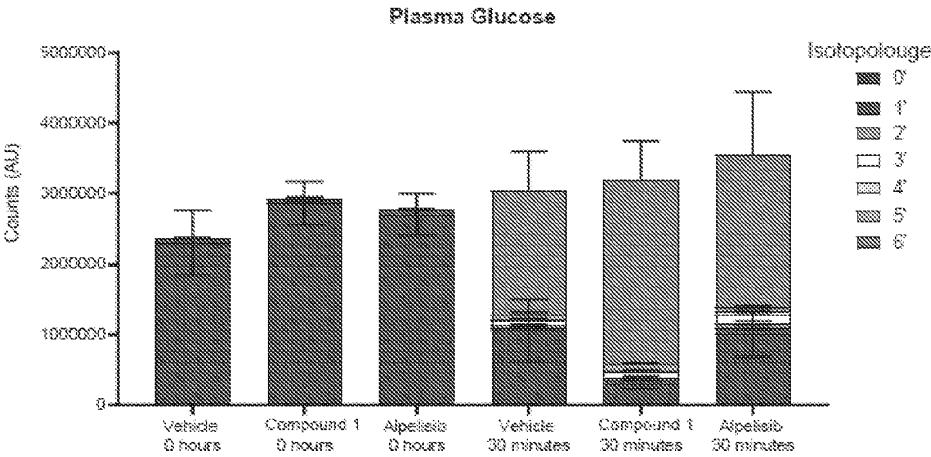


Fig. 8J

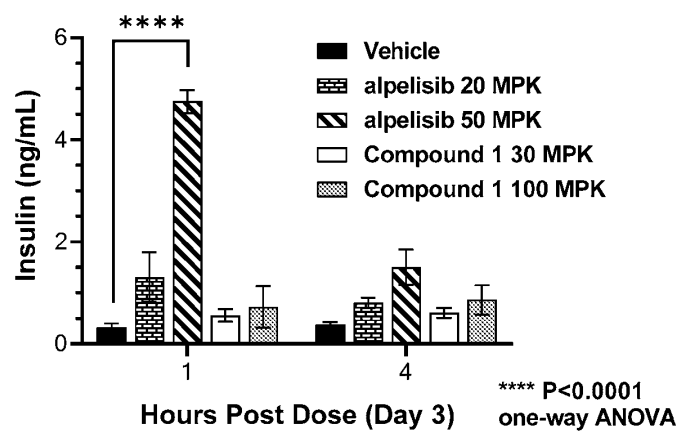


Fig. 9

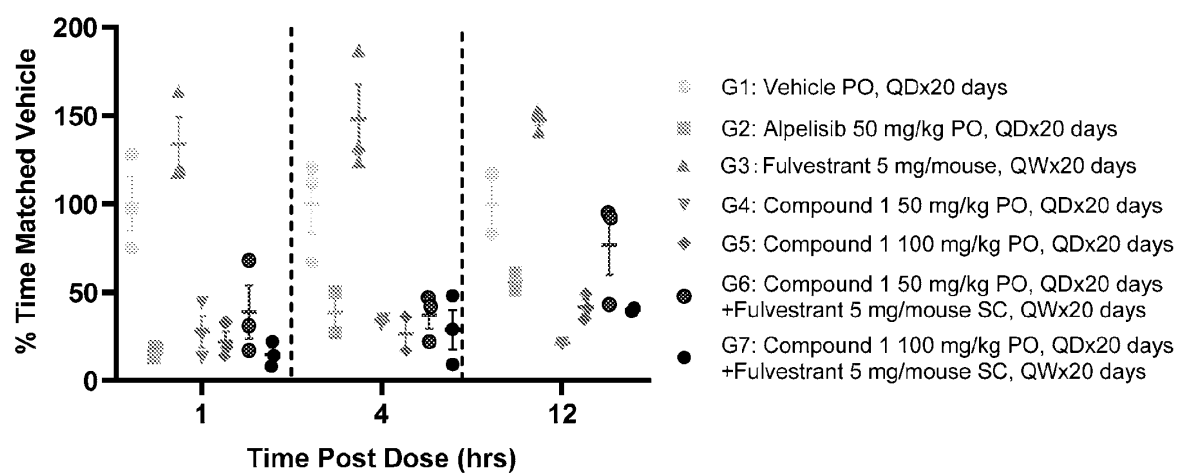


Fig. 10

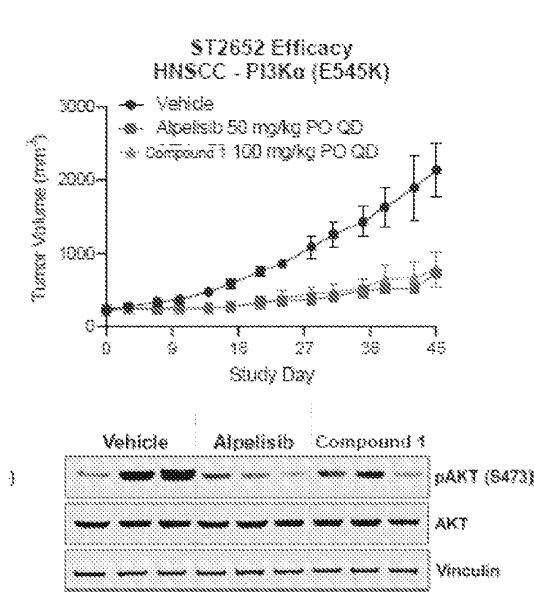


Fig. 11A

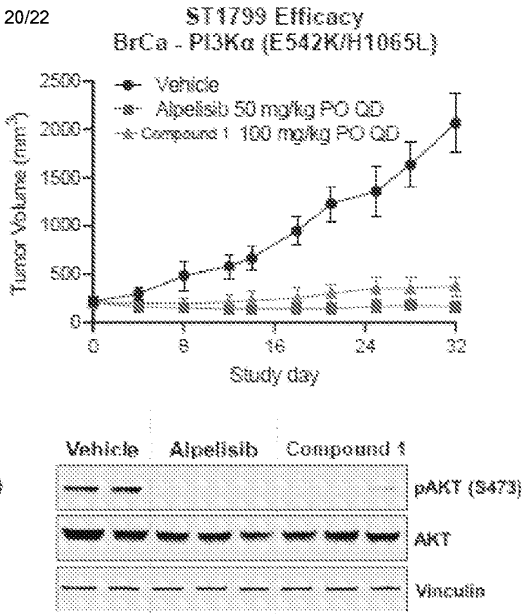


Fig. 11B

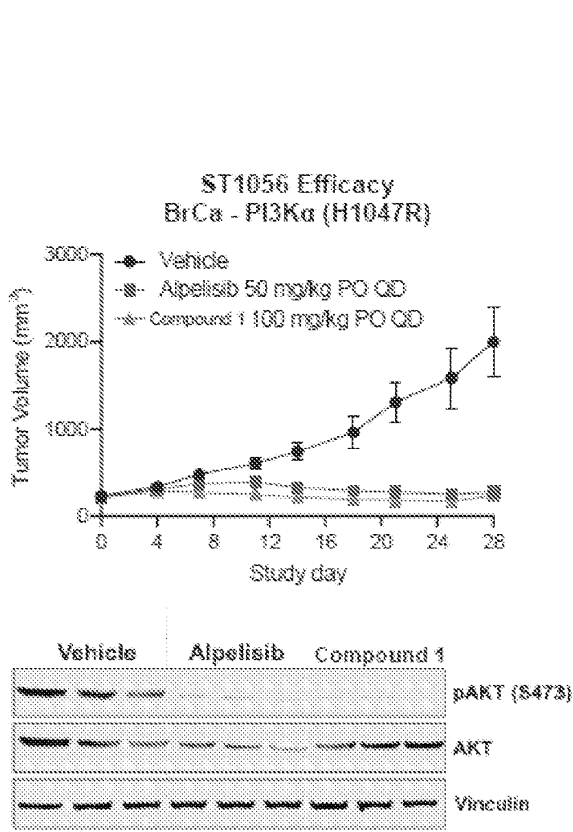


Fig. 11C

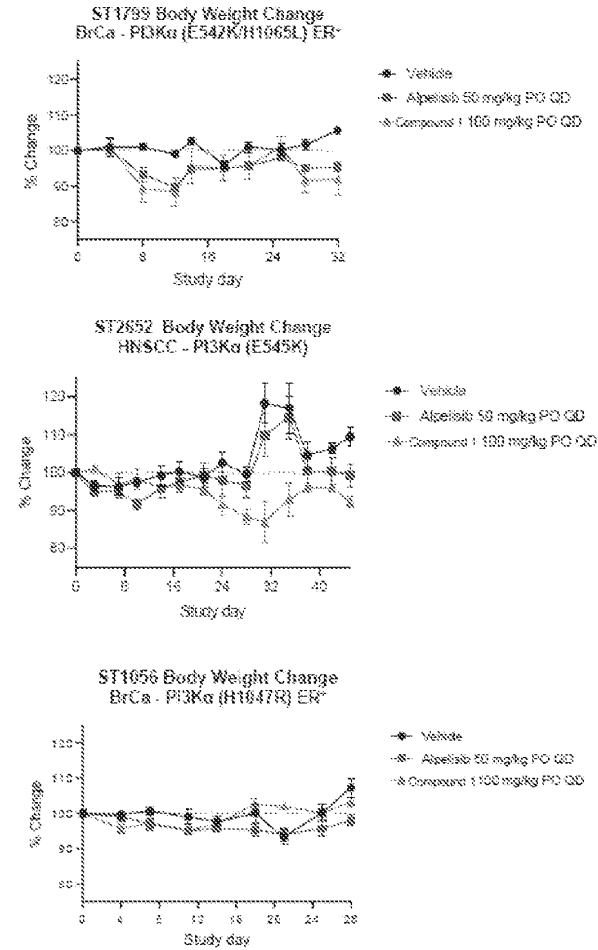


Fig. 11D

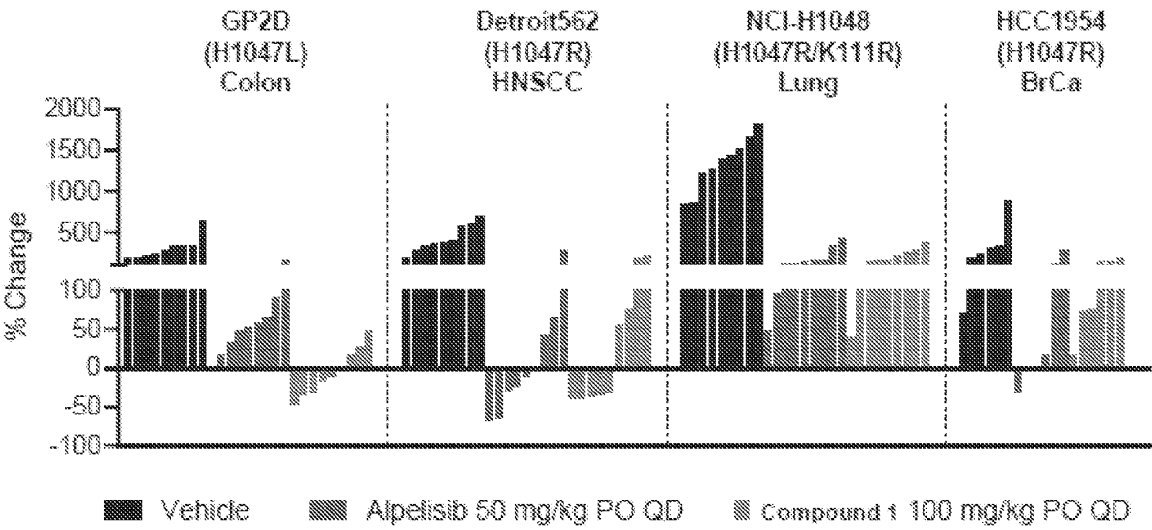


Fig. 11E

Fig. 11F

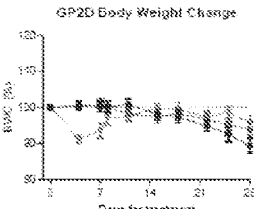
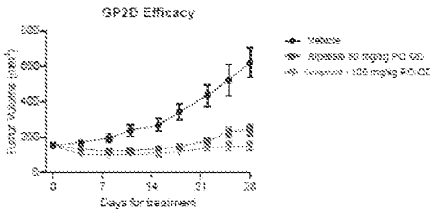


Fig. 11G

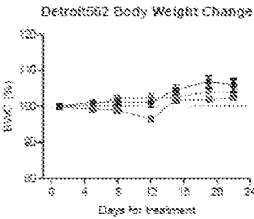
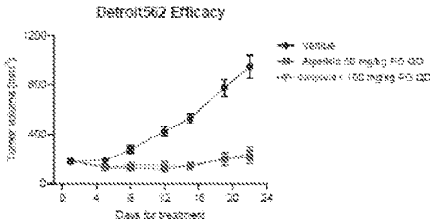


Fig. 11H

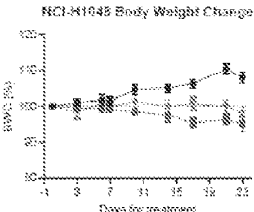
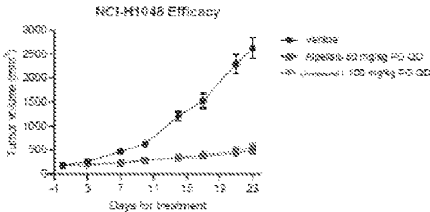
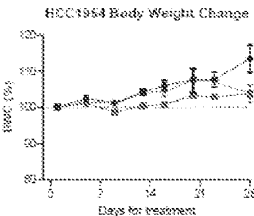
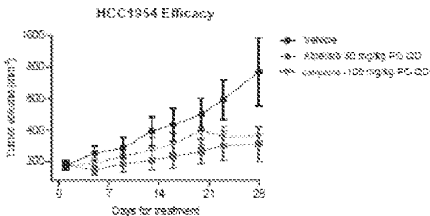


Fig. 11I



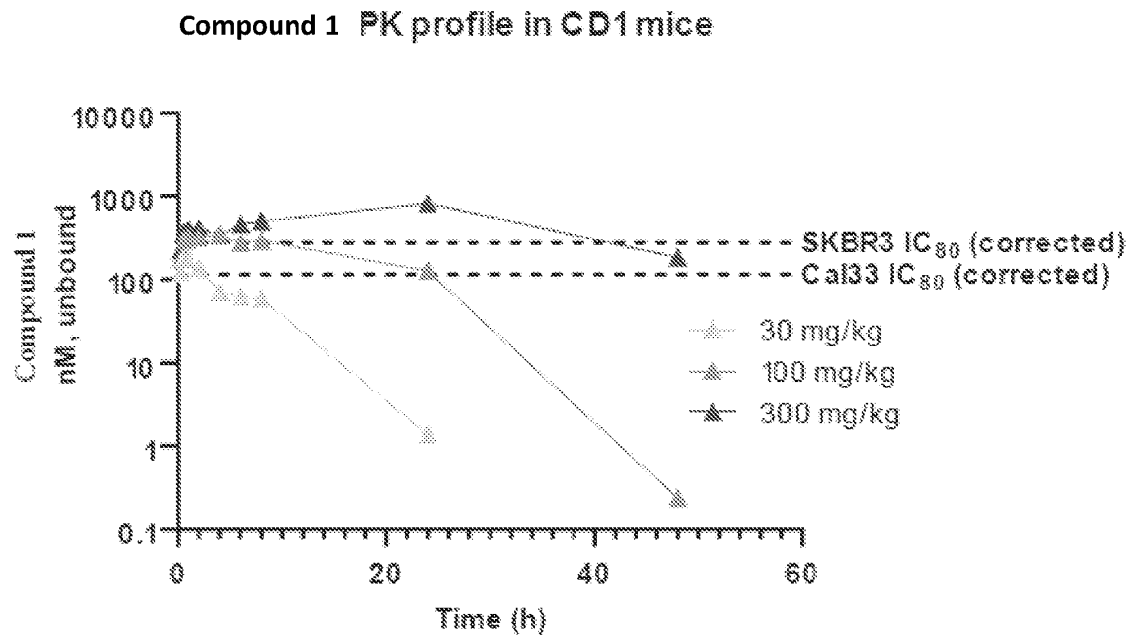


Fig. 12