

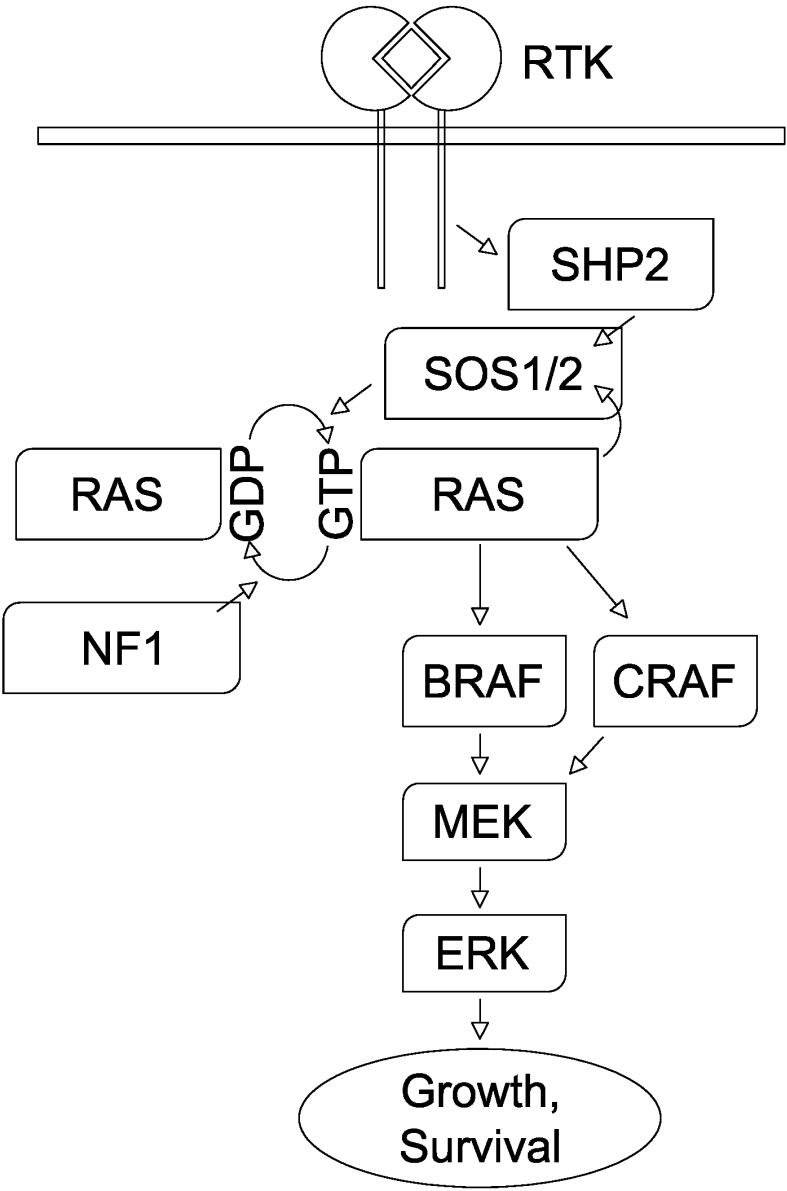


FIG. 1

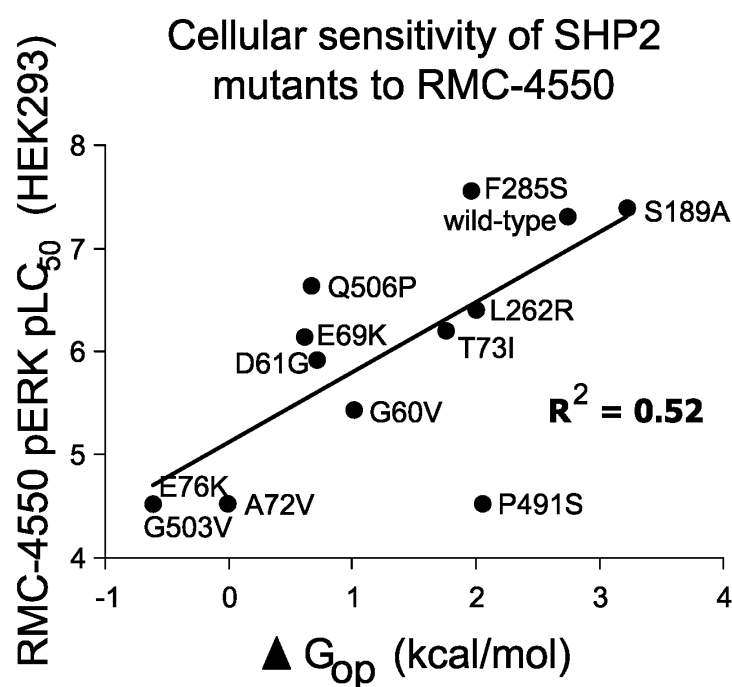


FIG. 2A

Variant	pERK IC ₅₀ (nM)
WT	49
F285S	27.4
S189A	40.7
S502P	179
Q506P	228
L262R	385
T73I	626
E69K	713
D61G	1190
G60V	3700
E76K	>30000
P491S	>30000
A72V	>30000
G503V	>30000
T253M/Q257L	>30000

FIG. 2B

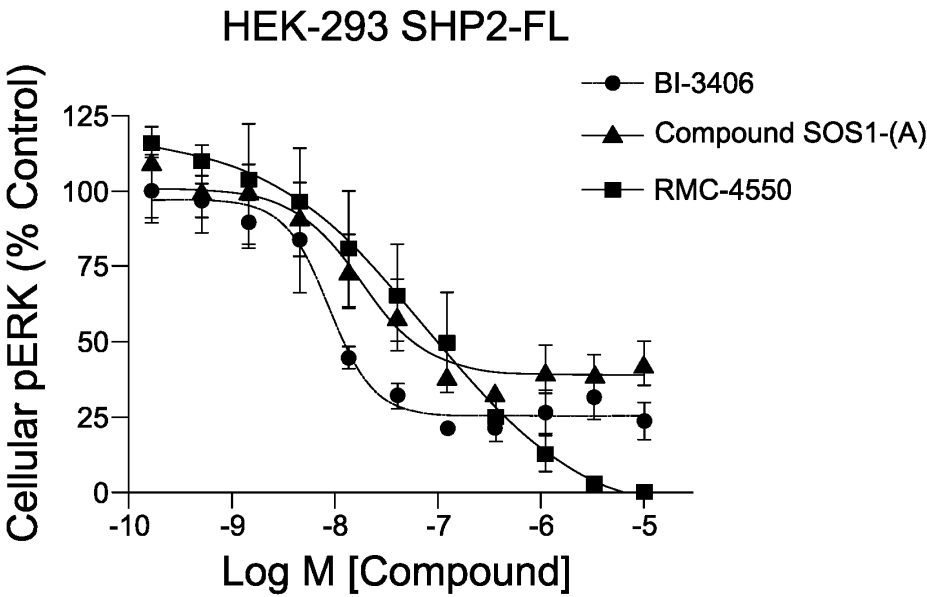


FIG. 3A

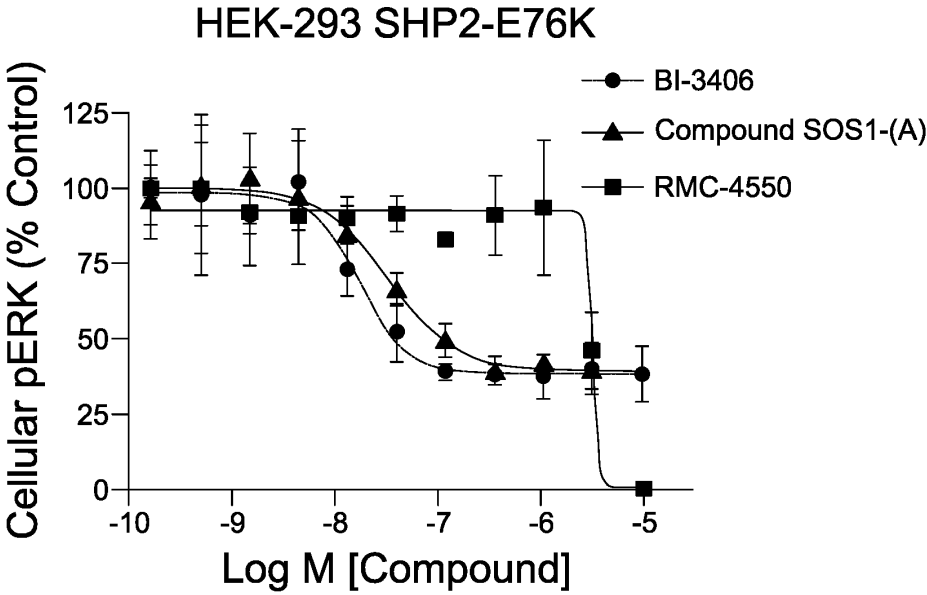


FIG. 3B

5/31

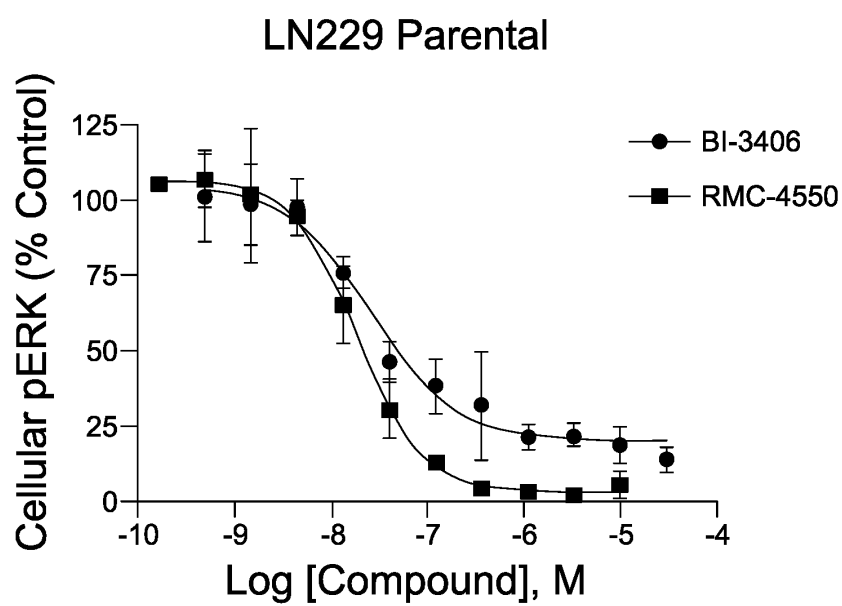


FIG. 4A

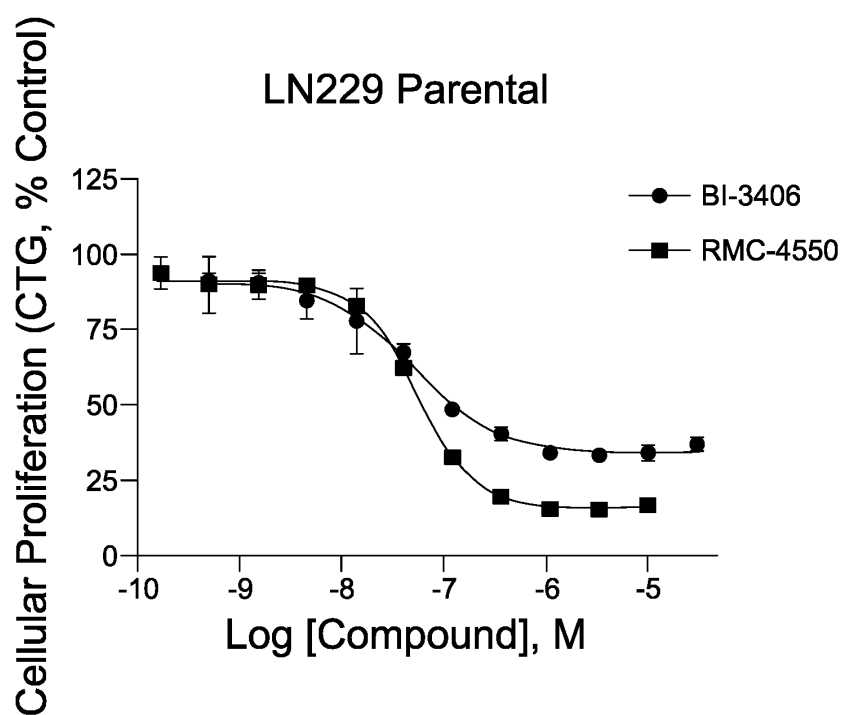


FIG. 4B

6/31

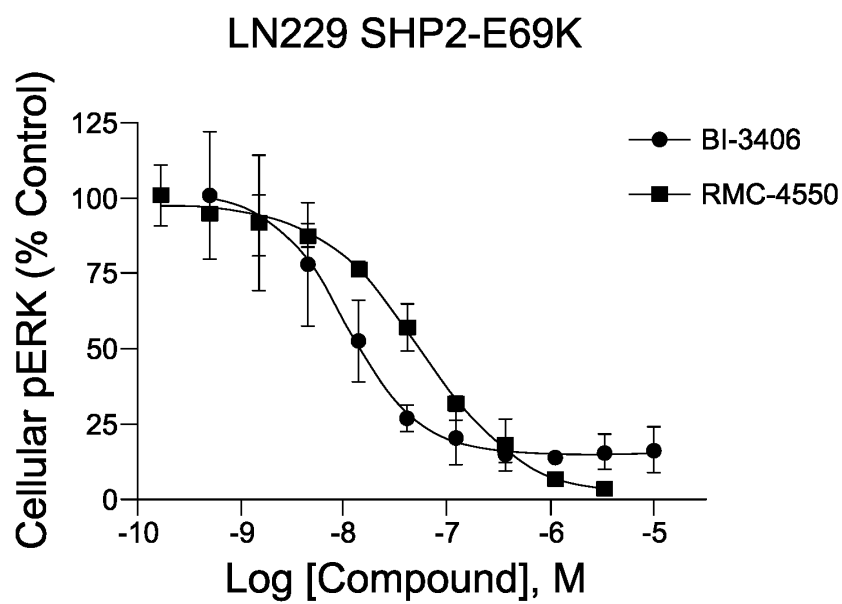


FIG. 4C

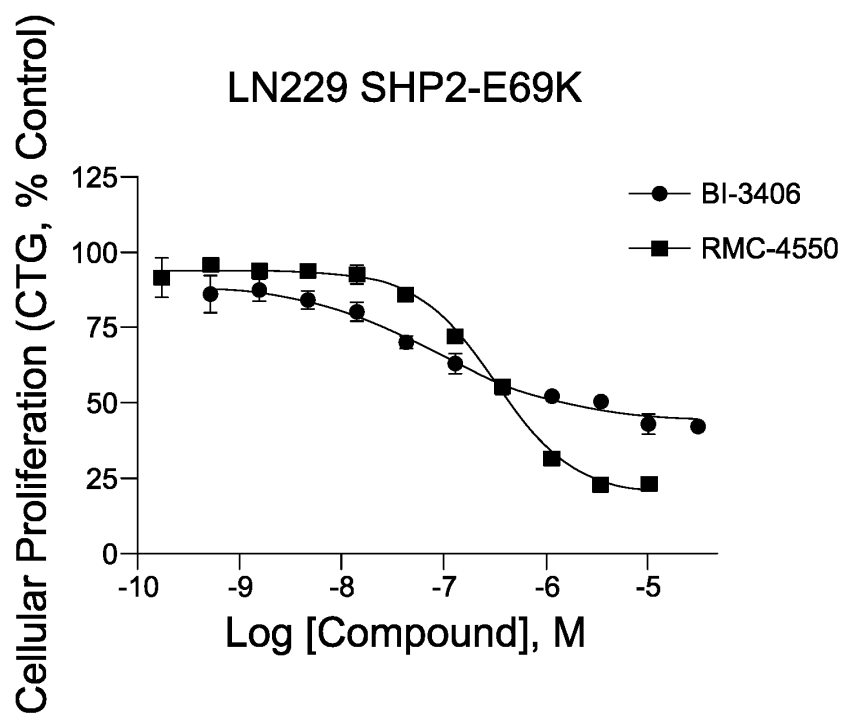


FIG. 4D

7/31

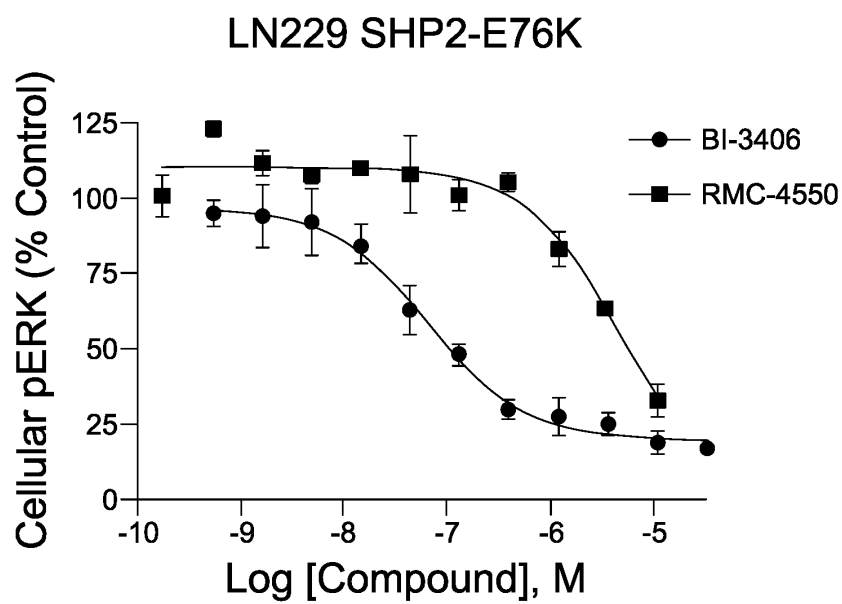


FIG. 4E

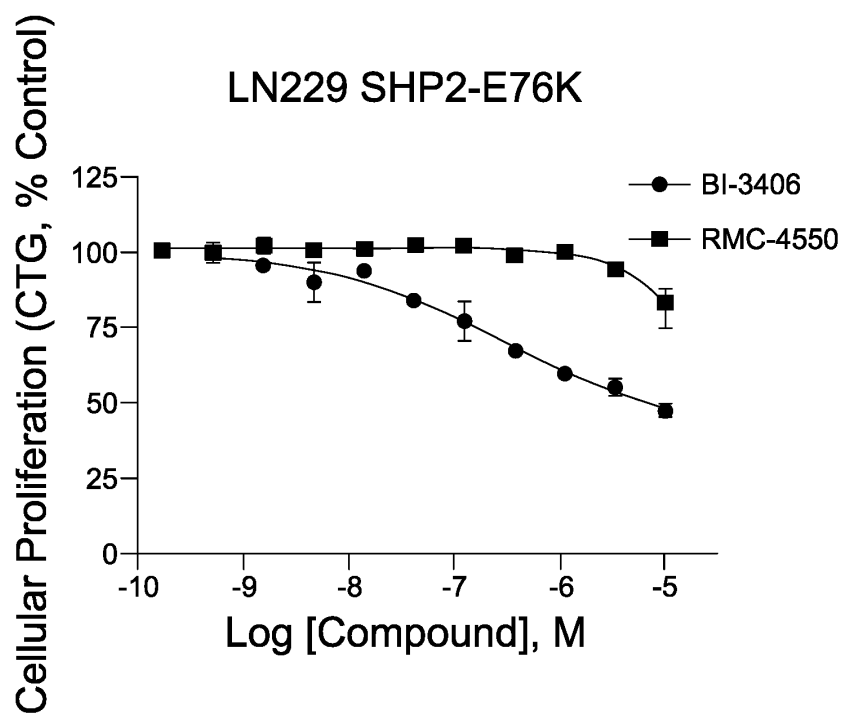


FIG. 4F

8/31

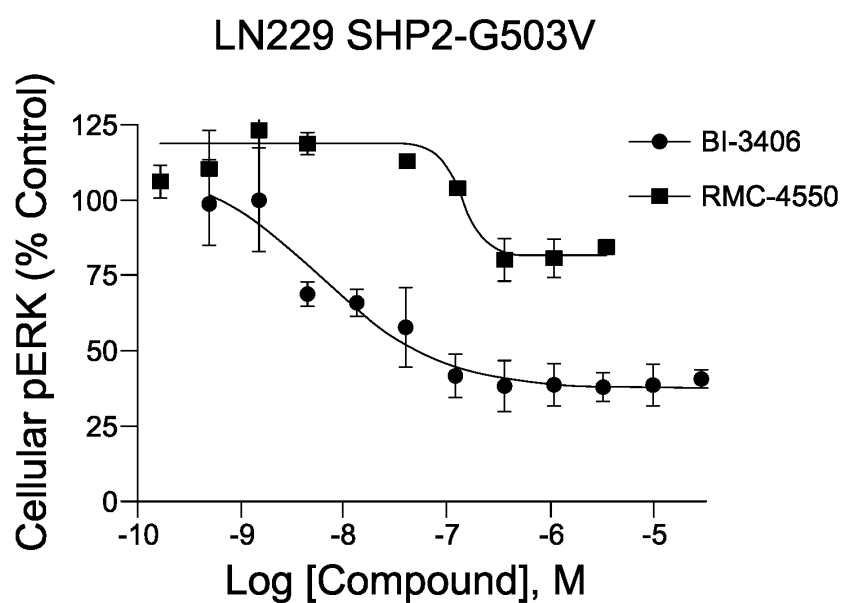


FIG. 4G

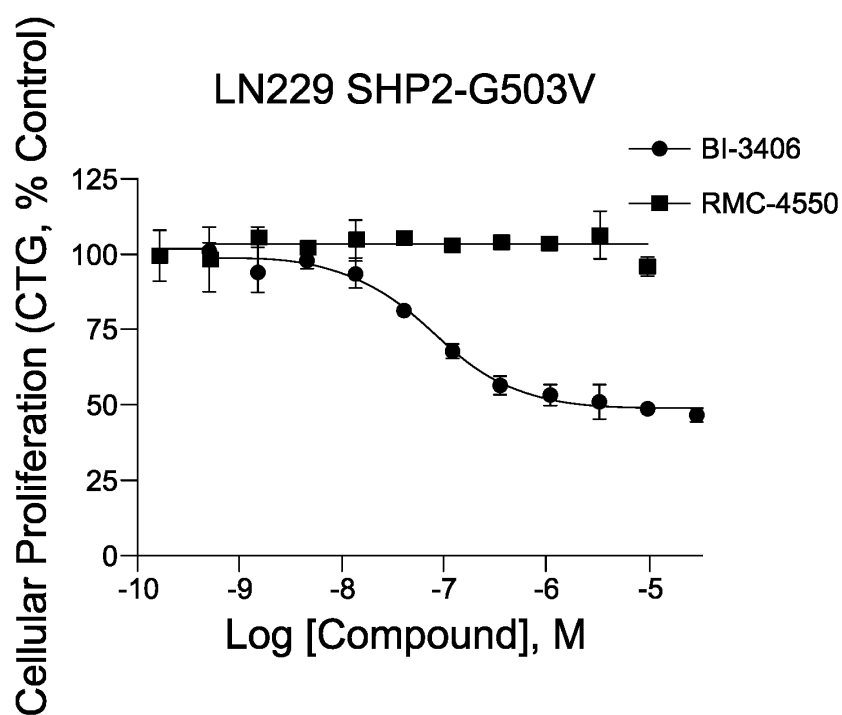
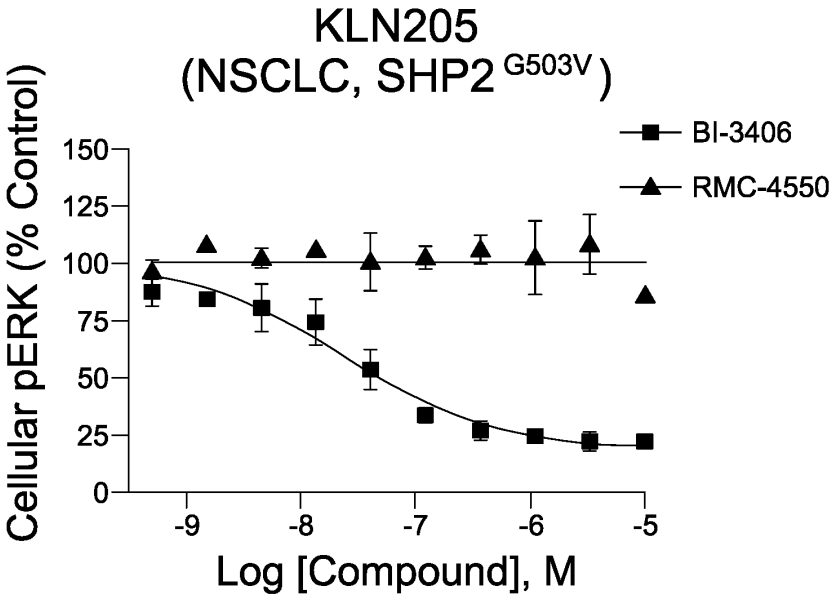


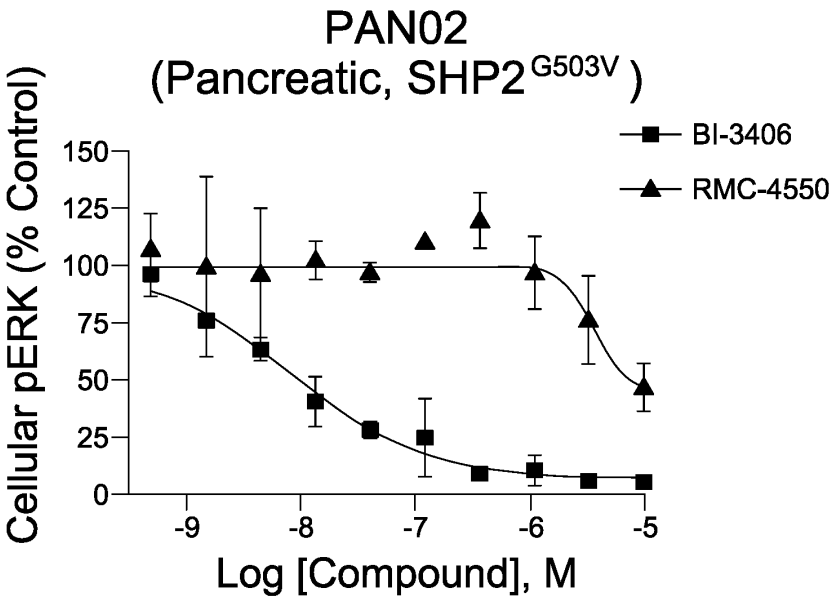
FIG. 4H



EC ₅₀ (nM)	KLN205	PAN02
BI-3406	25.5	8.08
RMC-4550	>10,000	>10,000

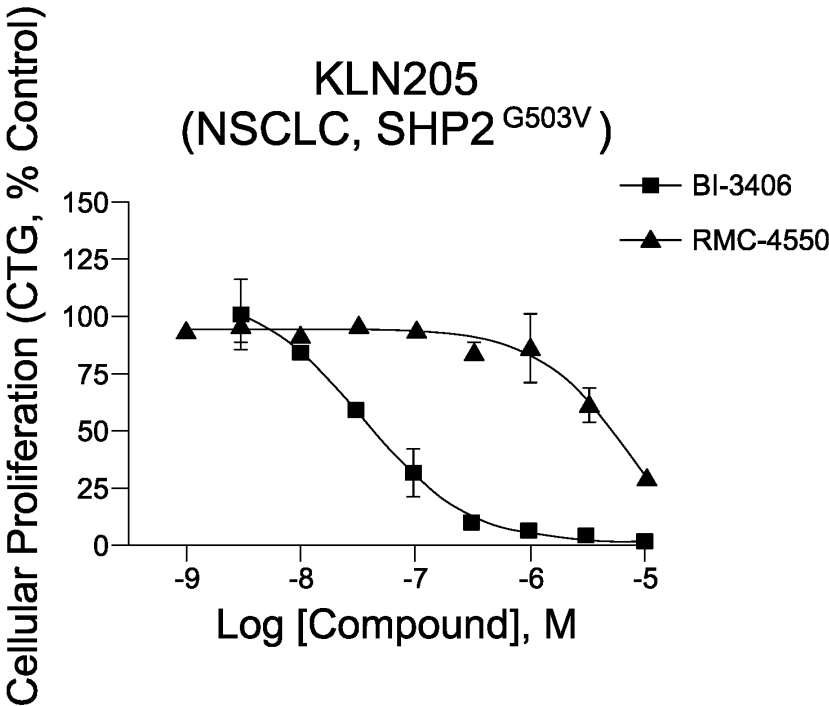
FIG. 5A

10/31



EC ₅₀ (nM)	KLN205	PAN02
BI-3406	25.5	8.08
RMC-4550	>10,000	>10,000

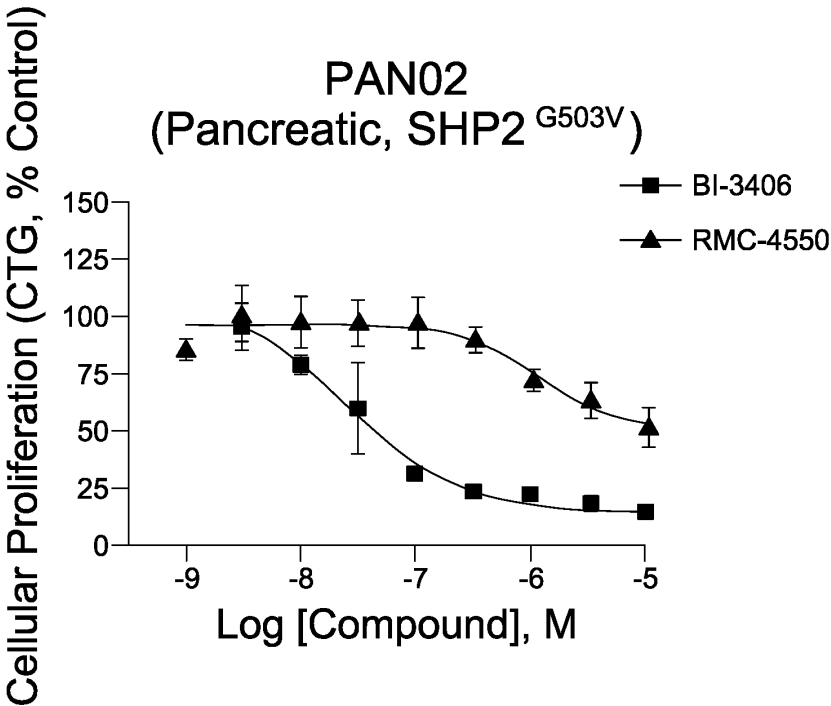
FIG. 5B



EC ₅₀ (nM)	KLN205	PAN02
BI-3406	46.0	41.3
RMC-4550	4867	>10,000

FIG. 5C

12/31



EC ₅₀ (nM)	KLN205	PAN02
BI-3406	46.0	41.3
RMC-4550	4867	>10,000

FIG. 5D

13/31

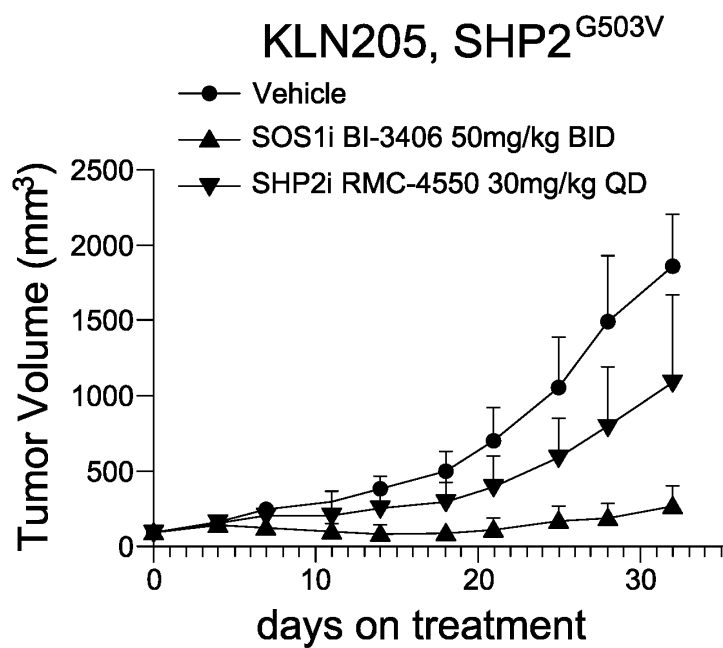


FIG. 6

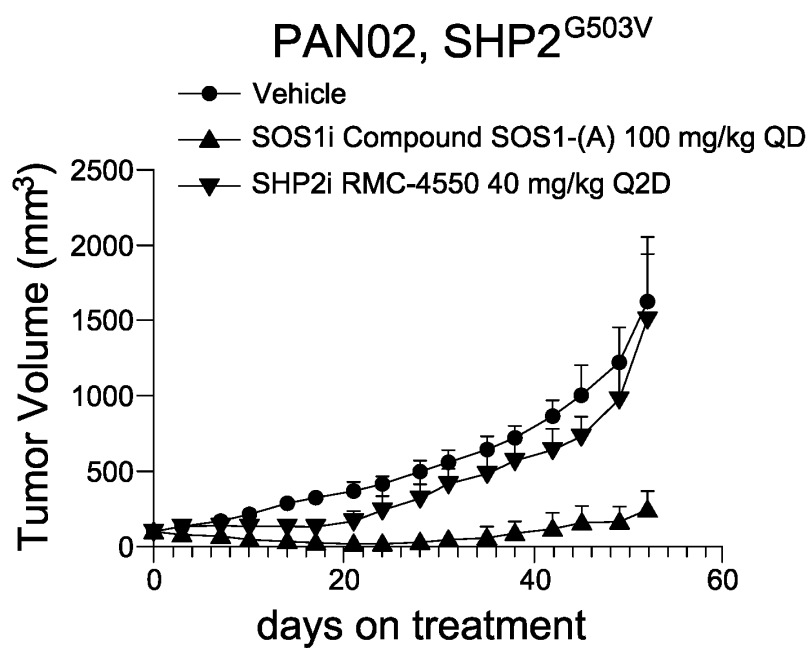


FIG. 7

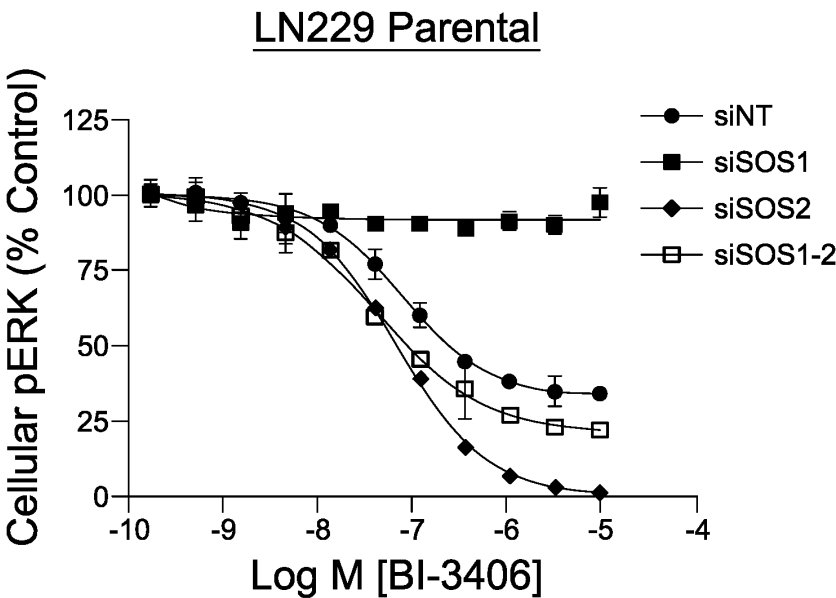


FIG. 8A

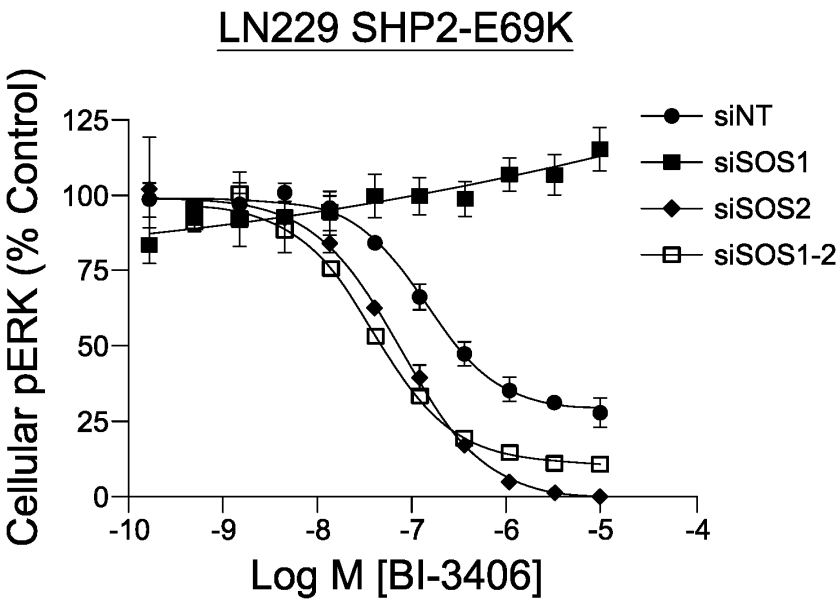


FIG. 8B

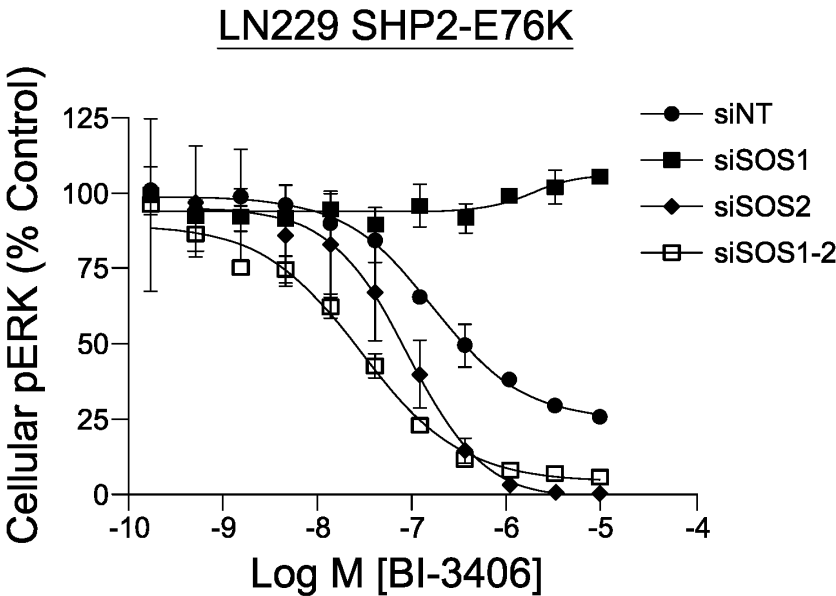


FIG. 8C

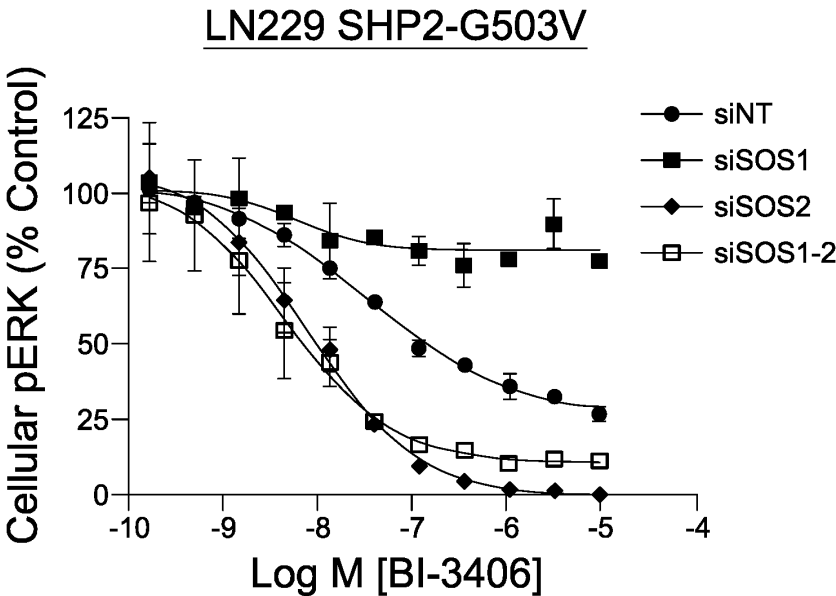


FIG. 8D

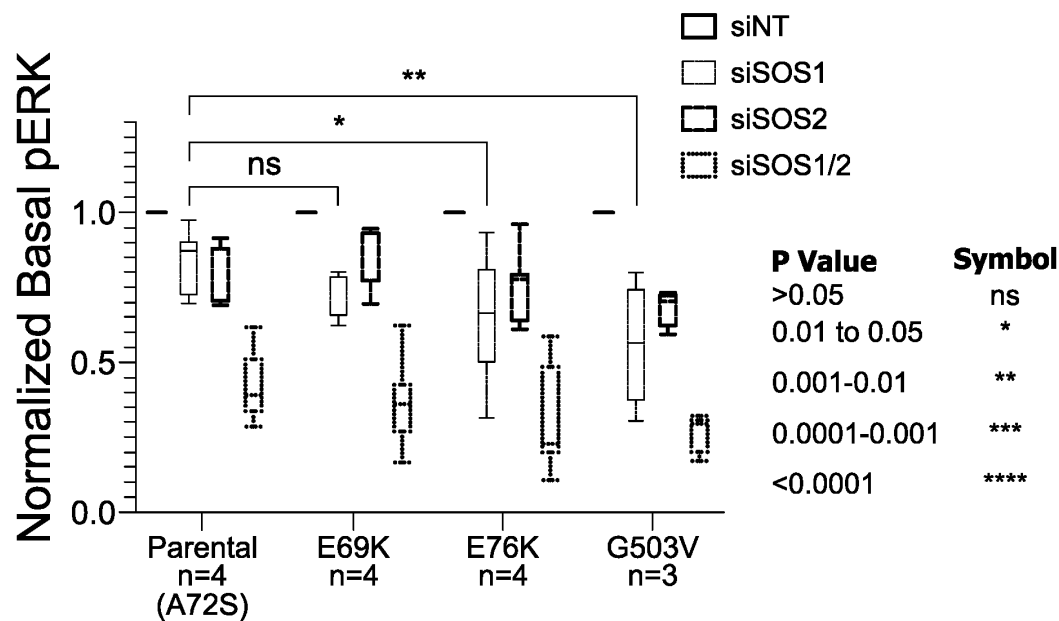


FIG. 9

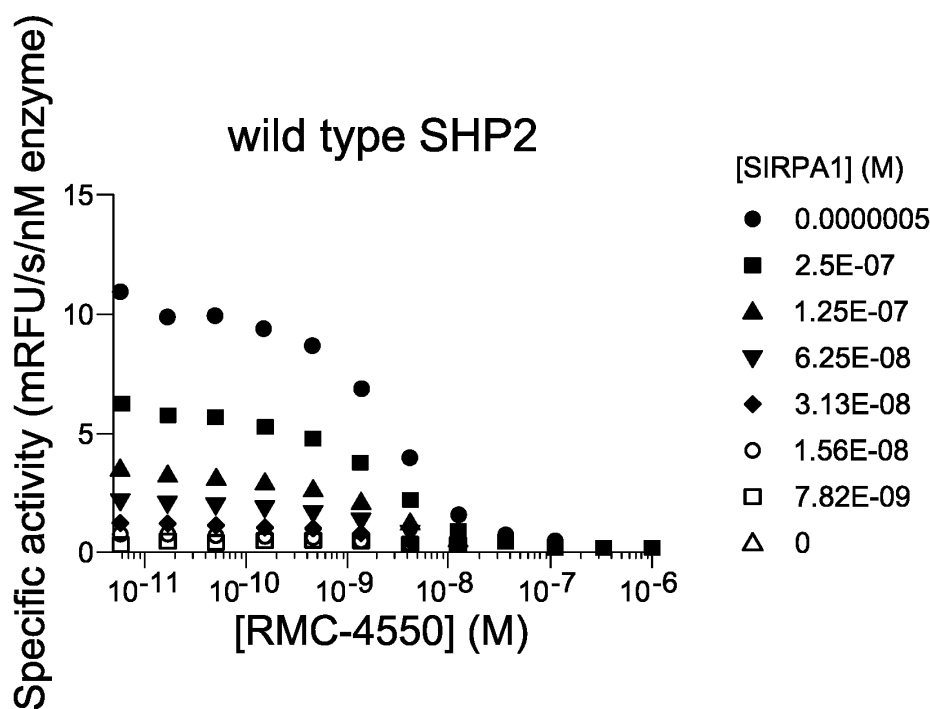


FIG. 10

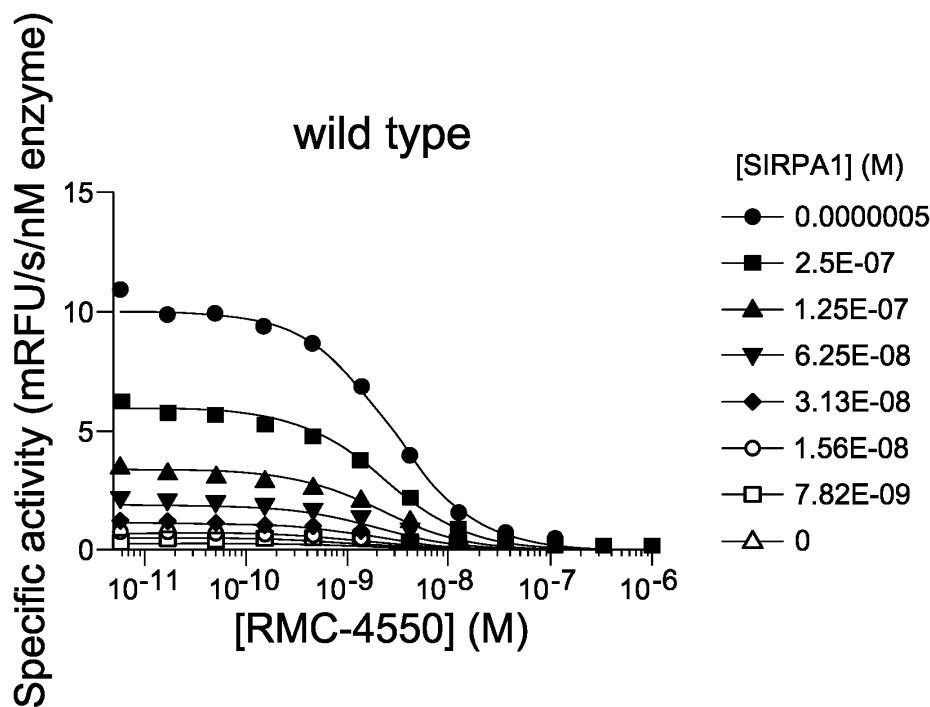


FIG. 11

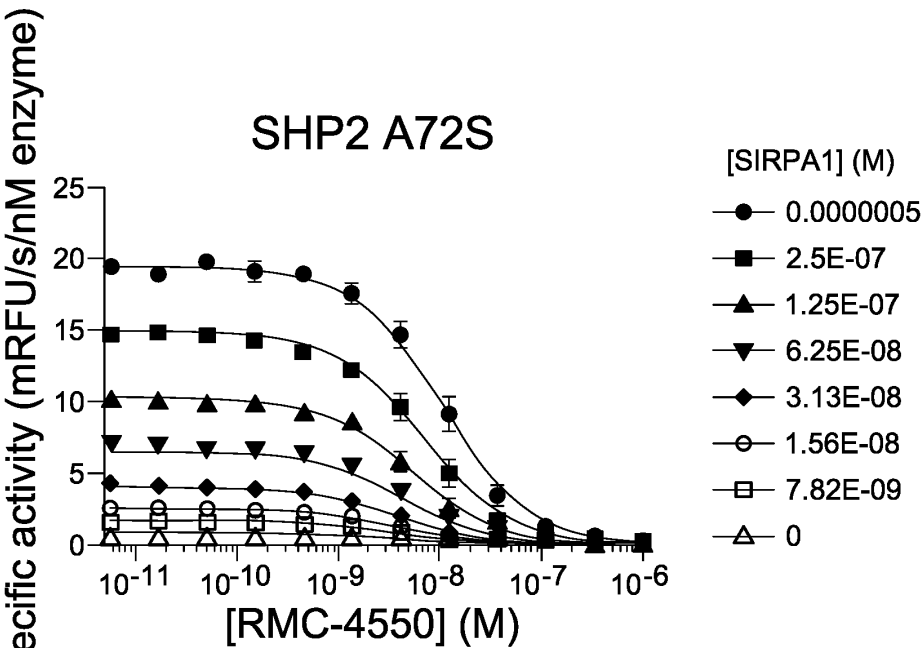


FIG. 12

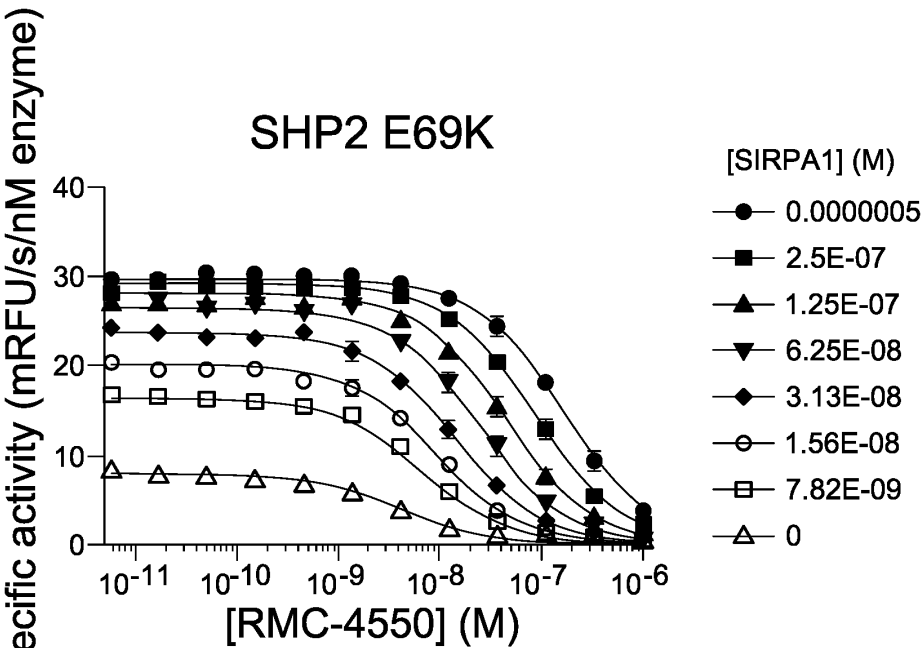


FIG. 13

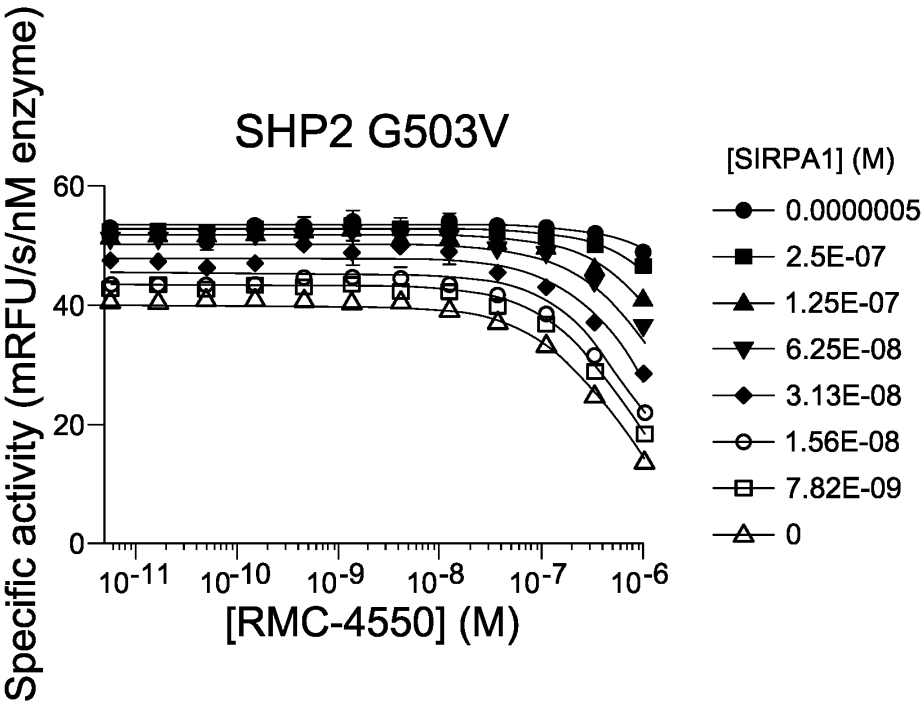


FIG. 14

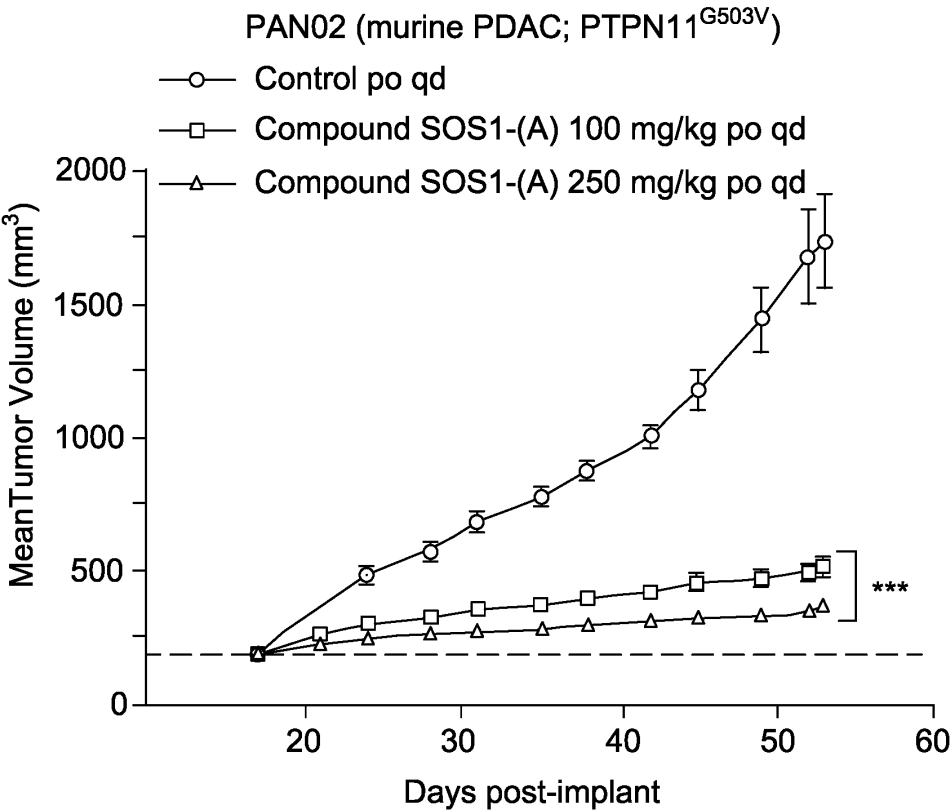


FIG. 15

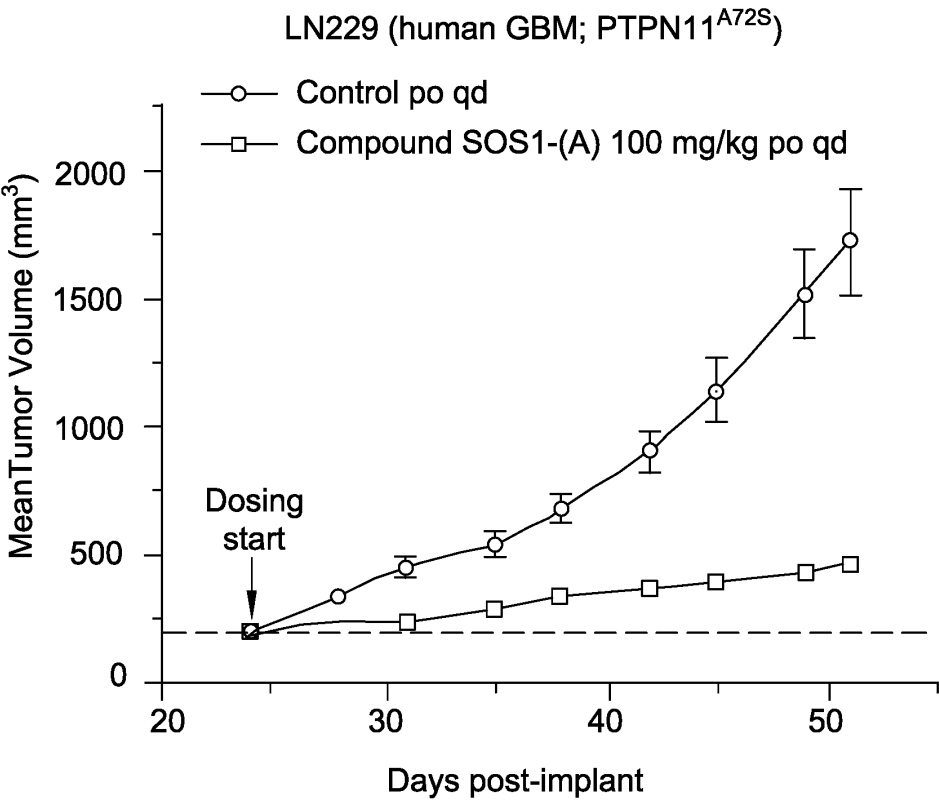


FIG. 16

22/31

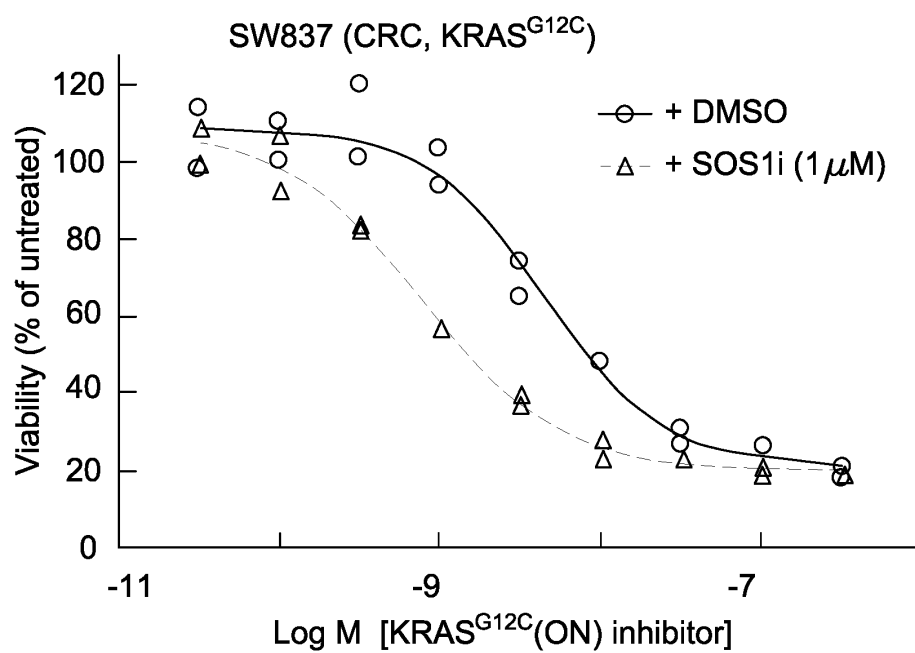


FIG. 17A

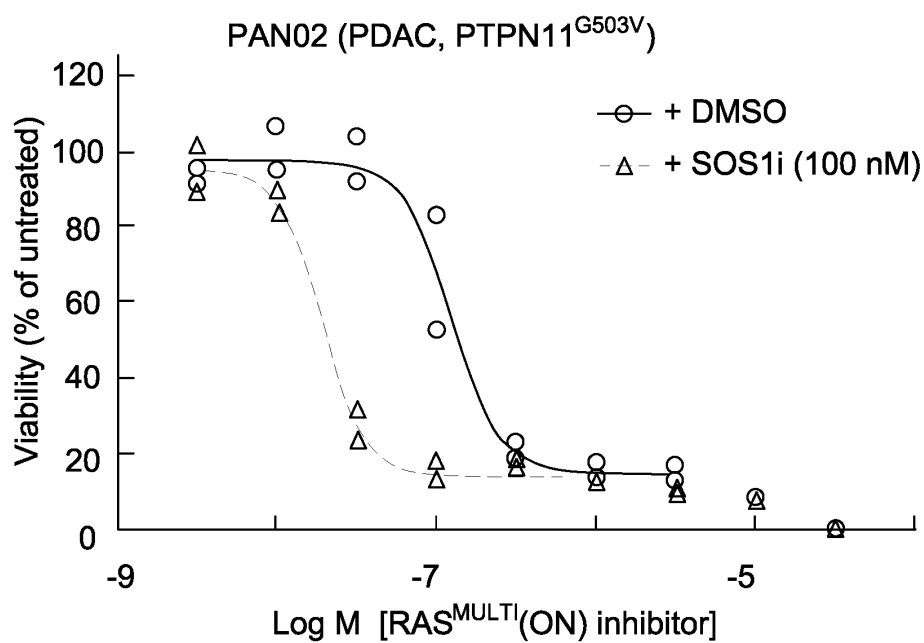


FIG. 17B

23/31

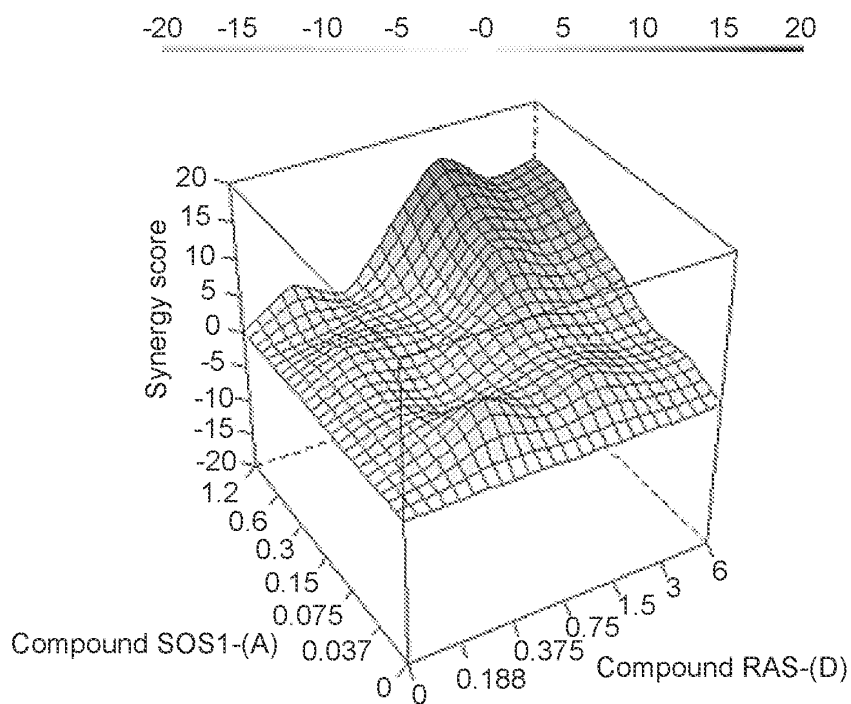


FIG. 18

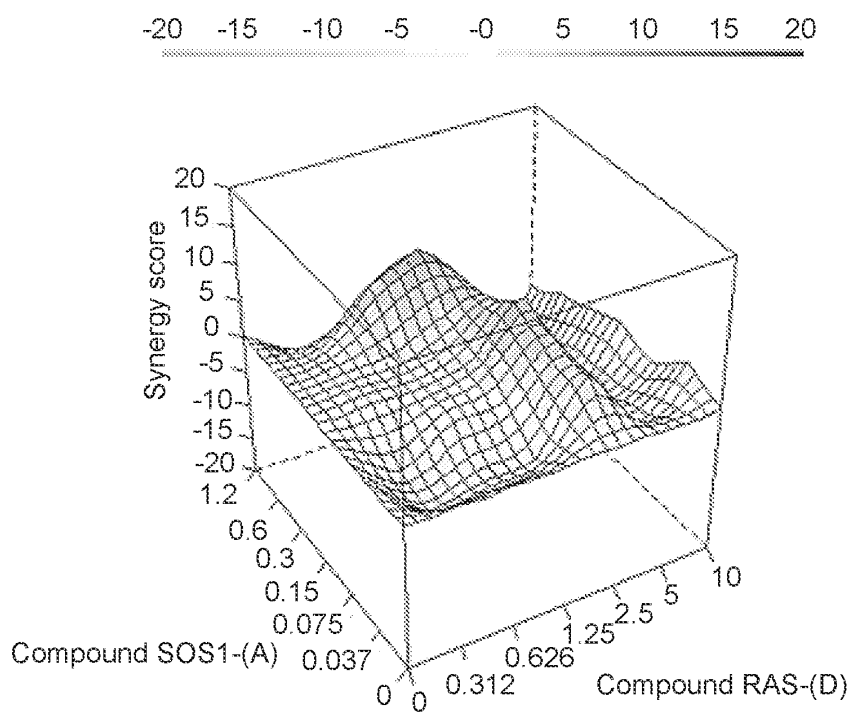


FIG. 19

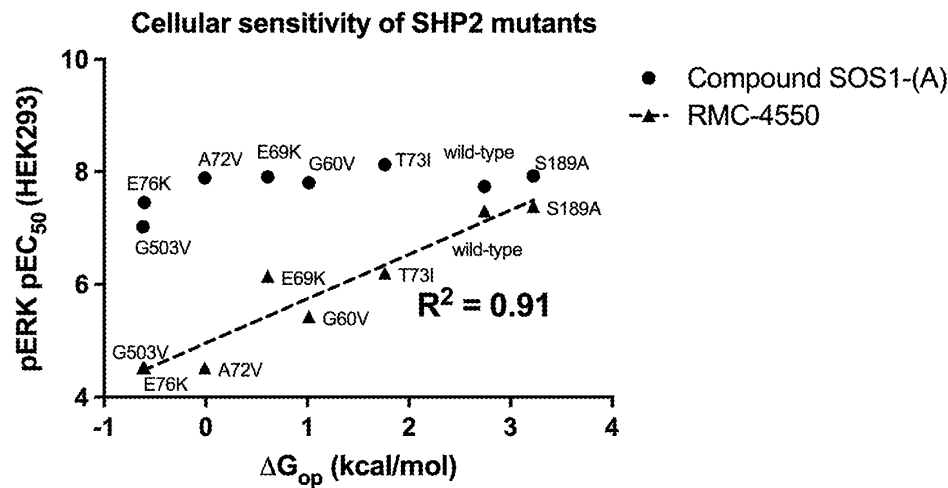


FIG. 20A

Variant	RMC-4550 pERK EC ₅₀ (nM)	Compound SOS1-(A) pERK EC ₅₀ (nM)
WT	49	18
S189A	41	12
T73I	626	7.5
E69K	713	12
G60V	3700	16
E76K	>30000	35
A72V	>30000	13
G503V	>30000	95

FIG. 20B

25/31

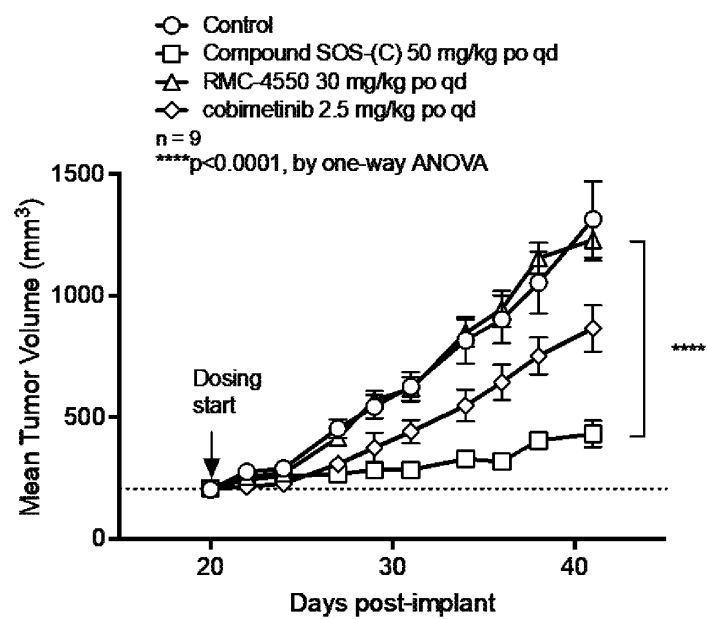


FIG. 21

26/31

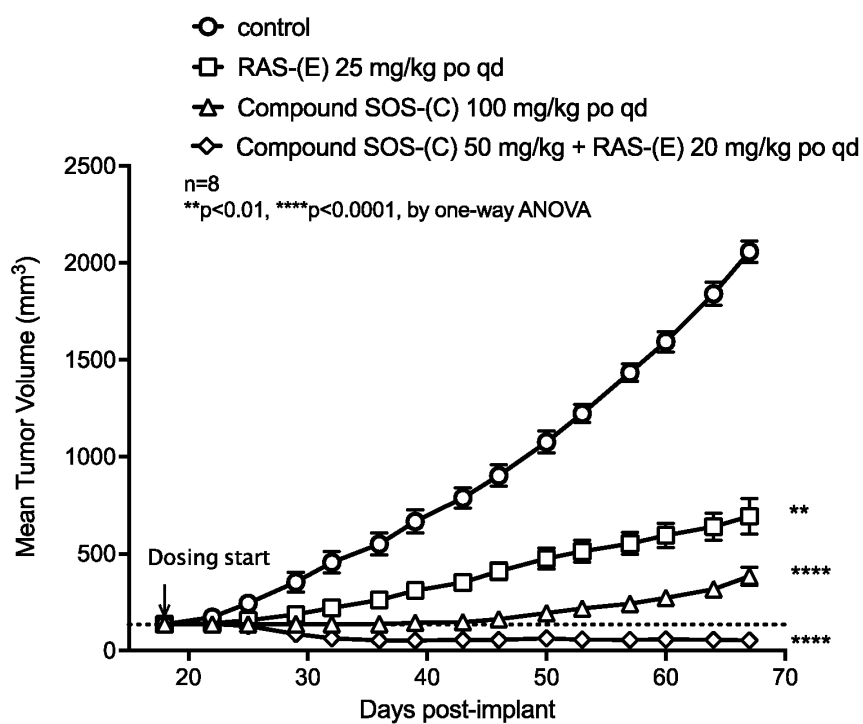


FIG. 22

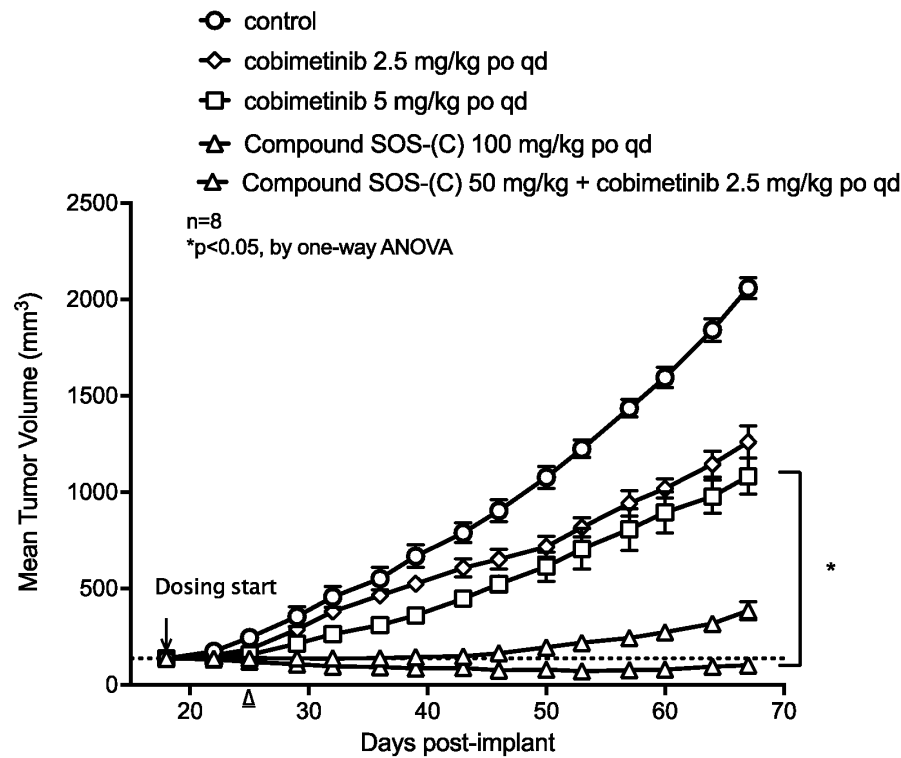


FIG. 23

28/31

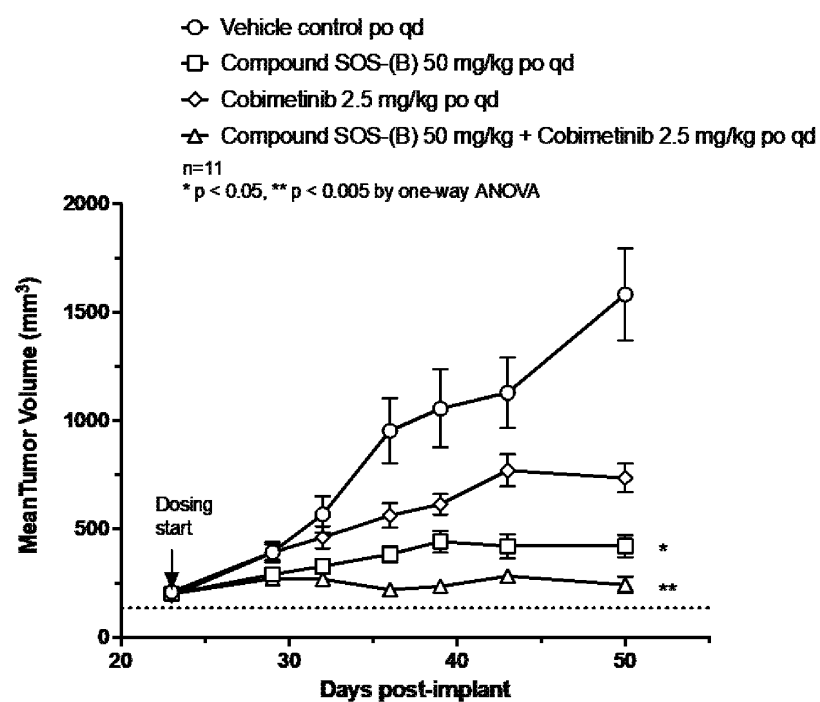


FIG. 24

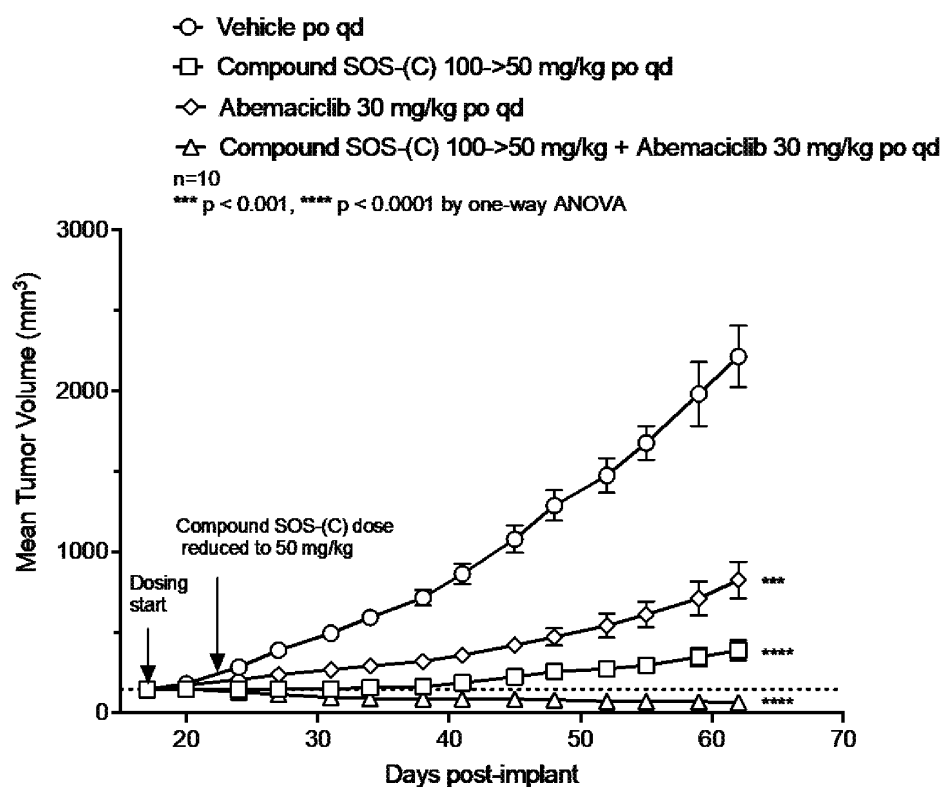


FIG. 25

FIG. 26A

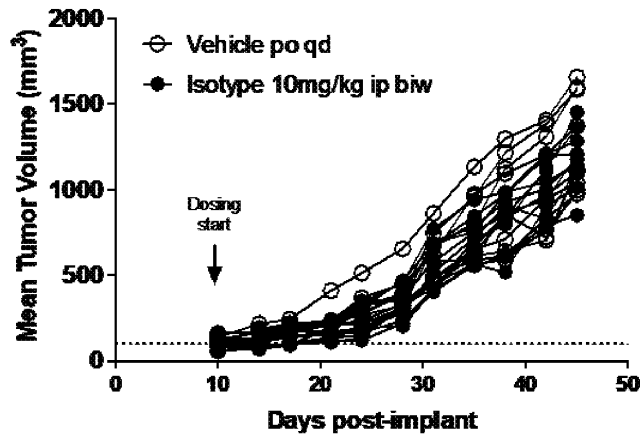


FIG. 26B

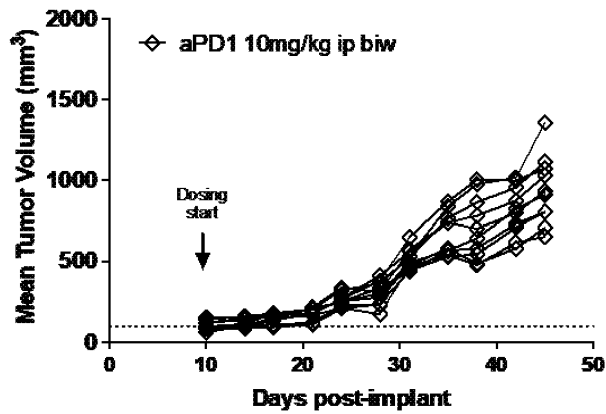


FIG. 26C

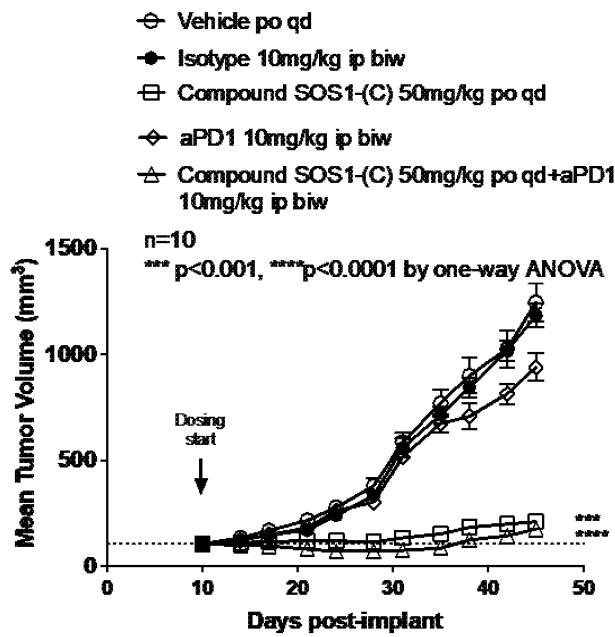


FIG. 26D

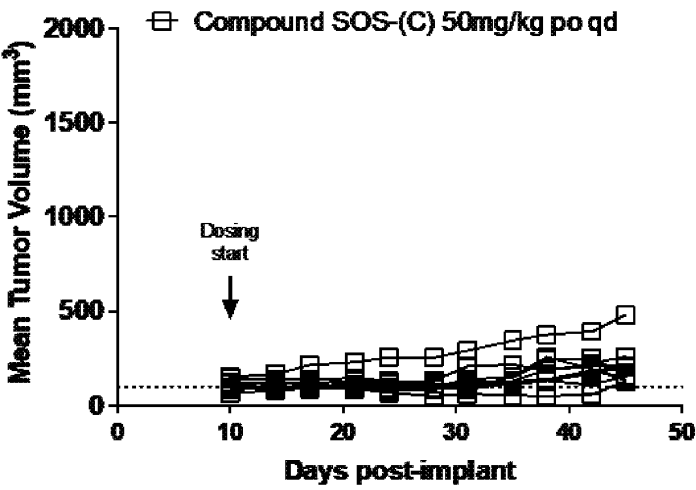


FIG. 26E

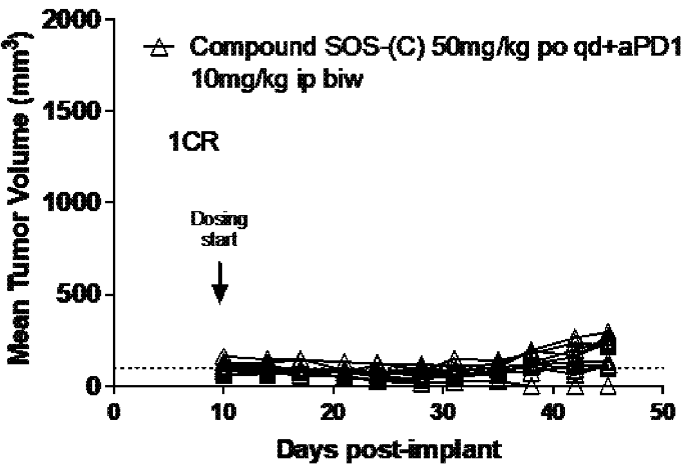


FIG. 26F

