FIG. 1

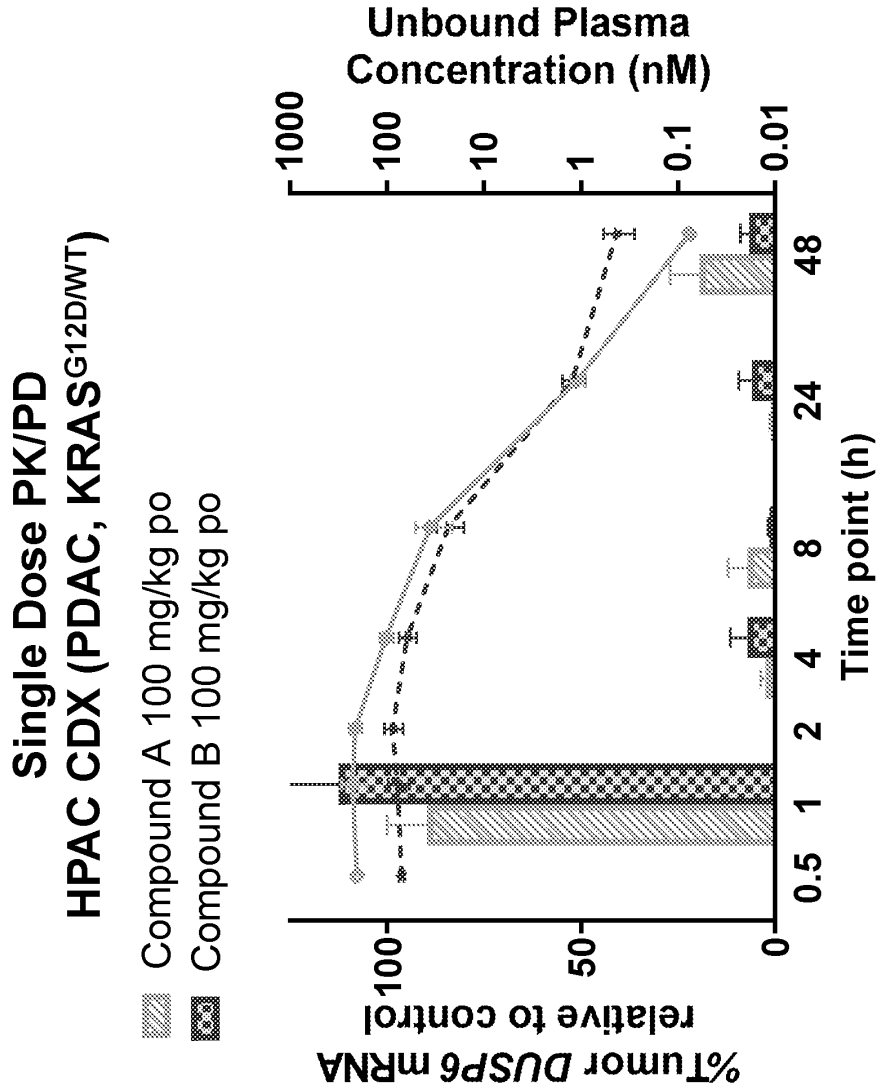

Single Dose PK/PD
HPAC CDX (PDAC, KRASG12D/WT)
Compound A 100 mg/kg po
Compound B 100 mg/kg po
%Tumor DUSP6 mRNA relative to control
100
50
0
Unbound Plasma Concentration (nM)
1000
100
10
1
0.1
0.01
0.5
1
2
4
8
24
48
Time point (h)

FIG. 2

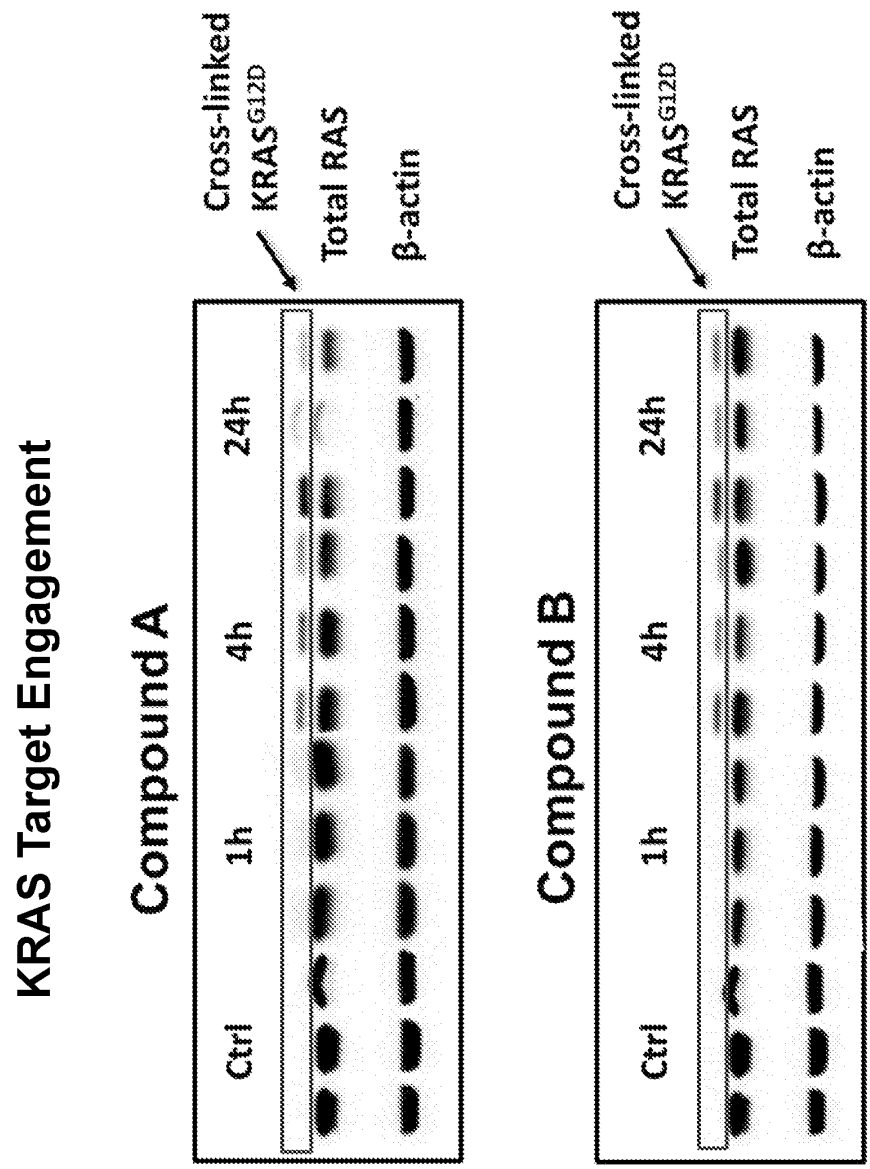

KRAS Target Engagement
Compound A
Ctrl
1h
4h
24h
Cross-linked KRAS^{G12D}
Total RAS
β-actin
Compound B
Ctrl
1h
4h
24h
Cross-linked KRAS^{G12D}
Total RAS
β-actin

FIG. 3A

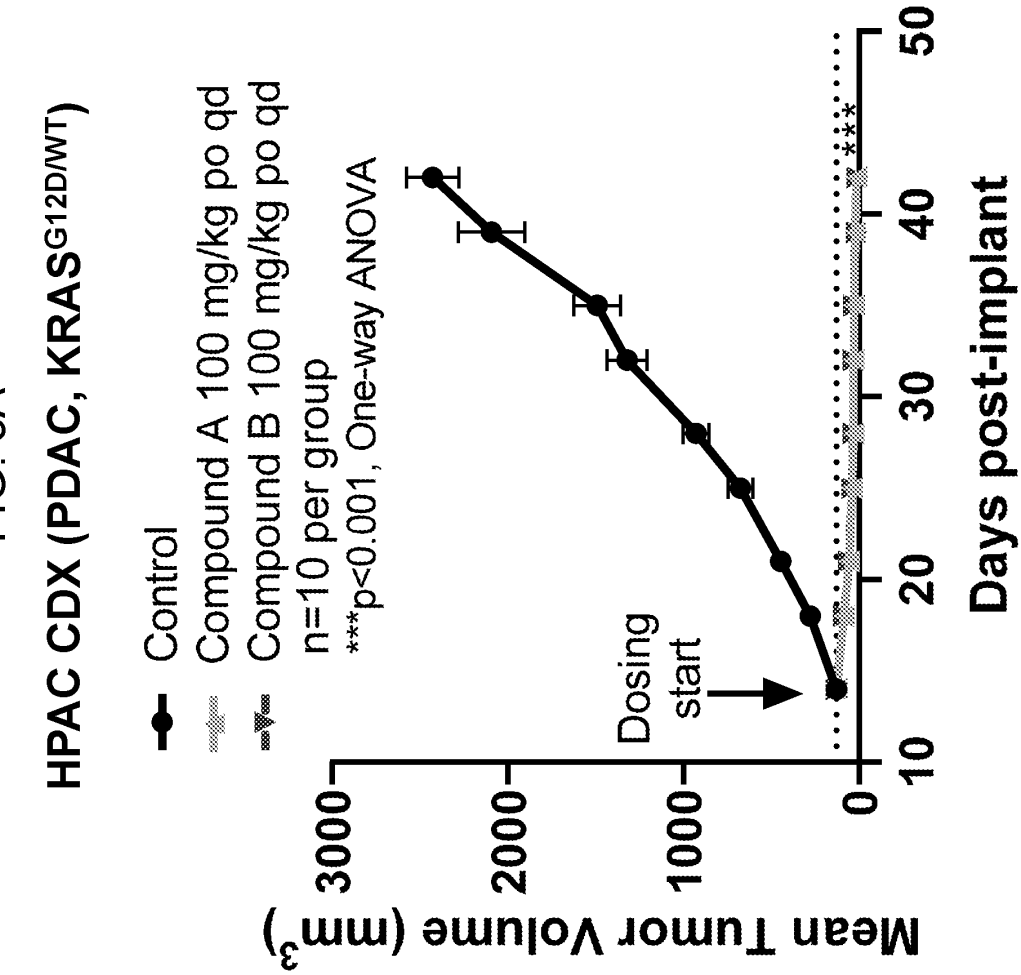

HPAC CDX (PDAC, KRASG12D/WT)
Control
Compound A 100 mg/kg po qd
Compound B 100 mg/kg po qd
n=10 per group
***p<0.001, One-way ANOVA
Mean Tumor Volume (mm3)
3000
2000
1000
0
Dosing start
10
20
30
40
50
Days post-implant
***
***

FIG. 3B

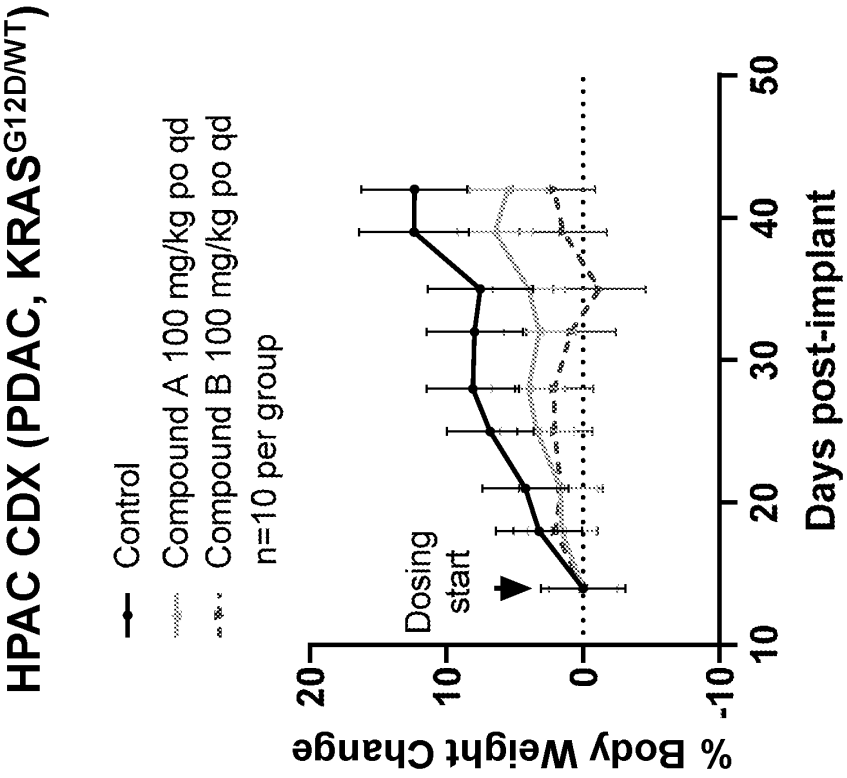
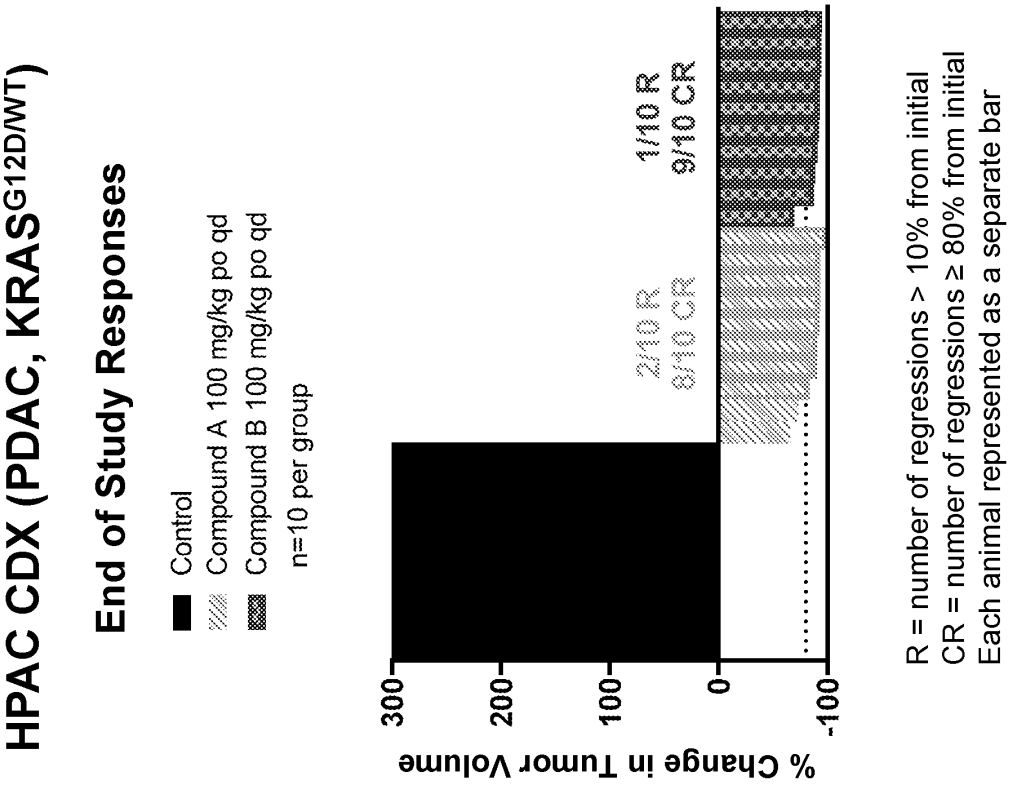

HPAC CDX (PDAC, KRASG12D/WT)
Control
Compound A 100 mg/kg po qd
Compound B 100 mg/kg po qd
n=10 per group
Dosing start
% Body Weight Change
20
10
0
-10
10
20
30
40
50
Days post-implant

FIG. 3C


HPAC CDX (PDAC, KRASG12D/WT)
End of Study Responses
Control
Compound A 100 mg/kg po qd
Compound B 100 mg/kg po qd
n=10 per group
% Change in Tumor Volume
300
200
100
0
-100
2/10 R
8/10 CR
1/10 R
9/10 CR
R = number of regressions > 10% from initial
CR = number of regressions ≥ 80% from initial
Each animal represented as a separate bar