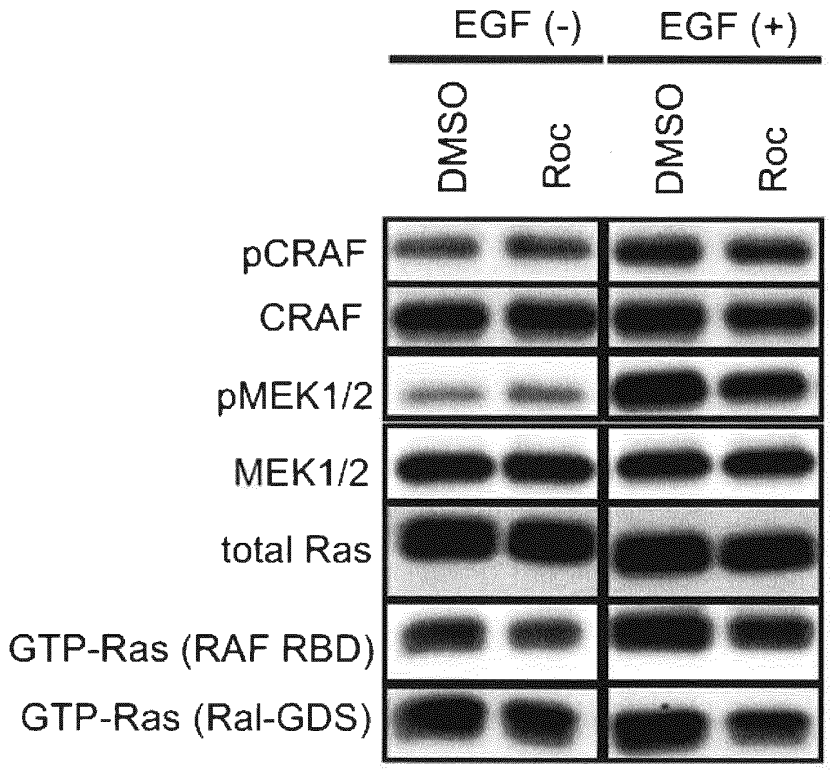

EGF (-)
EGF (+)
DMSO
Roc
DMSO
Roc
pCRAF
CRAF
pMEK1/2
MEK1/2
total Ras
GTP-Ras (RAF RBD)
GTP-Ras (Ral-GDS)

FIGURE 1

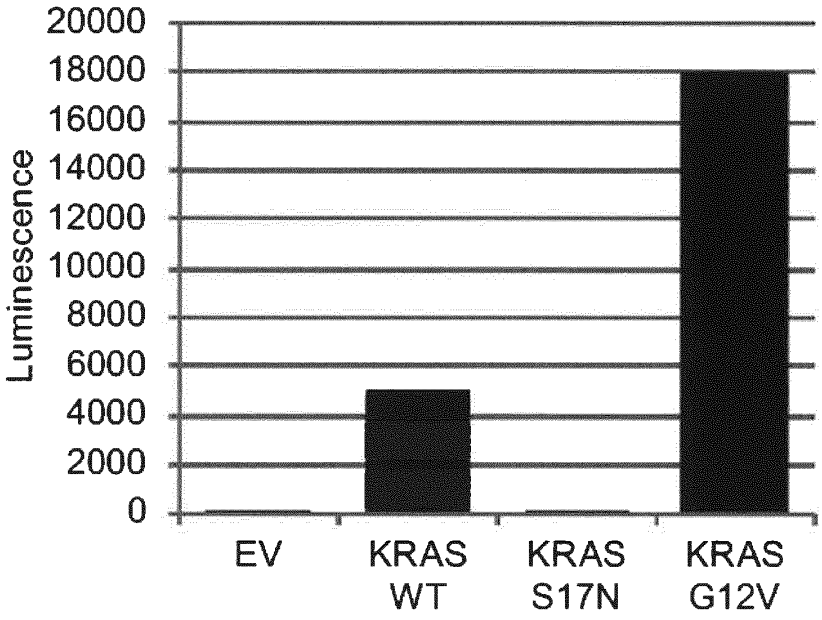

20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
Luminescence
EV
KRAS WT
KRAS S17N
KRAS G12V

FIGURE 2

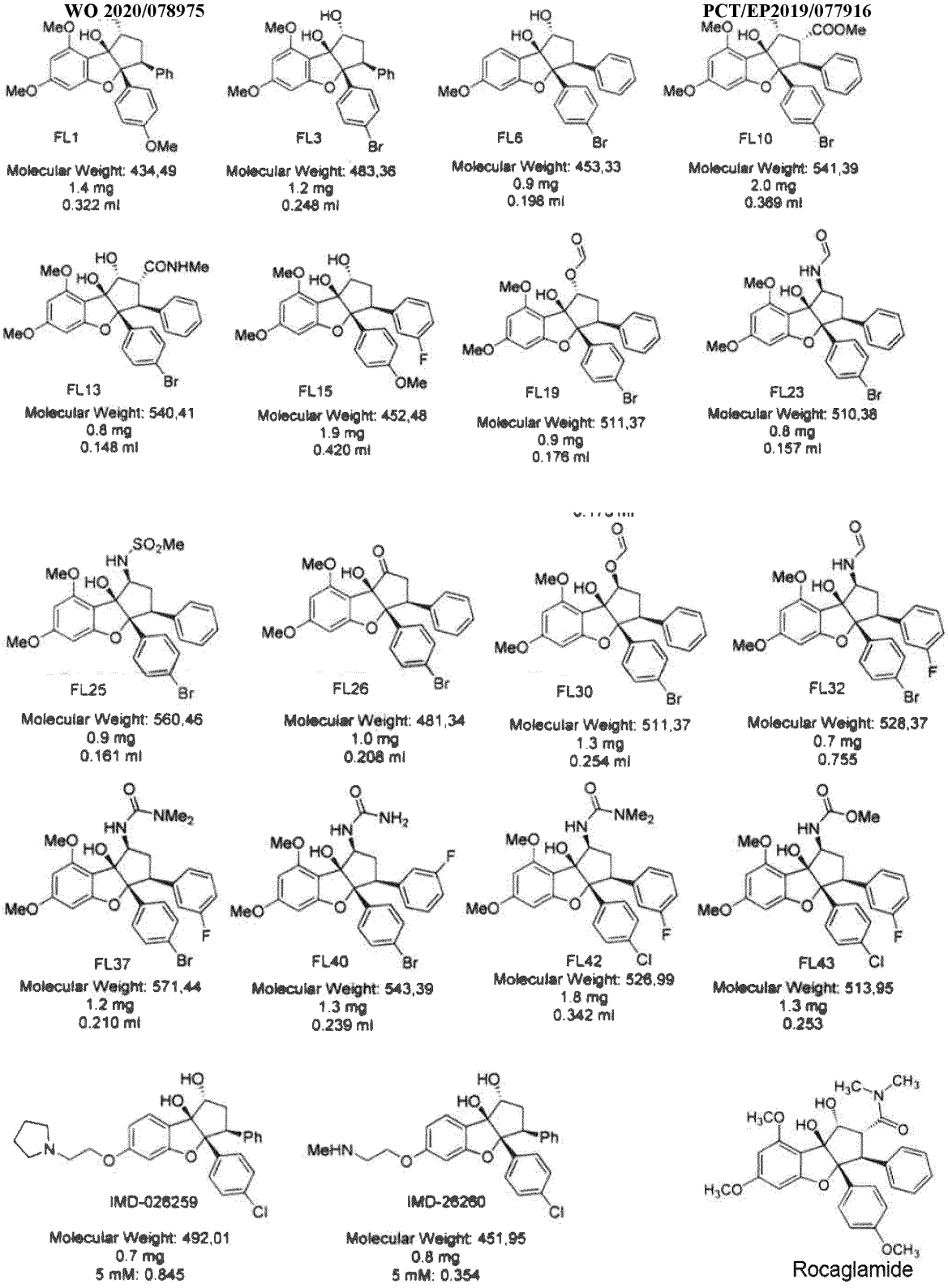

FL1
Molecular Weight: 434,49
1.4 mg
0.322 ml
FL3
Molecular Weight: 483,36
1.2 mg
0.248 ml
FL6
Molecular Weight: 453,33
0.9 mg
0.198 ml
FL10
Molecular Weight: 541,39
2.0 mg
0.369 ml
FL13
Molecular Weight: 540,41
0.8 mg
0.148 ml
FL15
Molecular Weight: 452,48
1.9 mg
0.420 ml
FL19
Molecular Weight: 511,37
0.9 mg
0.176 ml
FL23
Molecular Weight: 510,38
0.8 mg
0.157 ml
FL25
Molecular Weight: 560,46
0.9 mg
0.161 ml
FL26
Molecular Weight: 481,34
1.0 mg
0.208 ml
FL30
Molecular Weight: 511,37
1.3 mg
0.254 ml
FL32
Molecular Weight: 528,37
0.7 mg
0.755
FL37
Molecular Weight: 571,44
1.2 mg
0.210 ml
FL40
Molecular Weight: 543,39
1.3 mg
0.239 ml
FL42
Molecular Weight: 526,99
1.8 mg
0.342 ml
FL43
Molecular Weight: 513,95
1.3 mg
0.253
IMD-026259
Molecular Weight: 492,01
0.7 mg
5 mM: 0.845
IMD-26260
Molecular Weight: 451,95
0.8 mg
5 mM: 0.354
Rocaglamide

FIGURE 3

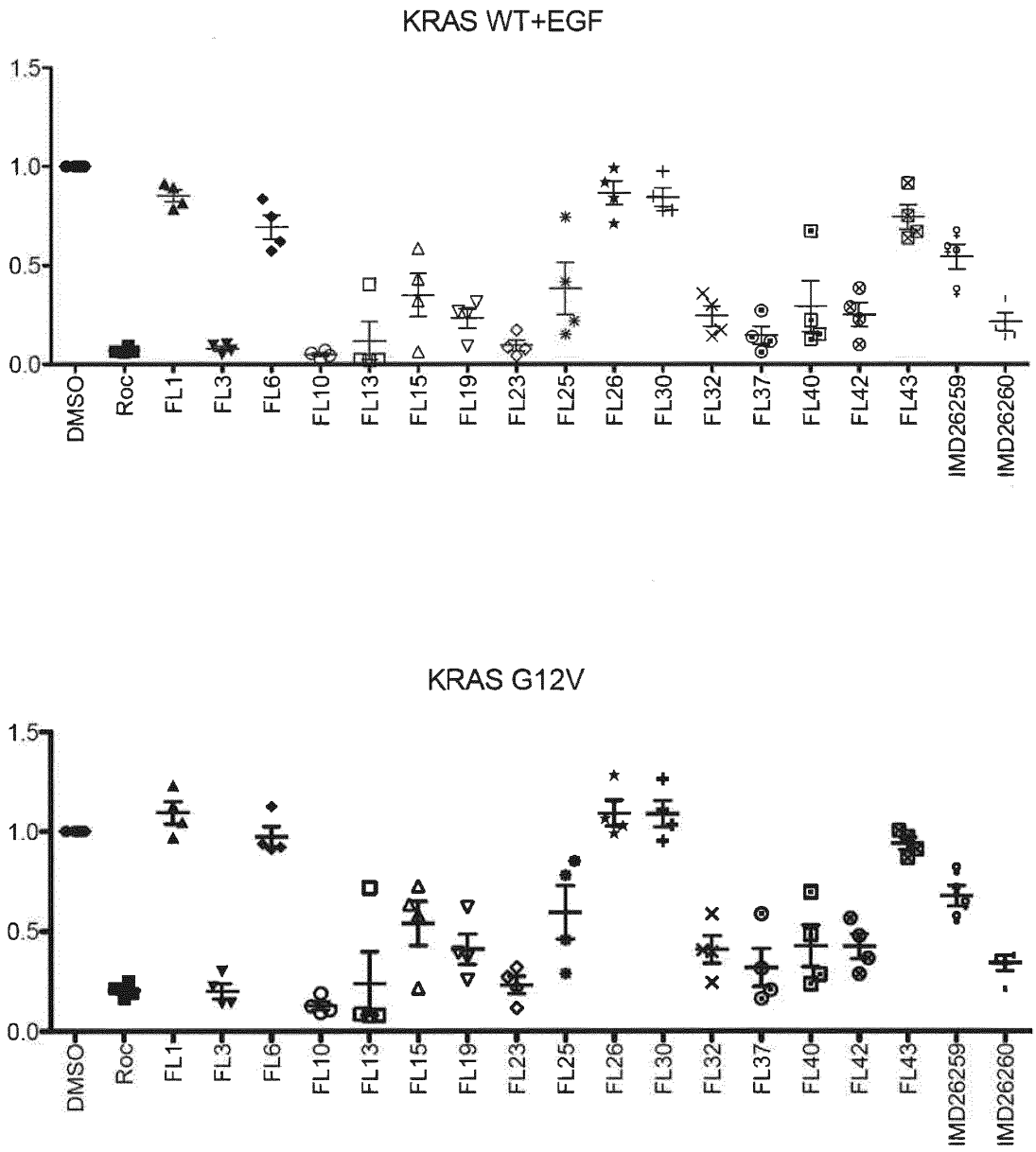
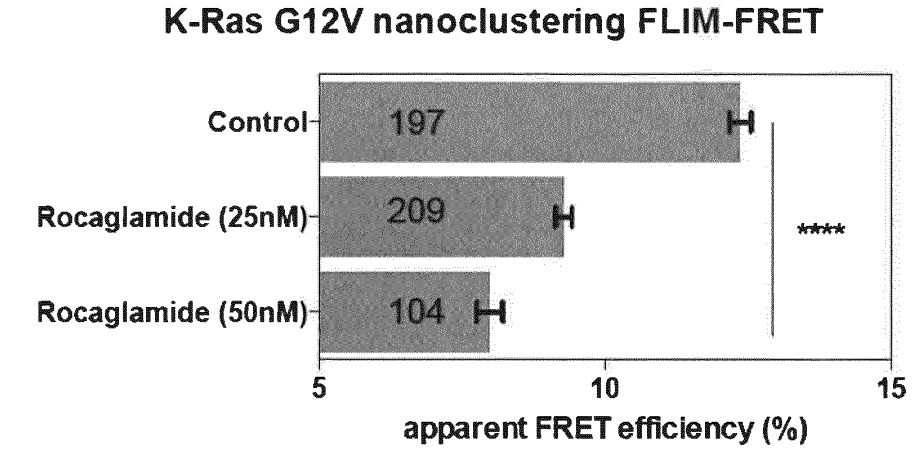
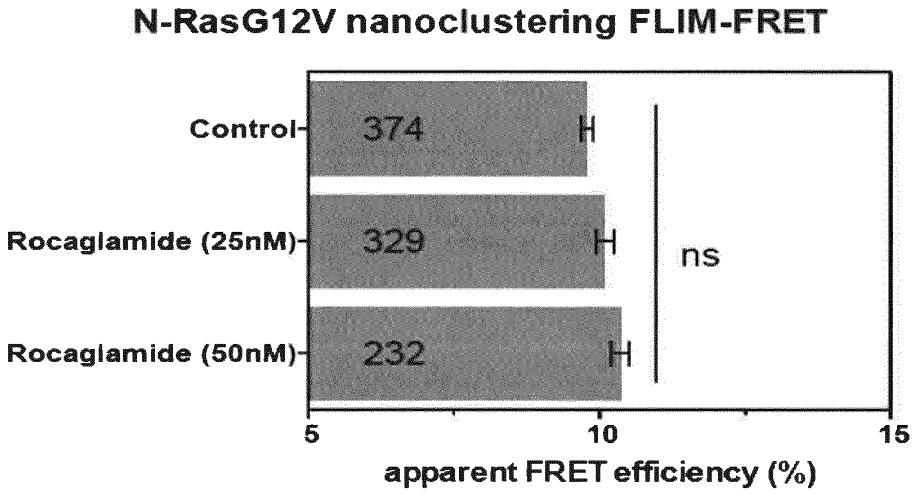

KRAS WT+EGF
1.5
1.0
0.5
0.0
DMSO
Roc
FL1
FL3
FL6
FL10
FL13
FL15
FL19
FL23
FL25
FL26
FL30
FL32
FL37
FL40
FL42
FL43
IMD26259
IMD26260
KRAS G12V
1.5
1.0
0.5
0.0
DMSO
Roc
FL1
FL3
FL6
FL10
FL13
FL15
FL19
FL23
FL25
FL26
FL30
FL32
FL37
FL40
FL42
FL43
IMD26259
IMD26260

FIGURE 4


K-Ras G12V nanoclustering FLIM-FRET
Control
Rocaglamide (25nM)
Rocaglamide (50nM)
197
209
104
****
5
10
15
apparent FRET efficiency (%)


N-RasG12V nanoclustering FLIM-FRET
Control
Rocaglamide (25nM)
Rocaglamide (50nM)
374
329
232
ns
5
10
15
apparent FRET efficiency (%)

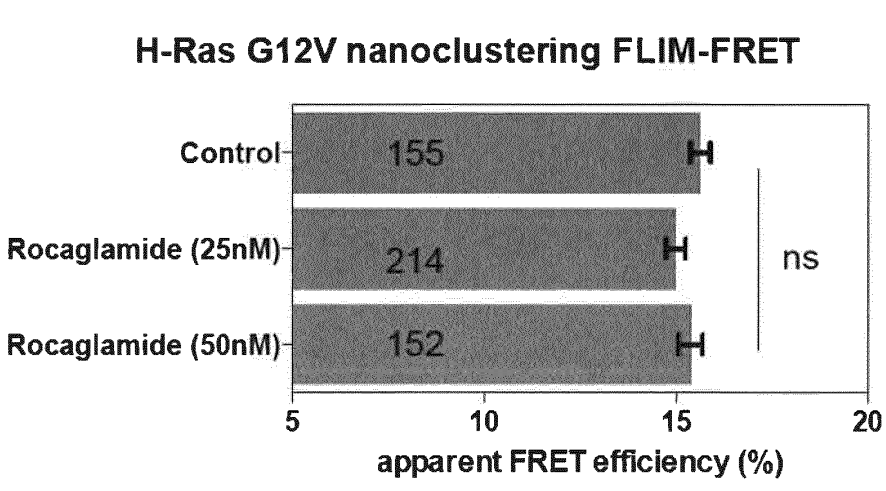

H-Ras G12V nanoclustering FLIM-FRET
Control
Rocaglamide (25nM)
Rocaglamide (50nM)
155
214
152
ns
5
10
15
20
apparent FRET efficiency (%)

FIGURE 5

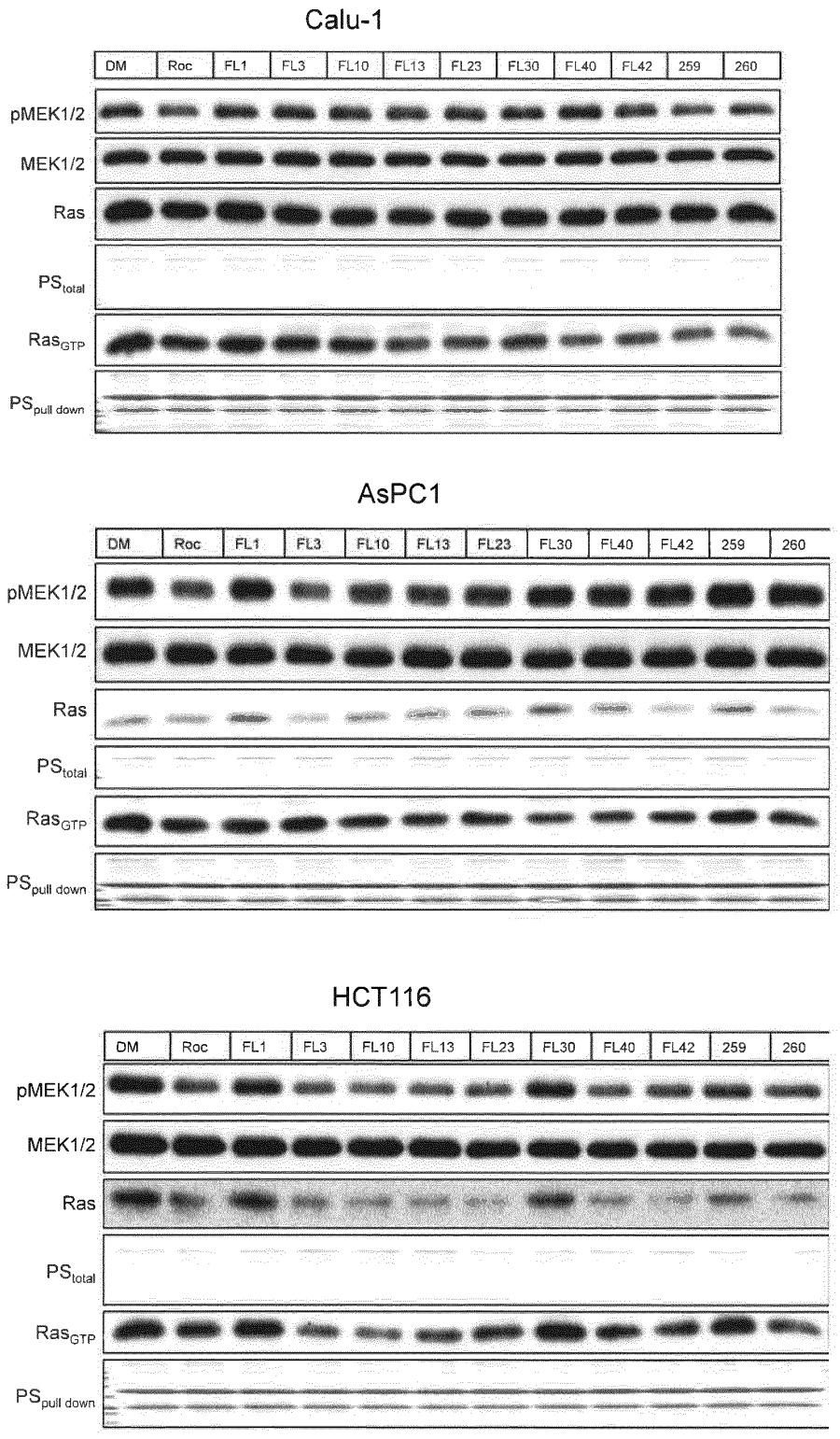

Calu-1
DM
Roc
FL1
FL3
FL10
FL13
FL23
FL30
FL40
FL42
259
260
pMEK1/2
MEK1/2
Ras
PS total
Ras GTP
PS pull down
AsPC1
DM
Roc
FL1
FL3
FL10
FL13
FL23
FL30
FL40
FL42
259
260
pMEK1/2
MEK1/2
Ras
PS total
Ras GTP
PS pull down
HCT116
DM
Roc
FL1
FL3
FL10
FL13
FL23
FL30
FL40
FL42
259
260
pMEK1/2
MEK1/2
Ras
PS total
Ras GTP
PS pull down

FIGURE 6

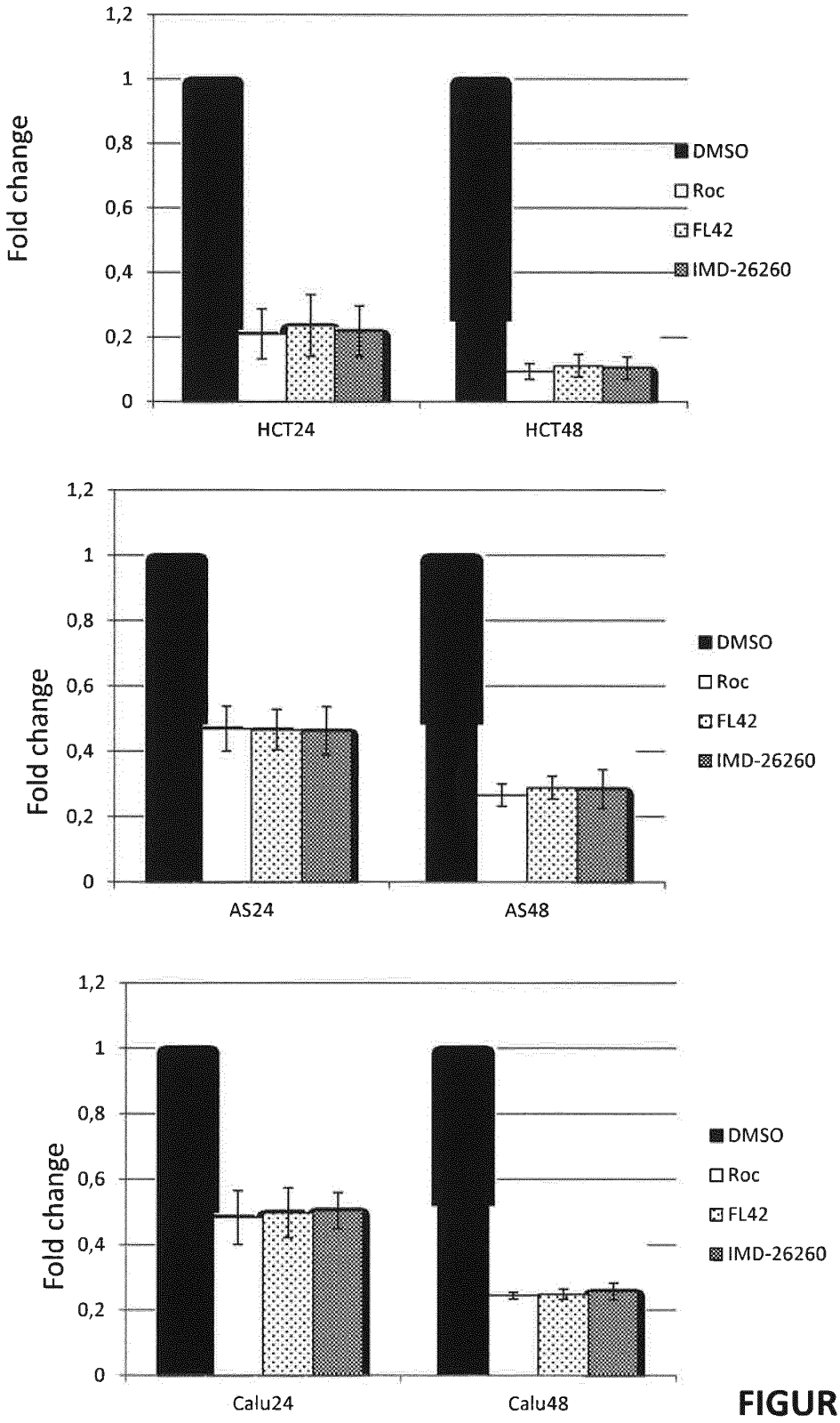
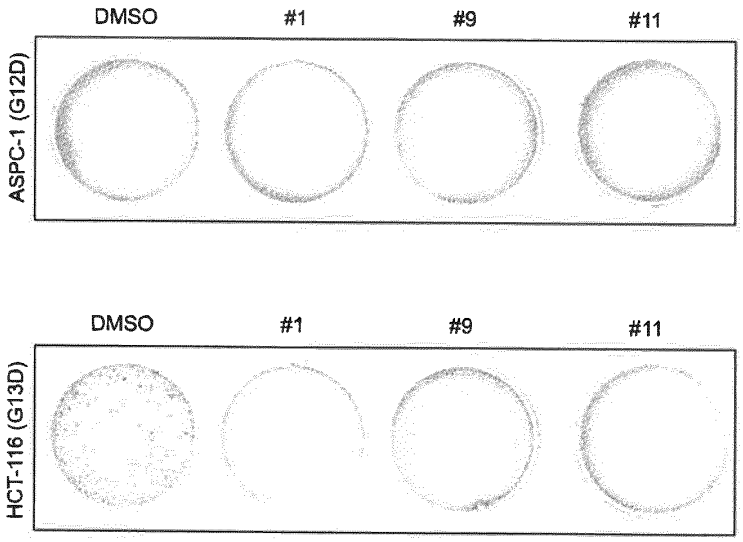

1,2
1
0,8
0,6
0,4
0,2
0
Fold change
HCT24
HCT48
DMSO
Roc
FL42
IMD-26260
AS24
AS48
Calu24
Calu48

FIGURE 7


DMSO
#1
#9
#11
ASPC-1 (G12D)
DMSO
#1
#9
#11
HCT-116 (G13D)

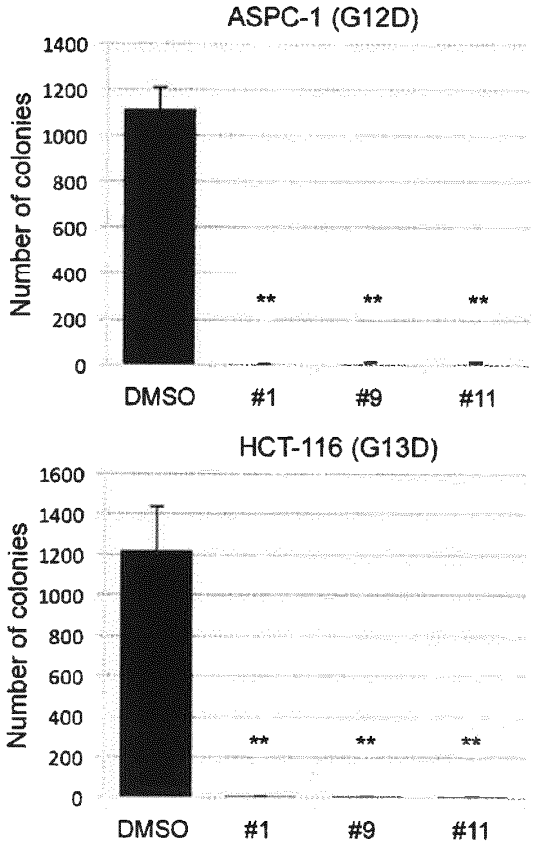

ASPC-1 (G12D)
Number of colonies
1400
1200
1000
800
600
400
200
0
**
**
**
DMSO
#1
#9
#11
HCT-116 (G13D)
Number of colonies
1600
1400
1200
1000
800
600
400
200
0
**
**
**
DMSO
#1
#9
#11

FIGURE 8