FIG. 1A

Cell line	Origins	CCNE1 Amplification	CCNE1 CN
COV318	Ovary	+	14
OVCAR3_OVARY	Ovary	+	10
Fu-OV1	Ovary	+	10
KLE	Uterus	+	7
COV504	Ovary	-	1
OV56	Ovary	-	2
Igrov1	Ovary	-	2

FIG. 1B

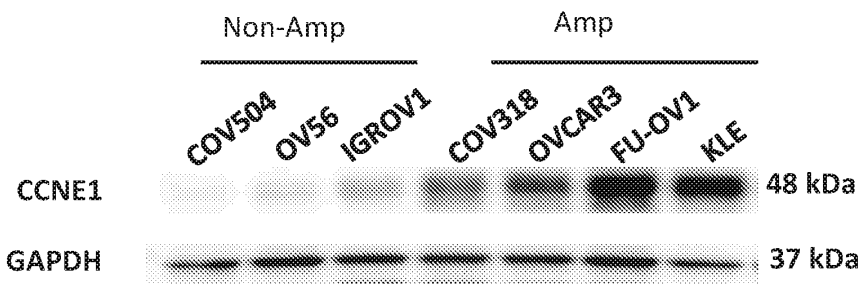


FIG. 2A

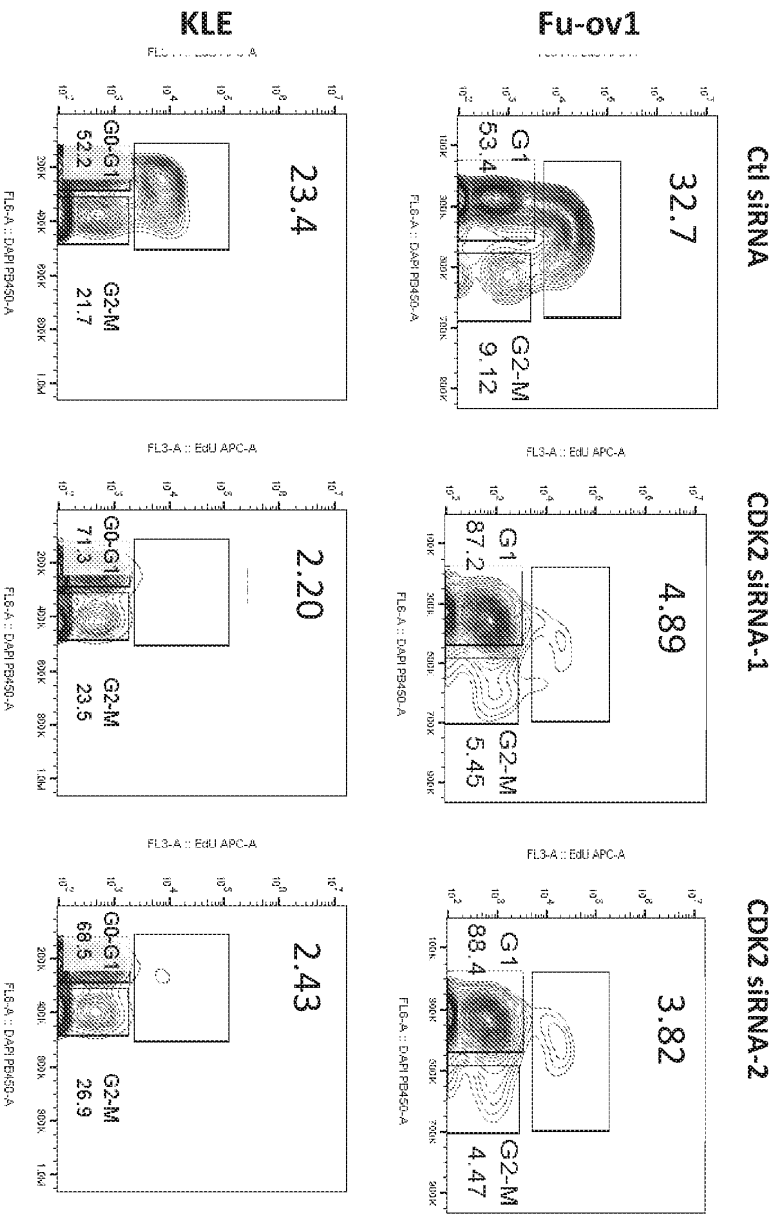

CCNE1 Amp
KLE
Fu-ov1
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
G0-G1
G1
G2-M
52.2
21.7
23.4
53.4
9.12
32.7
71.3
23.5
2.20
87.2
5.45
4.89
68.5
26.9
2.43
88.4
4.47
3.82
FL3-A :: EdU APC-A
FL6-A :: DAPI PB450-A

FIG. 2B

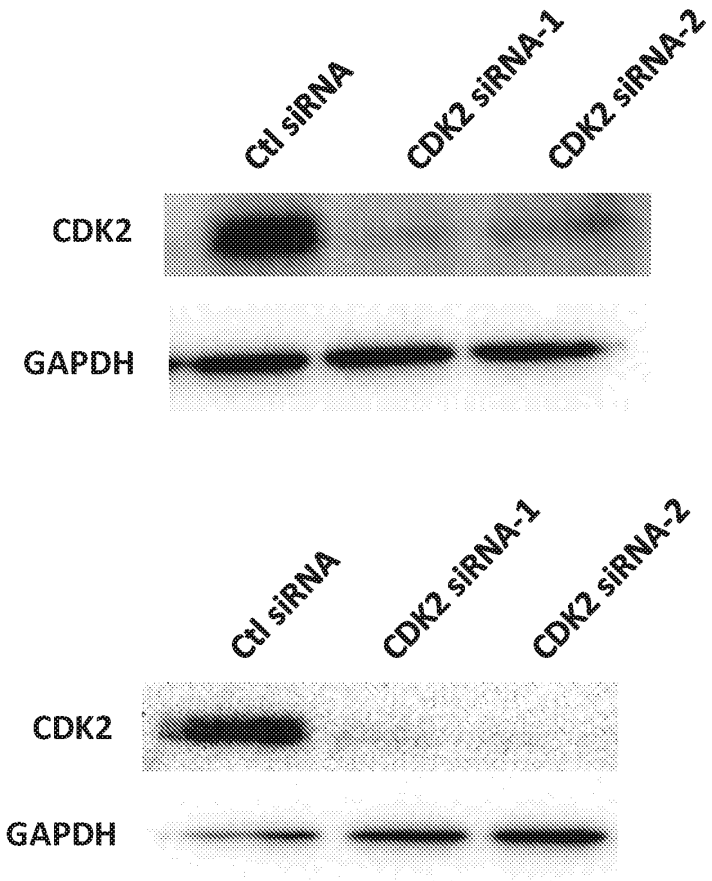

Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
CDK2
GAPDH
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
CDK2
GAPDH

FIG. 3A

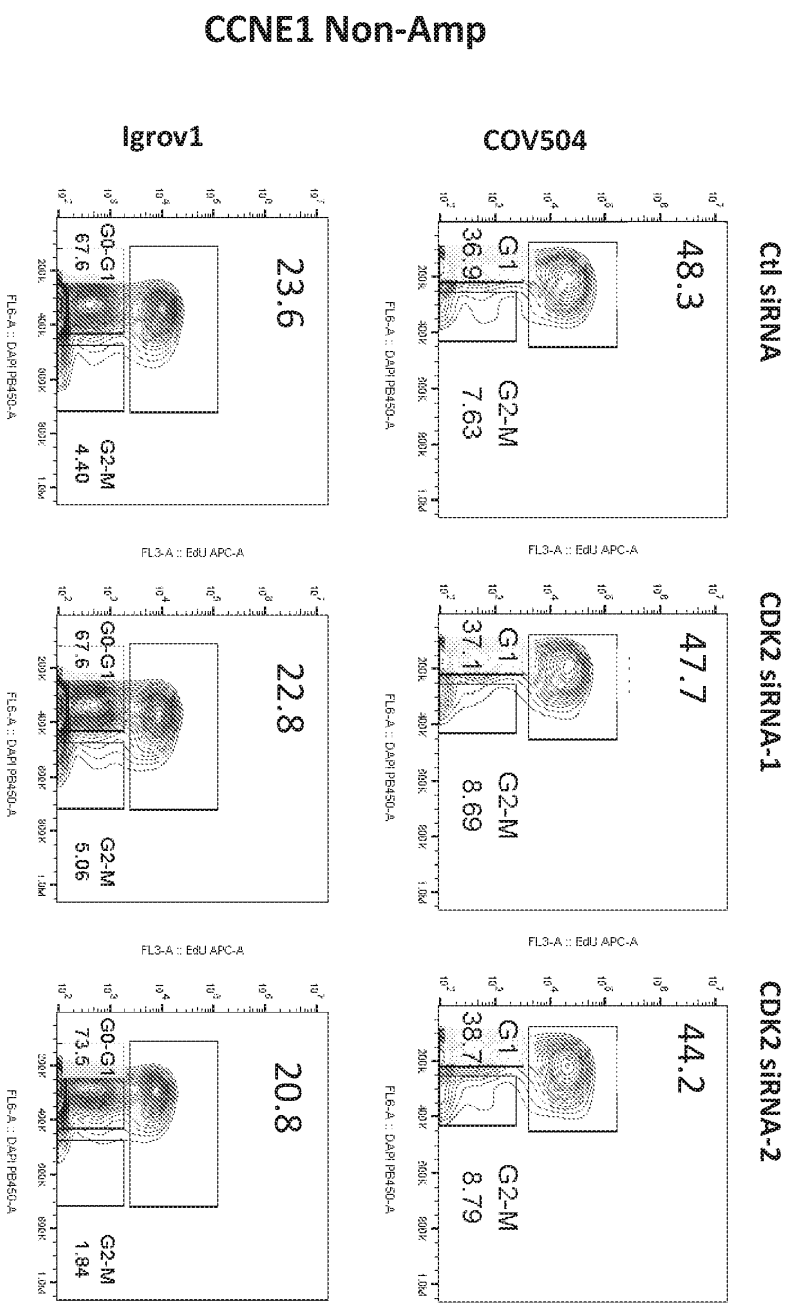

CCNE1 Non-Amp
Igrov1
COV504
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
G0-G1
G1
G2-M
67.6
36.9
7.63
4.40
23.6
48.3
37.1
8.69
5.06
22.8
47.7
38.7
8.79
1.84
20.8
44.2
73.5
FL3-A :: EdU APC-A
FL6-A :: DAPI PB450-A

FIG. 3B

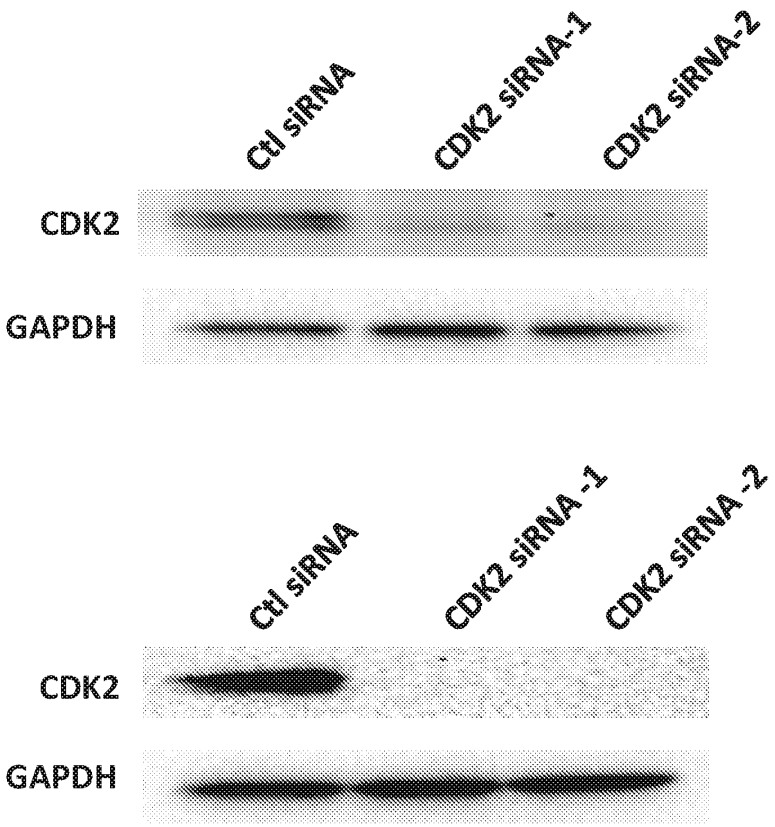

Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
CDK2
GAPDH
Ctl siRNA
CDK2 siRNA -1
CDK2 siRNA -2
CDK2
GAPDH

FIG. 4

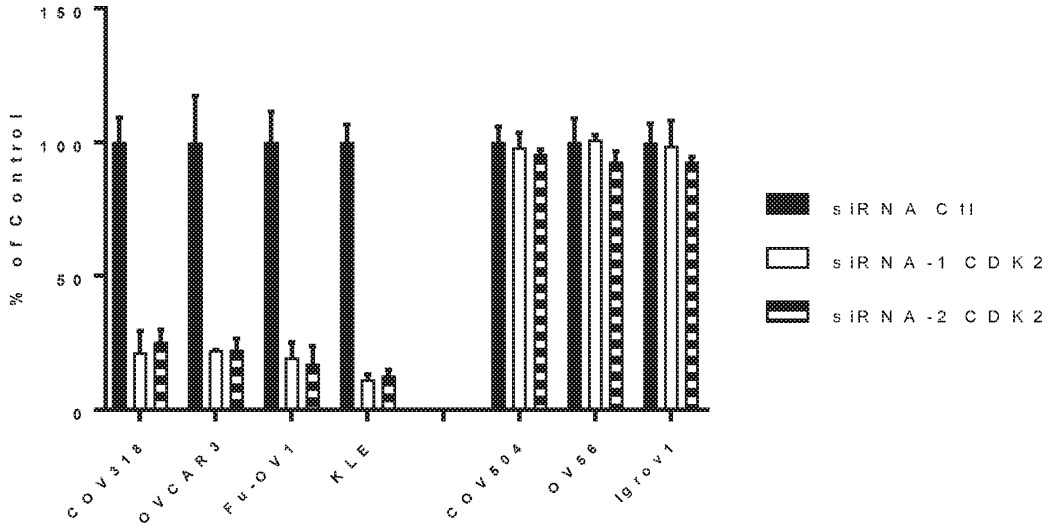

150
100
50
0
% of Control
siRNA Ctl
siRNA-1 CDK2
siRNA-2 CDK2
COV318
OVCAR3
Fu-OV1
KLE
COV504
OVSE
Igrov1

FIG. 5

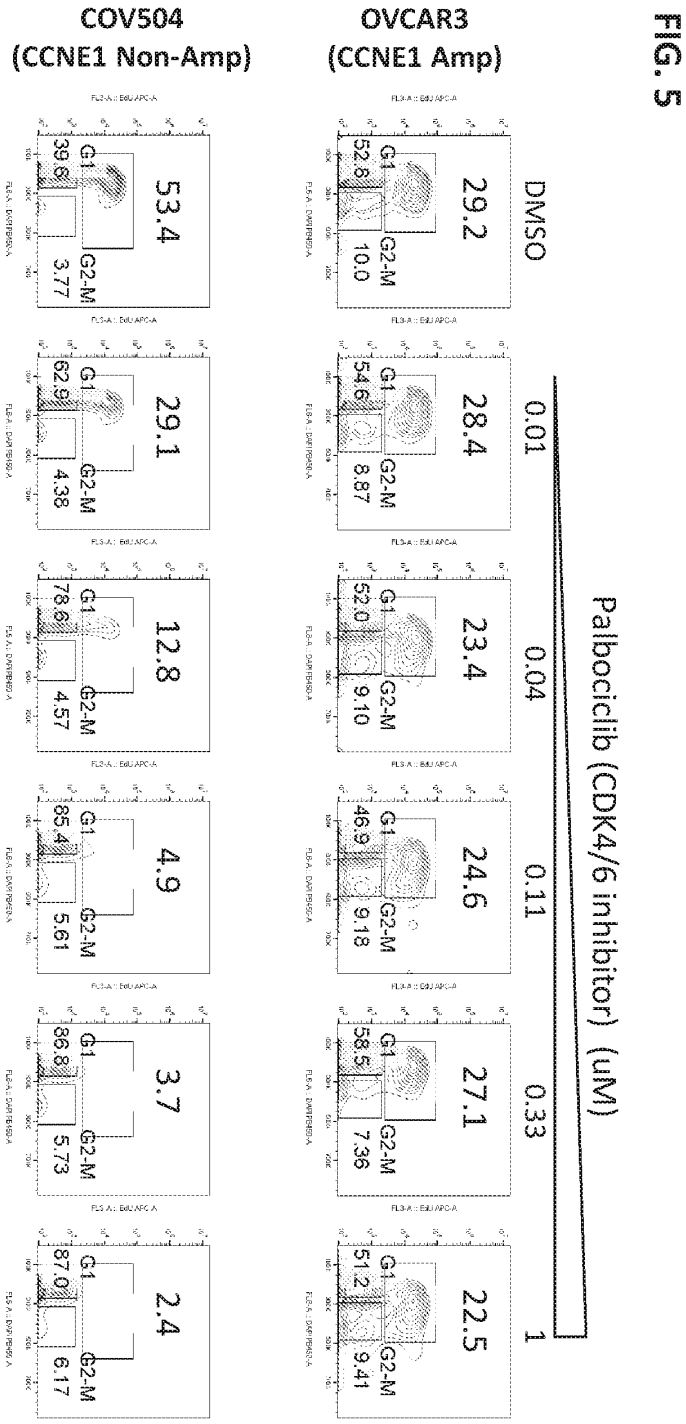
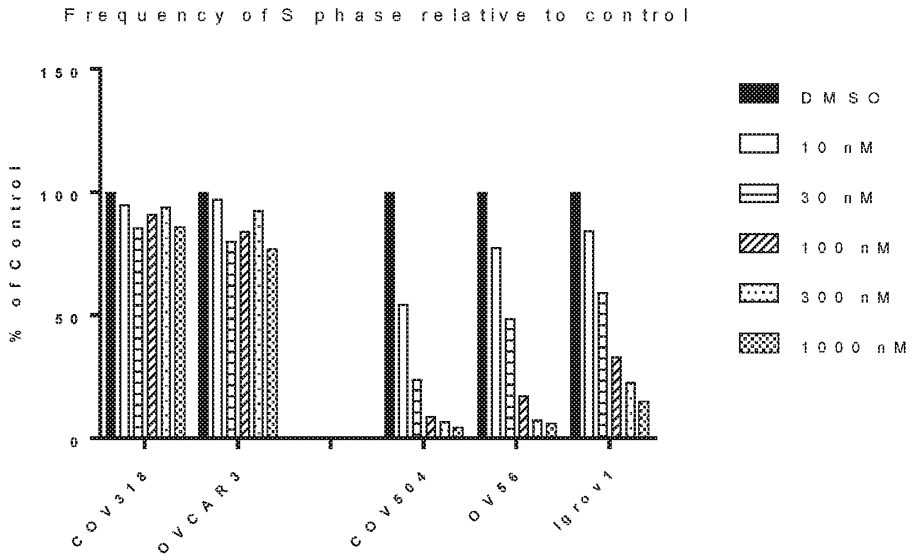

COV504
(CCNE1 Non-Amp)
OVCAR3
(CCNE1 Amp)
DMSO
0.01
0.04
0.11
0.33
1
Palbociclib (CDK4/6 inhibitor) (uM)
G1
G2-M
39.6
53.4
3.77
52.8
29.2
10.0
62.9
29.1
4.38
54.6
28.4
8.87
78.6
12.8
4.57
52.0
23.4
9.10
85.4
4.9
5.61
46.9
24.6
9.18
86.8
3.7
5.73
58.5
27.1
7.36
87.0
2.4
6.17
51.2
22.5
9.41

FIG. 6


Frequency of S phase relative to control
% of Control
150
100
50
0
COV318
OVCAR3
COV504
OV56
Igrov1
DMSO
10 nM
30 nM
100 nM
300 nM
1000 nM

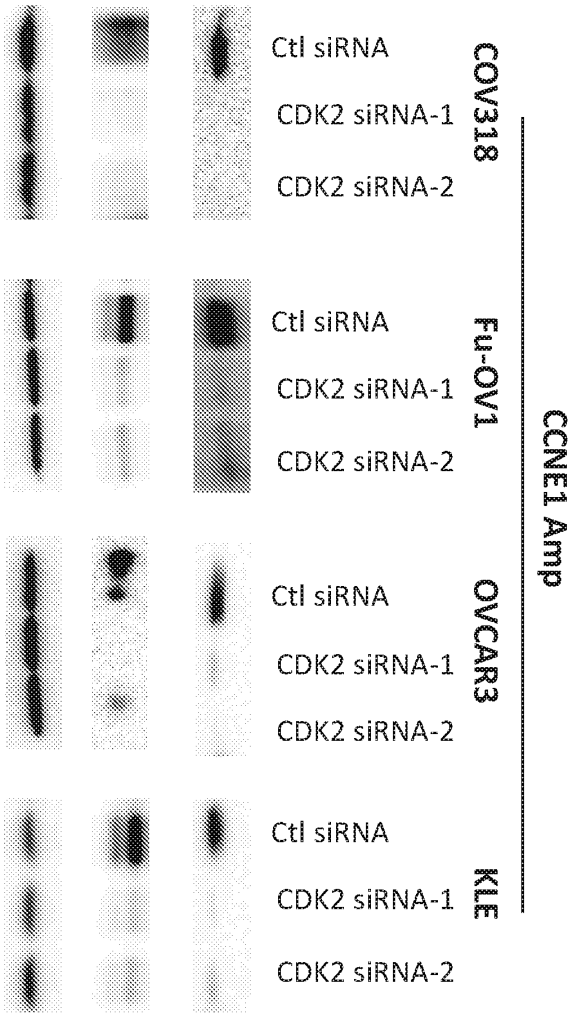

GAPDH
p-RB (S780)
CDK2
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
COV318
Fu-OV1
OVCAR3
KLE
CCNE1 Amp

FIG. 7A

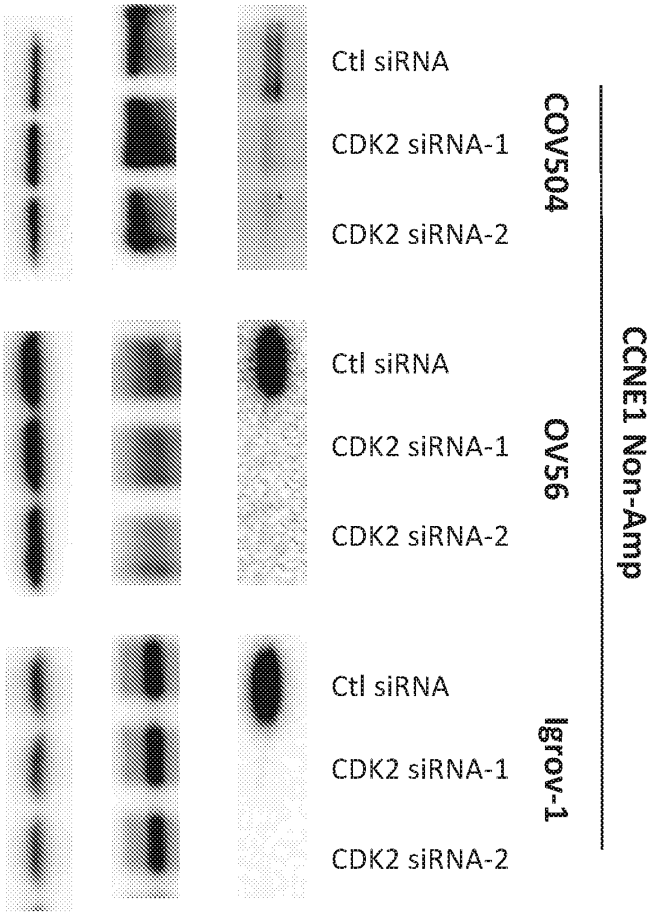

GAPDH
p-RB (S780)
CDK2
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
COV504
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
OV56
Ctl siRNA
CDK2 siRNA-1
CDK2 siRNA-2
Igrov-1
CCNE1 Non-Amp

FIG. 7B

FIG. 8A

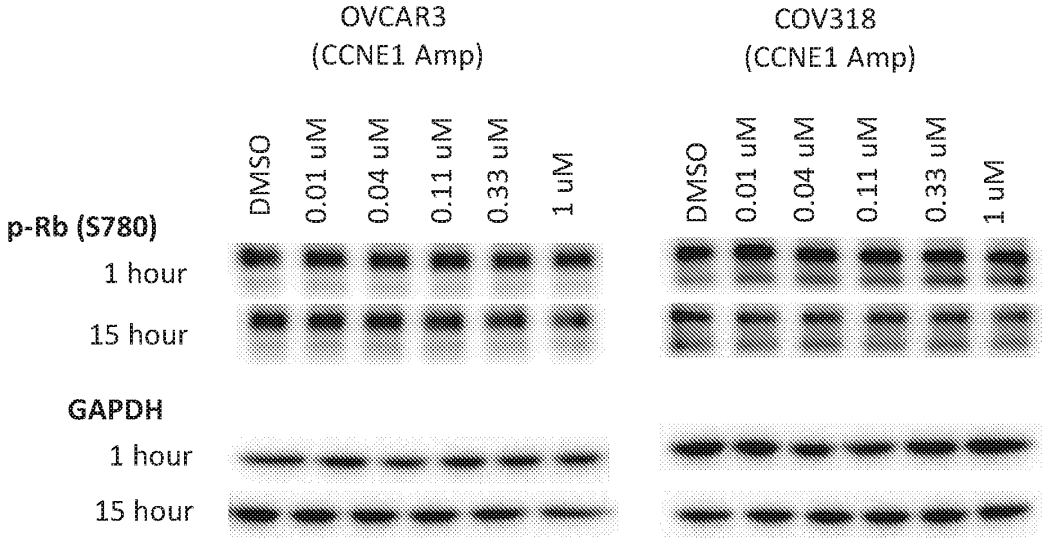

OVCAR3
(CCNE1 Amp)
COV318
(CCNE1 Amp)
DMSO
0.01 uM
0.04 uM
0.11 uM
0.33 uM
1 uM
p-Rb (S780)
1 hour
15 hour
GAPDH
1 hour
15 hour

FIG. 8B

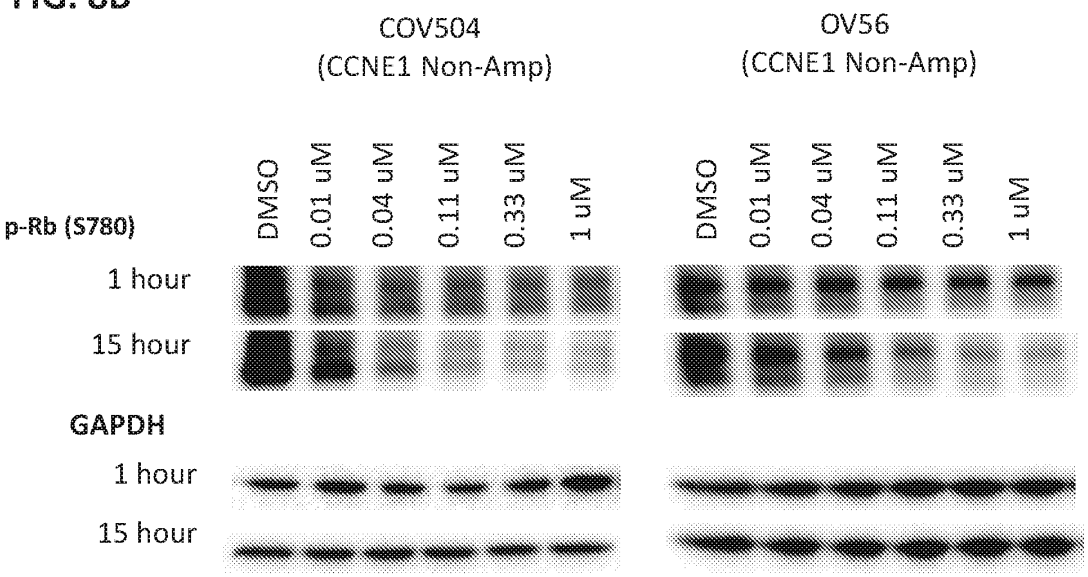

COV504
(CCNE1 Non-Amp)
OV56
(CCNE1 Non-Amp)
DMSO
0.01 uM
0.04 uM
0.11 uM
0.33 uM
1 uM
p-Rb (S780)
1 hour
15 hour
GAPDH
1 hour
15 hour

FIG. 9A

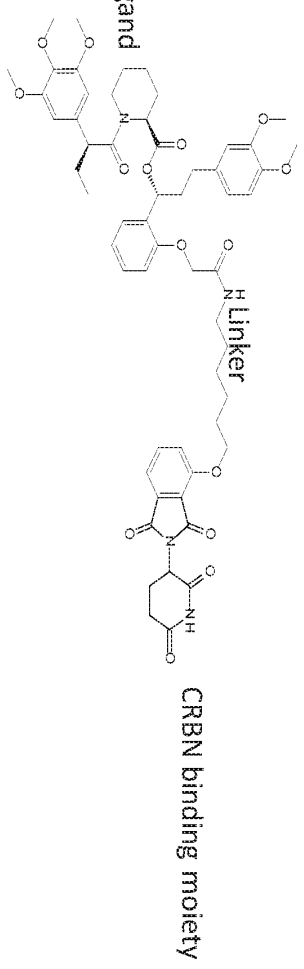

FKBP12F36V-binding ligand
Linker
CRBN binding moiety

FIG. 9B

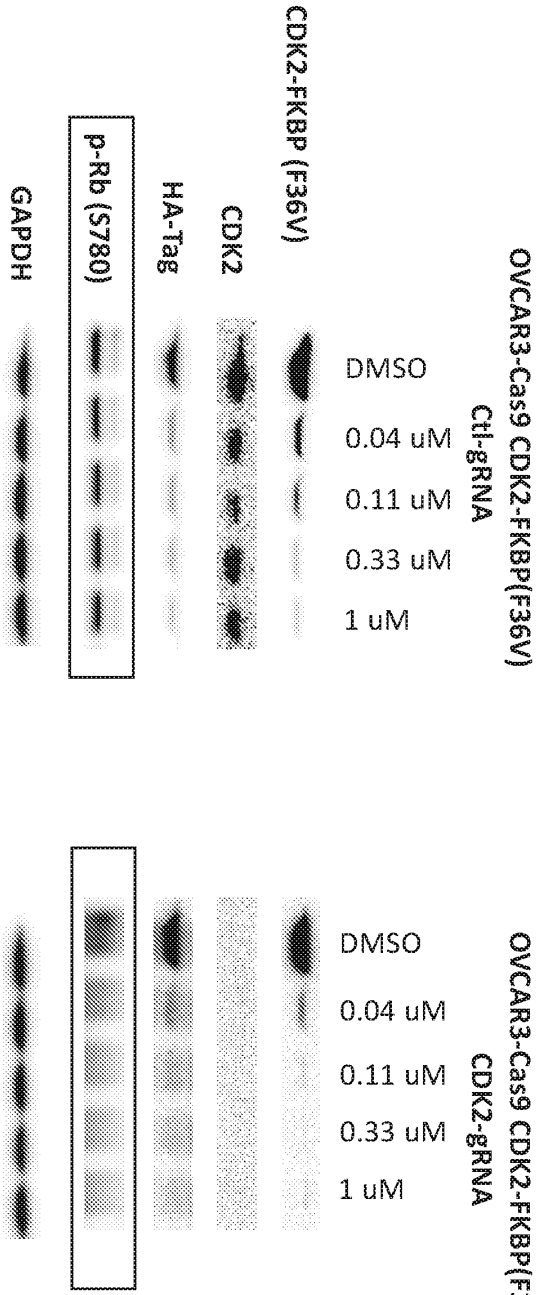
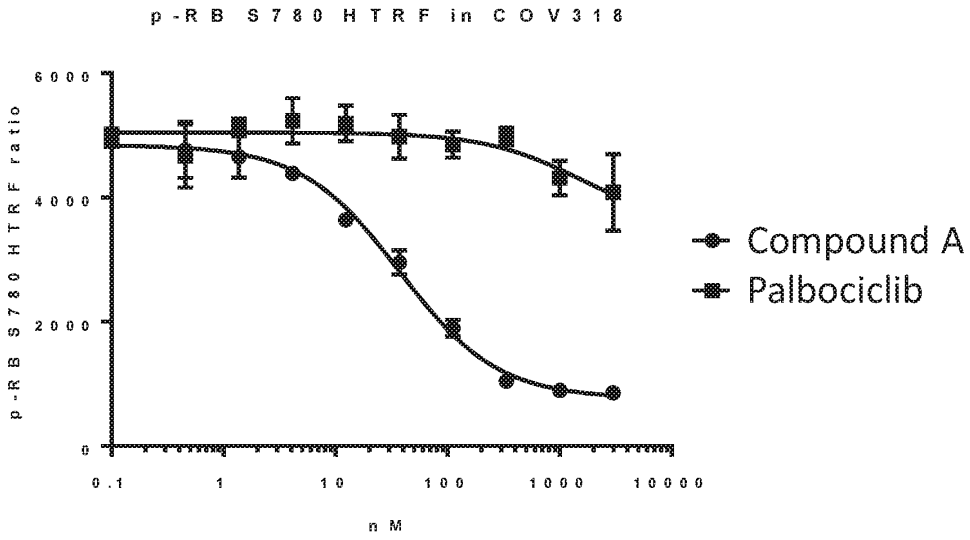

OVCAR3-Cas9 CDK2-FKBP(F36V)
Ctl-gRNA
DMSO
0.04 uM
0.11 uM
0.33 uM
1 uM
CDK2-FKBP (F36V)
CDK2
HA-Tag
p-Rb (S780)
GAPDH
OVCAR3-Cas9 CDK2-FKBP(F36V)
CDK2-gRNA
DMSO
0.04 uM
0.11 uM
0.33 uM
1 uM

FIG. 10A

CDK2/CCNE1 enzymatic assay	CDK2_IC50 (nM)
Compound A	1.1
Palbociclib	10000

FIG. 10B



P-RB S780 HTRF cellular assay	CDK2_IC50 (nM)
Compound A	37
Palbociclib	>3000

FIG. 11

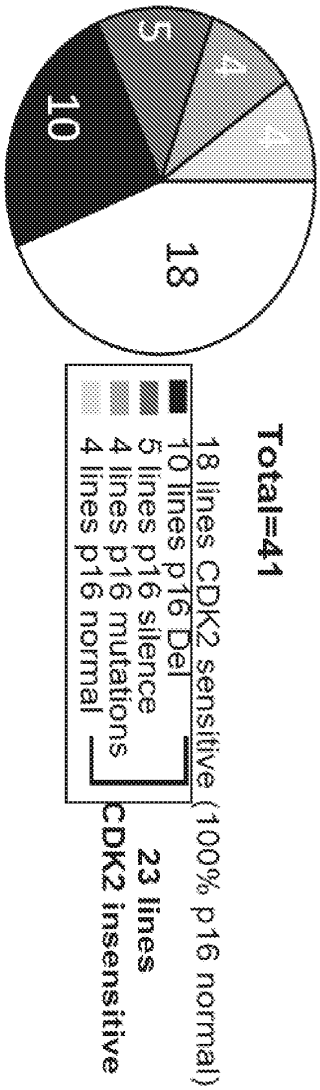

Total=41
18
10
5
4
4
18 lines CDK2 sensitive (100% p16 normal)
10 lines p16 Del
5 lines p16 silence
4 lines p16 mutations
4 lines p16 normal
23 lines
CDK2 insensitive

FIG. 12A

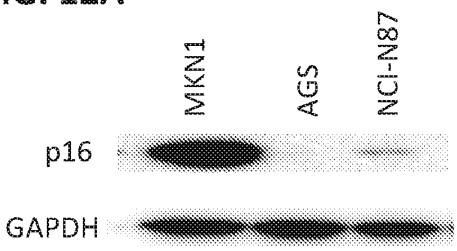


FIG. 12B

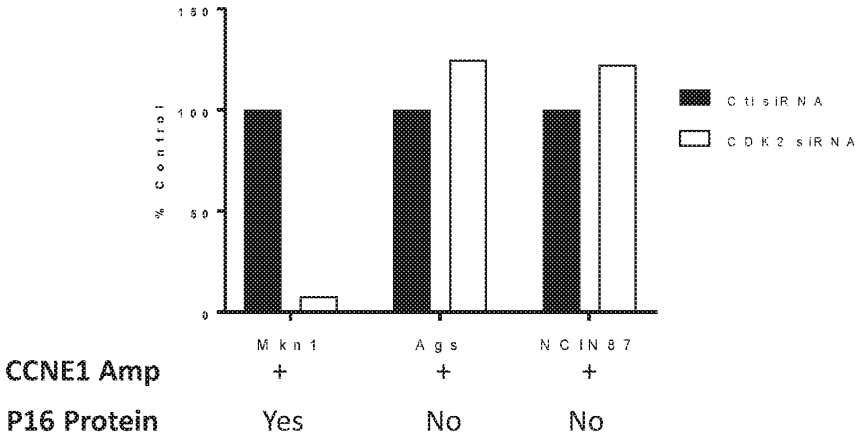
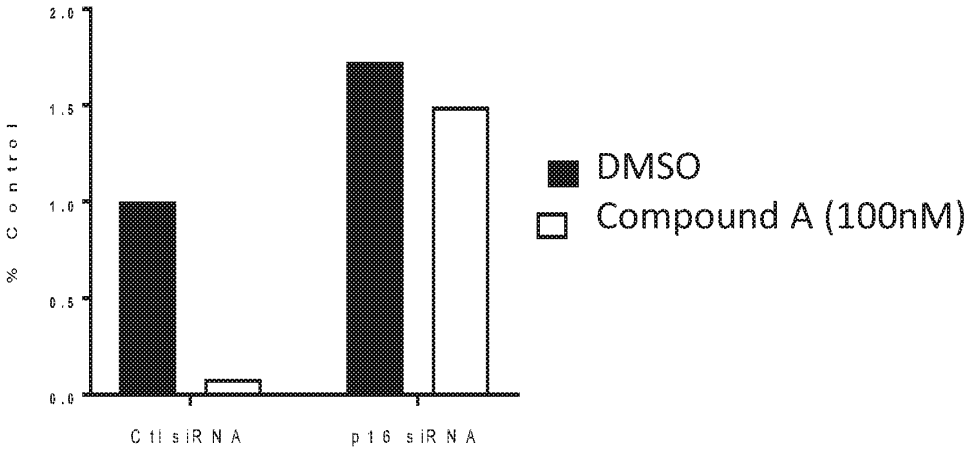


FIG. 13


2.0
1.5
1.0
0.5
0.0
% Control
Ctl siRNA
p16 siRNA
DMSO
Compound A (100nM)