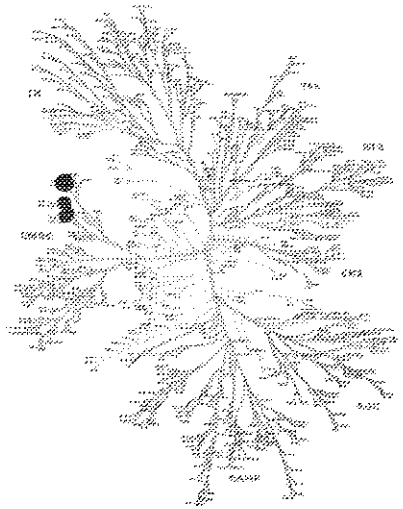
Figure 1

Lipid kinase selectivity

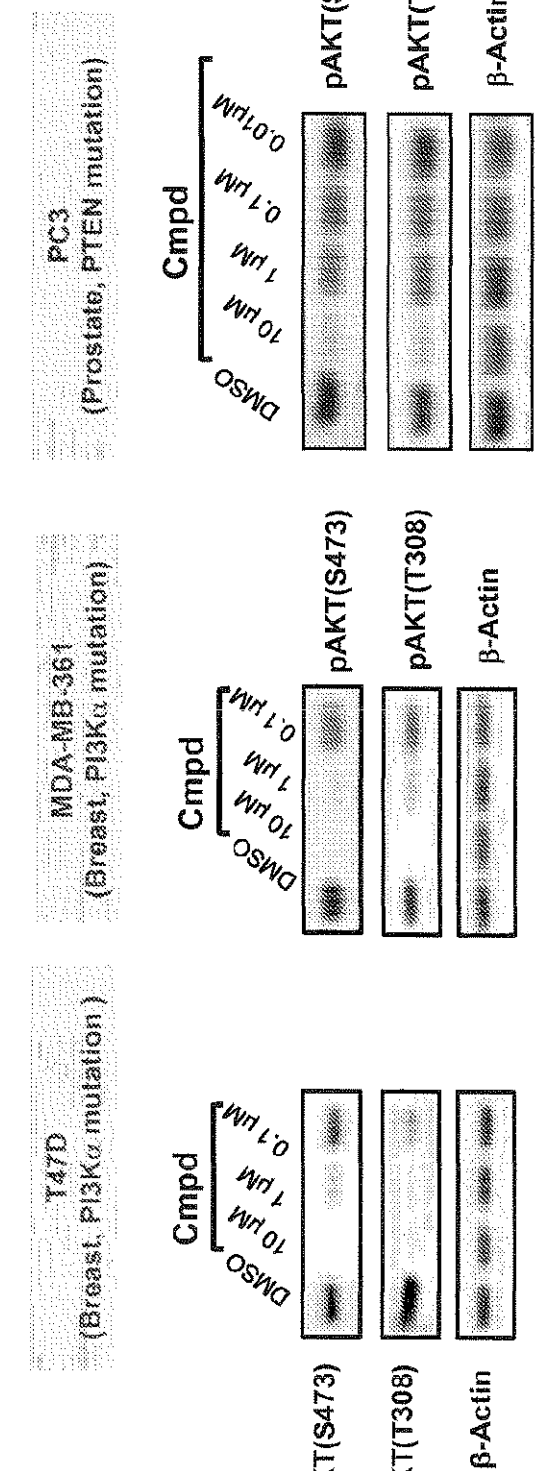
	IC50 (nM)						%inhibition @ 1000nM (Ambit)						
	PI3K Class I						PI3K Class II		PI4K	PI5K			
	PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ	mTor	DNA-PK	PI3KC2β	PI3KC2γ	PI4Kβ	PI5K1α	PI5K1C	PI5K2β	PI5K2C
Cmpd	++++	++	++	+	++	++	0%	22%,	28%	0%	0%	9%	17%



Protein kinase selectivity

Kinase	Ambit %Inhibition @ 1000nM	Invitrogen IC_{50} (nM)
DYRK1A	91	2080
HIPK3	68	>10,000
CLK1	73	3810

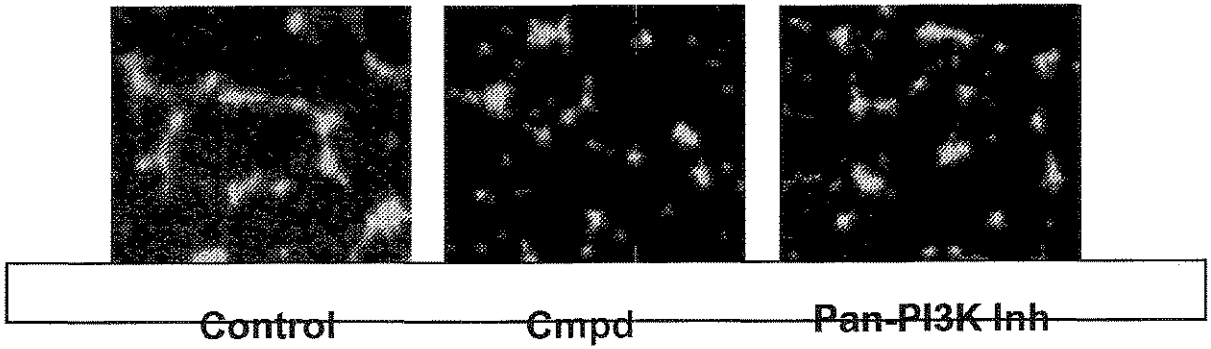
Figure 2



	pAKT inhibition IC_{50} (nM)			Cell Proliferation inhibition IC_{50} (nM)		
	T47D	MDA-MB-361	PC3	T47D	MDA-MB-361	PC3
Cmpd	~500	~500	~10,000	1190	1400	>10,000

Figure 3

Inhibition of Angiogenesis (*In-Vitro*)



Compound	Tube Formation Assay IC_{50} (μM)	Cell Viability Assay IC_{50} (μM)
Cmpd	0.41	>10
Pan-PI3K Inh	1.03	>10

Biochemical Potency (IC_{50} values)				
Compound	PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ
Cmpd	++++	++	++	+
Pan-PI3K Inh	++++	++++	++++	++++

Figure 4

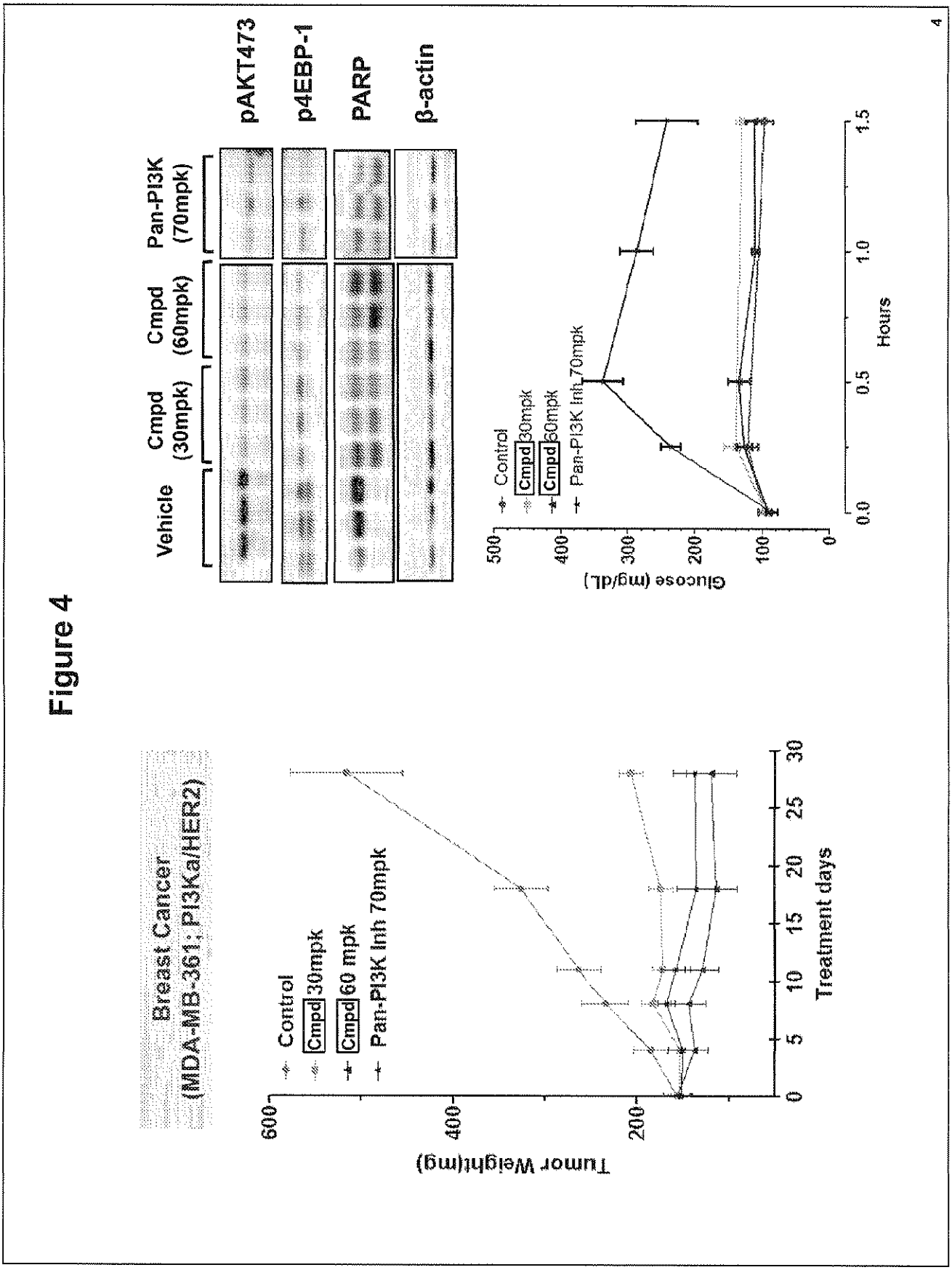

Breast Cancer
(MDA-MB-361; PI3Kα/HER2)
Control
Cmpd 30mpk
Cmpd 60 mpk
Pan-PI3K Inh 70mpk
Tumor Weight(mg)
Treatment days
Vehicle
Cmpd (30mpk)
Cmpd (60mpk)
Pan-PI3K (70mpk)
pAKT473
p4EBP-1
PARP
β-actin
Glucose (mg/dL)
Hours

Figure 5

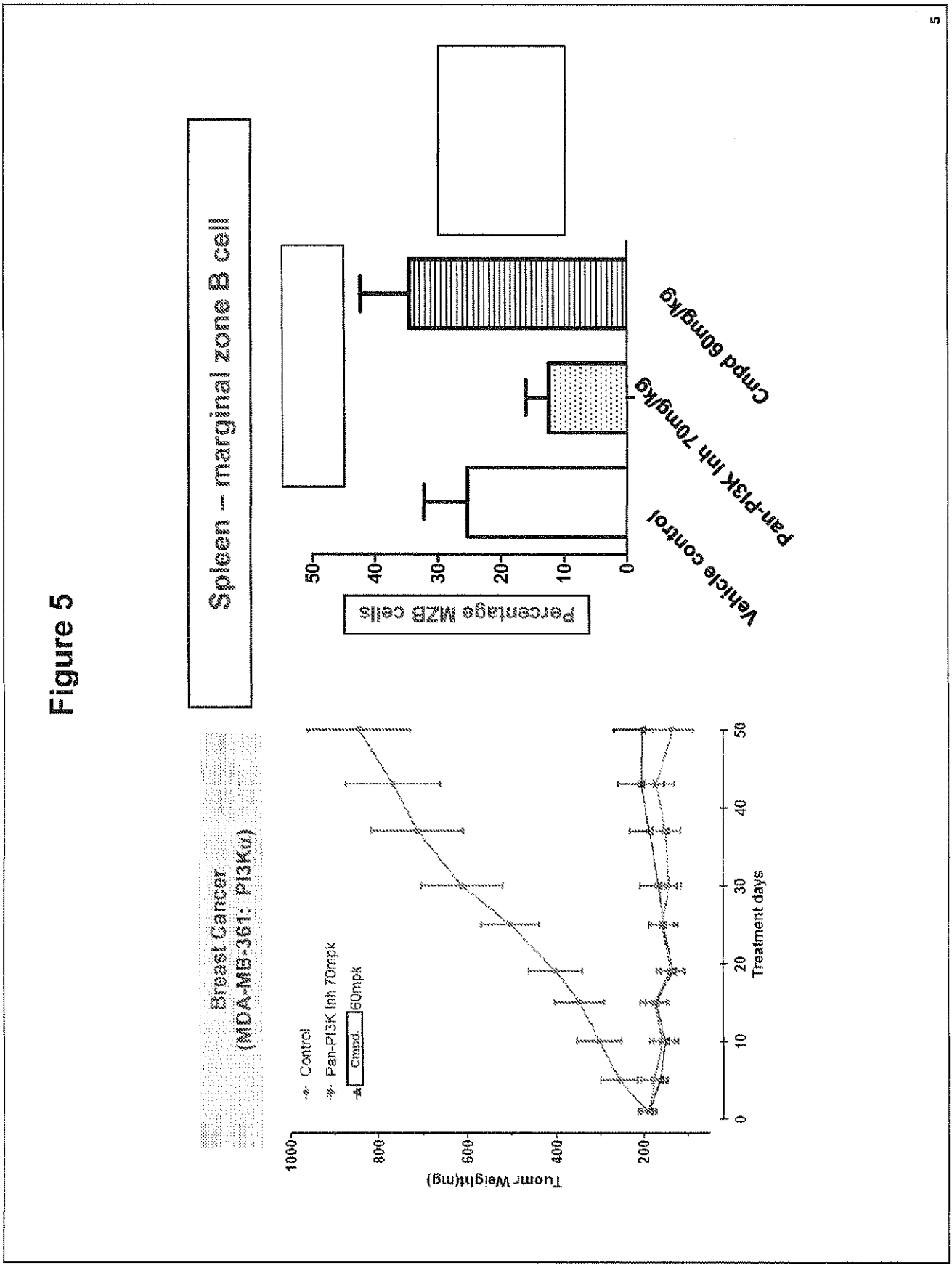
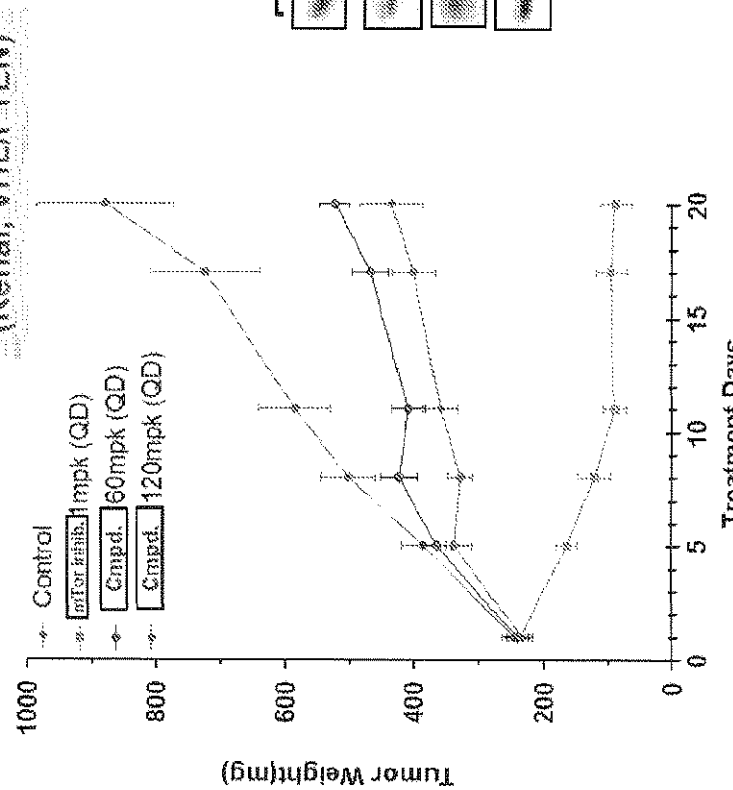
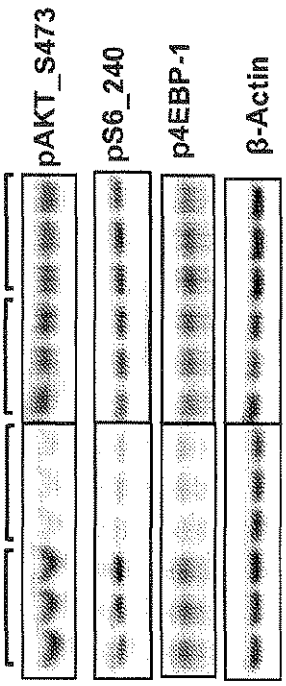

Breast Cancer
(MDA-MB-361: PI3Kα)
Control
Pan-PI3K Inh 70mpk
Cmpd 60mpk
Tuomr Weight(mg)
1000
800
600
400
200
0
10
20
30
40
50
Treatment days
Spleen – marginal zone B cell
Percentage MZB cells
50
40
30
20
10
0
Vehicle control
Pan-PI3K Inh 70mg/kg
Cmpd 60mg/kg

Figure 6

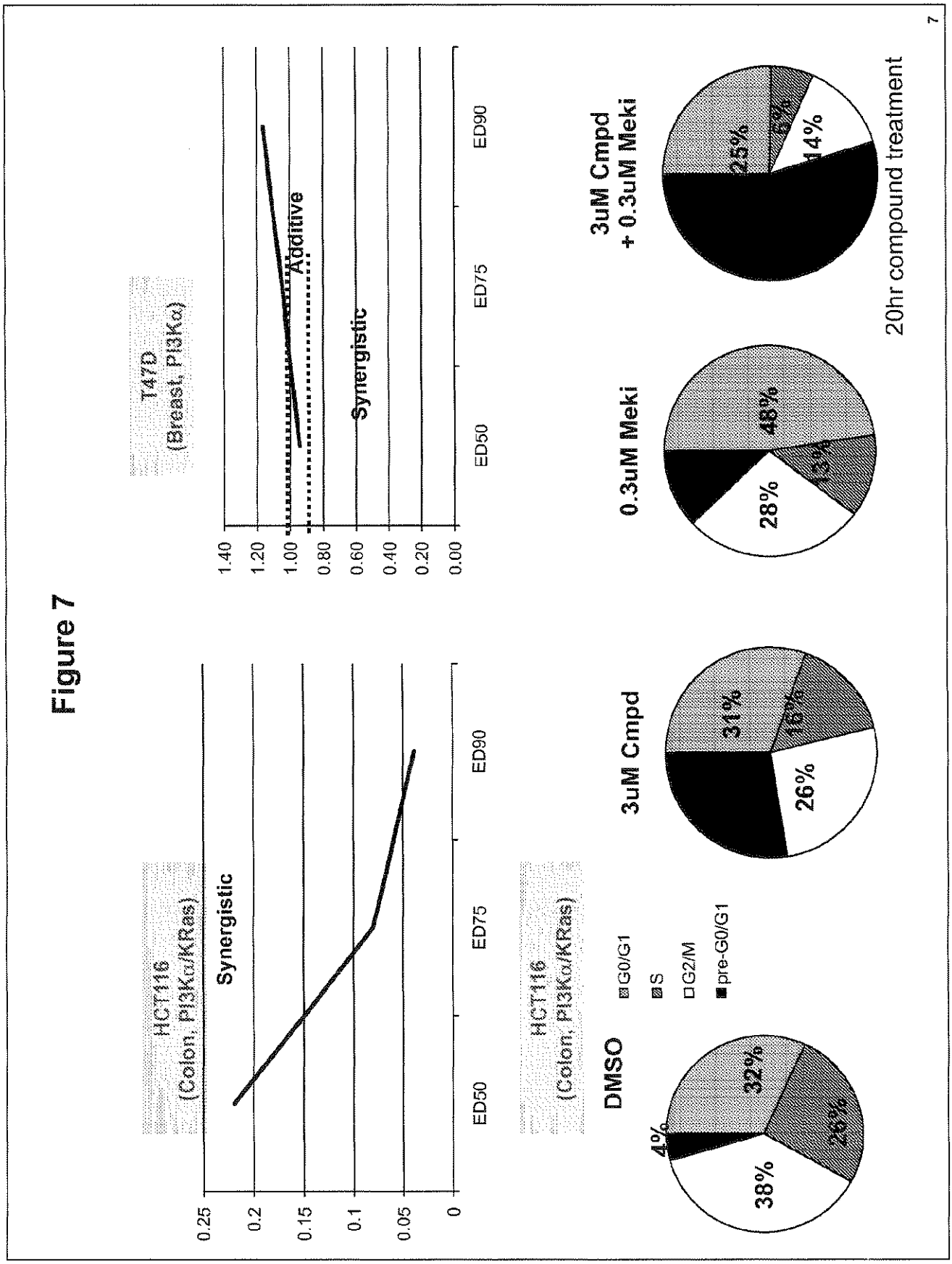




Biochemical Potency (IC_{50} values)					
Compound	PI3Kα	PI3Kβ	PI3Kγ	PI3Kδ	mTor
Cmpd	++++	++	++	+	++
mTor inhib.	+++	++	+++	+++	++++

6

Figure 7


HCT116
(Colon, PI3Kα/KRas)
Synergistic
0.25
0.2
0.15
0.1
0.05
0
ED50
ED75
ED90
T47D
(Breast, PI3Kα)
Additive
Synergistic
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
ED50
ED75
ED90
HCT116
(Colon, PI3Kα/KRas)
DMSO
3uM Cmpd
0.3uM Meki
3uM Cmpd
+ 0.3uM Meki
G0/G1
S
G2/M
pre-G0/G1
4%
32%
38%
26%
31%
16%
26%
28%
13%
48%
25%
6%
14%
20hr compound treatment
7