

SUPPLEMENTARY ONLINE DATA

A drug targeting only p110lpha can block phosphoinositide 3-kinase signalling and tumour growth in certain cell types

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	% Activity re A66 10 µM	PIK75 10 µM	TGX221 10 μM	IC87114 10 μM
MKK1	108	4	84	86
MKK2	116	9	114	105
MKK6	85	55	83	97
ERK1	99	16	103	100
ERK2	92	42	103	105
JNK1	90	19	102	95
JNK2	102	62	86	90
JNK3	106	56	104	101
p38a MAPK	96	98	92	93
p38b MAPK	98	62	99	94
p38g MAPK	90	4	78	100
p38d MAPK	95	2	74	93
ERK8	91	18	102	98
RSK1	84	3	88	99
RSK2	99	4	84	113
PDK1	94	22	99	100
PKBa	97	4	122	103
PKBb	99	70	79	105
SGK1	88	22	103	108
S6K1	98	3	101	104
PKA	89	4	93	94
ROCK 2	100	2	105	97
PRK2	90	1	82	80
PKCa	90	15	103	98
PKCz	110	39	102	106
PKD1	92	36	93	105
MSK1	115	11	90	93
MNK1	91	87	99	94
MNK2	102	47	99	96
MAPKAP-K	105	19	98	98
MAPKAP-K		96	83	106
PRAK	85	24	97	98
CAMKKb	93	24	102	116
CAMK1	109	61	92	98
SmMLCK	81	8	98	94
PHK	98	4	87	94

	% Activity re		TOVOOL	1007444
	A66 10 µM	PIK75 10 μM	TGX221 10 µM	IC87114 10 μM
D. D.				
DAPK1	81	2	102	110
CHK1	97	76	100	146
CHK2	117	34	105	88
GSK3b	95	1	28	98
CDK2-Cycli	103	2	81	90
PLK1	112	13	89	92
Aurora A	112	13	102	103
Aurora B	109	38	96	98
LKB1	105	10	85	89
AMPK	108	16	98	108
MARK1	97	5	94	96
MARK2	86	36	105	86
MARK3	83	2	99	98
MARK4	87	43	100	103
BRSK1	106	70	185	97
BRSK2	92	30	78	106
MELK	116	4	96	102
NUAK1	81	22	77	100
CK1	95	6	86	90
CK2	91	4	82	111
DYRK1A	96	0	83	94
DYRK2	86	5	89	87
DYRK3	83	-1	85	97
NEK2a	111	9	94	98
NEK6	89	112	95	111
IKKb	114	46	91	95
IKKe	68	8	86	95
TBK1	83	54	93	97
PIM1	111	8	76	102
PIM2	102	13	87	91
PIM3	97	12	64	81
SRPK1	95	83	98	117
EF2K	94	86	92	65
HIPK1	88	8	109	89
HIPK2	100	4	78	98
HIPK3	92	10	99	97
CLK2	20	1	41	89
PAK2	85	14	102	100
PAK2	85	14	102	100

	% Activity r			
	A66	PIK75	TGX221	IC87114
	10 µM	10 µM	10 µM	10 µM
PAK4	100	8	89	71
PAK5	85	29	86	85
PAK6	93	33	105	91
MST2	94	14	101	120
MST4	99	16	103	100
GCK	71	22	121	103
MINK1	100	6	101	106
MEKK1	135	13	92	97
MLK1	83	26	99	100
MLK3	99	13	104	93
TAO1	97	8	73	90
ASK1	93	12	94	94
TAK1	105	6	88	103
IRAK4	67	23	107	105
RIPK2	22	19	76	113
TTK	84	15	74	92
Src	115	19	84	95
Lck	111	6	61	96
CSK	108	22	88	92
YES1	113	19	58	88
BTK	96	6	67	105
JAK2	95	2	99	88
SYK	118	20	101	88
EPH-A2	126	71	76	111
EPH-A4	114	13	63	107
EPH-B1	106	77	99	108
EPH-B2	87	8	84	101
EPH-B3	114	8	115	108
EPH-B4	95	27	73	94
FGF-R1	116	11	86	93
HER4	108	13	111	108
IGF-1R	90	7	105	104
IR	108	4	97	96
IRR	99	12	85	97
TrkA	103	8	70	91
VEG-FR	97	11	78	93

Figure S1 Activity of kinases after addition of A66, PIK-75, TGX-221 or IC87114

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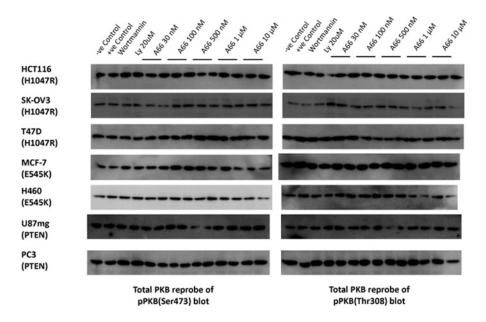
Enzyme ABL1	% Inhibition
	by 10 μM A66
ABL1 ABL1 E255K	11
ABL1 G250E ABL1 T315I	8
ABL1 13151 ABL1 Y253F	- 8 - 8
ABL2 (Arg)	-3
ACVR1 (ALK2)	47
ACVR1B (ALK4) ACVR2B	-2
ADRBK1 (GRK2)	-1
ADRBK2 (GRK3)	-4
AKT1 (PKB alpha)	-1
AKT2 (PKB beta) AKT3 (PKB gamma)	-13
AMPK A1/B1/G1	-1
AMPK A2/B1/G1 AURKA (Aurora A)	-3
AURKB (Aurora B)	2
AURKC (Aurora C)	12
AXL	14
BLK	6
BMPR1A (ALK3)	12
BMX BRAF	3 -10
BRAF	4
BRAF V599E BRAF V599E BRSK1 (SAD1)	-13
BRAF V599E	7
BRSK1 (SAD1) BTK	-4
CAMK1 (CaMK1)	29
CAMK1D (CaMKI delta)	-3
CAMK2A (CaMKII alpha) CAMK2B (CaMKII beta)	-2 -4
CAMK2B (CaMKII beta) CAMK2D (CaMKII delta)	-3
CAMK4 (CaMKIV)	-8
CAMKK1 (CAMKKA)	2
CAMKK2 (CaMKK beta)	14 -14
CDC42 BPA (MRCKA) CDC42 BPB (MRCKB)	7
CDK1/cyclin B	-1
CDK2/cyclin A CDK5/p25	3
CDK5/p35	-1
CDK7/cyclin H/MNAT1	-20
CDK8/cyclin C	13
CDK9/cyclin K CDK9/cyclin T1	-1 -16
CHEK1 (CHK1)	19
CHEK2 (CHK2)	-3
CHUK (IKK alpha)	11
CLK1 CLK2 CLK3	58
	28
CLK4 CSF1R (FMS)	87 9
CSF IR (FINS)	
CSK	7
CSK CSNK1A1 (CK1 alpha 1)	7 0
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta)	7 0 3
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1E (CK1 epsilon)	7 0 3 7
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1E (CK1 epsilon) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2)	7 0 3
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1E (CK1 epsilon) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2)	7 0 3 7 -5
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1E (CK1 epsilon) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2)	7 0 3 7 -5 10 3 7
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1D (CK1 delta) CSNK1G1 (CK1 gaslion) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2)	7 0 3 7 -5 10 3 7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1B (CK1 gasilon) CSNK1G1 (CK1 garmna 1) CSNK1G2 (CK1 garmna 2) CSNK1G3 (CK1 garmna 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK)	7 0 3 7 -5 10 3 7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1G (CK1 geslion) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DCAMKL2 (DK2)	7 0 3 7 -5 10 3 7 1 -37 0
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1B1 (CK1 gesilon) CSNK1G1 (CK1 gemma 1) CSNK1G2 (CK1 gemma 2) CSNK1G3 (CK1 gemma 2) CSNK1G3 (CK1 gemma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DAAMKL2 (DCK2) DCAMKL2 (DCK2) DCAMKL2 (DCK2)	7 0 3 7 -5 10 3 7 1 -37
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1B1 (CK1 genma 1) CSNK1G1 (CK1 gamma 1) CSNK1G3 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DCAMKL2 (DCK2) DCMKL2 (DCK2) DDR1 DDR2 DMPK	7 0 3 7 -5 10 3 7 1 -37 0 0 0 3 2 1
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1G (CK1 epsilon) CSNK1G1 (CK1 gamma 2) CSNK1G2 (CK1 gamma 3) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DAPK3 (ZIPK) DCAMKL2 (CK2) DDR1 DDR1 DDR2 DMPK DNA-PK	7 0 3 7 -55 10 3 7 7 1 -37 0 0 0 3 2 1 1-37
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 delta) CSNK1E (CK1 gesilon) CSNK1G1 (CK1 gamma 1) CSNK1G3 (CK1 gamma 2) CSNK1G3 (CK1 gamma 2) CSNK1G3 (CK1 gamma 2) CSNK2A2 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK) DCAMKL2 (ICK2 glba 2)	7 0 3 7 -5 10 3 7 7 1 13 -37 0 0 0 3 2 2
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 delta) CSNK1B (CK1 genma 1) CSNK1G1 (CK1 gamma 1) CSNK1G3 (CK1 gamma 2) CSNK1G3 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 1) DAPK1 DAPK1 DAPK3 (ZIPK) DCAMKL2 (DCK2) DDR1 DDR2 DMPK DNA-PK DYRK1A DYRK1B DYRK1B	7 0 3 7 7 5 5 10 3 7 7 1 1 3 3 7 0 0 0 3 3 2 2 1 1 1 1 2 1 4 4
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1B (CK1 epsilon) CSNK1B1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK) DCAMKL2 (CCK2) DCR1 DDR2 DMPK DDR4 DNAPK DNA-PK DYRK1A DYRK1A DYRK1B DYRK3 DYRK3	77 00 3 77 -55 110 3 77 1 -37 0 0 3 2 1 1 12 114 4 -12
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1E (CK1 epsilon) CSNK161 (CK1 gamma 1) CSNK162 (CK1 gamma 2) CSNK163 (CK1 gamma 2) CSNK163 (CK1 gamma 2) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK) DCAMKL2 (DCK2) DDR1 DDR2 DMPK DNA-PK DNA-PK DYRK1A DYRK1A DYRK1B DYRK3	7 0 3 7 7 -5 10 3 3 7 7 10 3 3 7 7 1 1 -37 0 0 0 3 3 2 2 1 1 12 14 4 4 4 12 -2 -5 5
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B1 (CK1 pasion) CSNK1B1 (CK1 pasion) CSNK1B2 (CK1 parma 1) CSNK1B2 (CK1 parma 2) CSNK1B2 (CK1 parma 2) CSNK1B2 (CK1 parma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 1) DAPK1 DAPK2 (CIPK) DAPK3 (ZIPK) DCAMKL2 (DCK2) DDR1 DDR2 DMPK DNA-PK DNA-PK DYRK1B DYRK1B DYRK1B DYRK1B DYRK1B DYRK1B EEF2K EGFR (Er/BB1)	77 00 3 77 -55 110 3 77 1 -37 0 0 3 2 1 1 12 114 4 -12
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1E (CK1 epsilon) CSNK161 (CK1 gamma 1) CSNK162 (CK1 gamma 2) CSNK163 (CK1 gamma 2) CSNK163 (CK1 gamma 2) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK) DCAMKL2 (DCK2) DDR1 DDR2 DMPK DNA-PK DNA-PK DYRK1A DYRK1A DYRK1B DYRK3	7 0 3 7 7 -5 10 3 3 7 7 10 3 3 7 7 1 1 -37 0 0 0 3 3 2 2 1 1 12 14 4 4 4 12 -2 -5 5
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1G (CK1 epsilon) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DOR1 DDR2 DMPK DNA-PK DYRK1A DYRK1B DYRK3 DYRK1B DYRK3 DYRK3 DYRK3 DYRK4 EEF2K EGFR (ErbB1) EGFR (ErbB1) EGFR (ErbB1) EGFR (ErbB1) EGFR (ErbB1)	7 7 0 3 7 7 5 5 10 10 3 3 7 7 1 1 3 7 7 1 1 2 1 2 1 1 4 4 1 1 2 2 5 5 0 3 3 1 1 7 7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B1 (CK1 pasion) CSNK1B1 (CK1 pasion) CSNK1B2 (CK1 pamma 1) CSNK1B2 (CK1 pamma 2) CSNK1B2 (CK1 pamma 2) CSNK1B2 (CK1 pamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A2 (CK2 alpha 1) DAPK1 DAPK2 (CPK2 plbha 2) DAPK1 DAPK3 (ZIPK) DCAMKL2 (DCK2) DDR1 DDR2 DMPK DNA-PK DNA-PK DYRK1B DYRK1B DYRK1B DYRK1B DYRK1B EEF2K EGFR (ErbB1) L858R EGFR (ErbB1) L859R EGFR (ErbB1) T190M EGFR (ErbB1) T790M EGFR (ErbB1) T790M EGFR (ErbB1) T790M	7 0 3 7 7 -5 10 10 3 7 7 1 1 -37 0 0 0 3 3 2 2 1 1 12 14 4 4 -12 -5 0 0 -3 -1 1 7 6 6
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 delta) CSNK1B (CK1 epsilon) CSNK1G1 (CK1 gesilon) CSNK1G1 (CK1 gamma 2) CSNK1G2 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DCAMKL2 (CK2) DDR1 DDR2 DMPK DNA-PK DYRK1A DYRK1A DYRK1B DYRK3 EGFR (ErbB1)	7 7 0 3 7 7 5 5 10 10 3 3 7 7 1 1 3 7 7 1 1 2 1 2 1 1 4 4 1 1 2 2 5 5 0 3 3 1 1 7 7
CSK CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1D (CK1 delta) CSNK1G (CK1 delta) CSNK1G (CK1 geslion) CSNK1G1 (CK1 gamma 1) CSNK1G2 (CK1 gamma 2) CSNK1G3 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DAPK1 DAPK3 (ZIPK) DCAMKL2 (CK2 alpha 2) DPR1 DDR2 DMPK DNR4 DPR1 DNR1 DPR1 DNR-PK DYRK1A DYRK1A DYRK1B DYRK3 EEFZK EGFR (ErbB1) L85R EGFR (ErbB1) EFHA1	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B1 (CK1 gesilon) CSNK1G1 (CK1 gesilon) CSNK1G2 (CK1 germa 1) CSNK1G3 (CK1 germa 2) CSNK1G3 (CK1 germa 2) CSNK1G3 (CK1 germa 2) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK4 (DCK2) DDR1 DDR2 DMPK DNA-PK DYRK1A DYRK1B DYRK1B DYRK1B DYRK3 EGFR (ErbB1)11858R EGFR (ErbB1)11858R EGFR (ErbB1)1790M	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1D (CK1 delta) CSNK1B (CK1 epsilon) CSNK1B (CK1 genima 1) CSNK1G1 (CK1 gamma 2) CSNK1G2 (CK1 gamma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DCAMK12 (CK2 alpha 2) DAPK1 DAPK3 (ZIPK) DCAMK12 (CK2) DOR1 DOR2 DMPK DNA-PK DYRK1A DYRK1A DYRK1B DYRK3 DYRK1A CFF (ErbB1) EGFR (ErbB1)	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B1 (CK1 gesilon) CSNK1G1 (CK1 gesilon) CSNK1G2 (CK1 germa 1) CSNK1G3 (CK1 germa 2) CSNK1G3 (CK1 germa 2) CSNK1G3 (CK1 germa 2) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK4 (DCK2) DDR1 DDR2 DMPK DNA-PK DYRK1A DYRK1B DYRK1B DYRK1B DYRK3 EGFR (ErbB1)11858R EGFR (ErbB1)11858R EGFR (ErbB1)1790M	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 gellon) CSNK1G1 (CK1 gellon) CSNK1G3 (CK1 gellon) CSNK1G3 (CK1 gellon) CSNK1G3 (CK1 gellon) CSNK1G3 (CK1 gellon) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK1 DAPK3 (ZIPK) DCAMKL2 (CK2 alpha 2) DPR1 DDR2 DMPK DNA-PK DVRK1A DYRK1A DYRK1B DYRK1A DYRK1B CFR (ErbB1) EGFR (ErbB1) EGFR (ErbB1) L85R EFHA1 EPHA3 EPHA4 EPHA5 EPHA6 EPHA6 EPHA6 EPHA8	7 0 3 7 7 -5 10 10 10 3 7 7 1 1 -3 7 0 0 0 3 3 2 2 1 1 12 14 4 4 -112 -2 5 0 0 3 3 -1 1 7 7 6 6 -1 1 6 6 -1 1 6 6 -1 1 9 2 2 -2 -3 2 2 2
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 gesion) CSNK1G1 (CK1 gemma 1) CSNK1G2 (CK1 gemma 2) CSNK1G3 (CK1 gemma 2) CSNK1G3 (CK1 gemma 3) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DR1 DDR2 DMPK DNA-PK DYRK1B DYRK3 DYRK1B DYRK3 DYRK1B DYRK3 EEFFAK EGFR (ErbB1) L856Y EGFR (ErbB1) L856Y EGFR (ErbB1) L856Y EGFR (ErbB1) T790M EGFR (ErbB1) T790M EGFR (ErbB1) T790M EFPHA3 EPHA3 EPHA4 EPHA5 EPHA5 EPHA6 EPHA6 EPHA7 EPHA6 EPHA7 EPHA6 EPHA7 EPHA6 EPHB1	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 gellan) CSNK1B (CK1 gellan) CSNK1G1 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK2A2 (CK2 alpha 2) DAPK1 DAPK3 (ZPK) DR1 DR2 DMPK DNA-PK DYRK1A DYRK1B DYRK1B DYRK1B DYRK3 EGFR (ErbB1) EFHA1 EFHA3 EFHA4 EFHA5 EFHA6 EFHB1 EFHB1 EFHB2	7 0 3 7 7 -5 10 10 10 3 7 7 1 1 -3 7 0 0 0 3 3 2 2 1 1 12 14 4 4 -112 -2 5 0 0 3 3 -1 1 7 7 6 6 -1 1 6 6 -1 1 6 6 -1 1 9 2 2 -2 -3 2 2 2
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 gellan) CSNK1B (CK1 gellan) CSNK1G1 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK2G3 (CK2 alpha 2) CSNK2G3 (CK2 alpha 2) DAPK3 (CK2 alpha 2) DYRK3 DYRK4 EGFR (ErbB1) EGFR (ErbB1) L85R EFHA1 EPHA2 EPHA3 EPHA4 EPHA5 EPHA6 EPHA6 EPHB1 EPHB1 EPHB2 EPHB1 EPHB2	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B1 (CK1 gesilon) CSNK1G1 (CK1 german 1) CSNK1G2 (CK1 german 2) CSNK1G3 (CK1 german 3) CSNK3G1 (CK2 alpha 1) CSNK3G1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK1 DAPK3 (ZIPK) DAPK1 DAPK3 (ZIPK) DCAMKL2 (DCK2) DDR1 DDR2 DMPK DNA-PK DVRK1 DVRK1 DVRK1 DYRK1B DYRK1B DYRK1B DYRK3 EGFR (ErbB1) EFPHA1 EFPHA3 EFPHA3 EFPHA4 EFPHA5 EFPHA5 EFPHA5 EFPHA6 EFPHB1 EFPHB1 EFPHB2 EFPHB8 EFPHB8 EFPBB2 (EFBB2) EFBBB4 (HER4)	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 gellan) CSNK1B (CK1 gellan) CSNK1G1 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK1G3 (CK1 gellan) CSNK2A2 (CK2 alpha 1) CSNK2A2 (CK2 alpha 2) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DOR1 DDR2 DMPK DNA-PK DYRK1A DYRK1A DYRK1B DYRK1B DYRK3 EGFR (ErbB1) EFHA1 EFHA2 EFHA3 EFHA4 EFHA5 EFHA6 EFHB1 EFHB2 EFHBB2 EFHBB2 EFRBB2 (HER2) ERBB4 (HER2)	7 7 0 3 7 7 -5 10 3 3 7 7 1 1 37 7 1 1 2 1 2 1 2 1 2 1 4 4 -12 -2 -5 0 0 3 3 -1 1 7 6 6 1 1 1 6 1 1 1 6 1
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B1 (CK1 gealion) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK1 DAPK3 (ZIPK) DAPK1 DAPK3 (ZIPK) DAPK1 DPR1 DDR2 DMPK DNA-PK DYRK1A DYRK1B DYRK1B DYRK1B DYRK1B EFF2K EGFR (ErbB1) EFPHA1 EFPHA2 EFPHA3 EFPHA4 EFPHA5 EFPHA5 EFPHB1 EFPHB2 EFPHB2 ERBB2 (HER2) ERBB2 (HER2) EFRBB1 (HER2) EFRBB1 (HER2) EFRBB1 (HER2) EFRBB1 (HER2) EFRBB1 (HER2) EFRBB1 (HER2)	7
CSK CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1A1 (CK1 alpha 1) CSNK1B (CK1 gesilon) CSNK1B (CK1 gesilon) CSNK1G1 (CK1 gesilon) CSNK1G3 (CK1 gamma 2) CSNK1G3 (CK1 gamma 2) CSNK2A1 (CK2 alpha 1) CSNK2A1 (CK2 alpha 1) DAPK1 DAPK1 DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK3 (ZIPK) DAPK1 DDR2 DMPK DNA-PK DYRK1A DYRK1A DYRK1B DYRK1B DYRK3 EGFR (ErbB1) FEFHA1 EPHA3 EPHA4 EPHA5 EPHA6 EPHB1 EPHB1 EPHB1 EPHB2 EFHB3 EPHB4 EFBB2 (HER4) FER	7

	% Inhibition
Enzyme	by 10 µM A66
Enzyme FGFR4 FGR	16
FLT1 (VEGFR1)	6 0
FLT3	12
FLT3 D835Y	14
FLT4 (VEGFR3) FRAP1 (mTOR)	2
FRK (PTK5) FYN	2
FYN GRK4	6
GRK5	-0
GRK6	8
GRK7	-14
GSG2 (Haspin) GSK3A (GSK3 alpha)	-14 -6
GSK3B (GSK3 beta)	-1
HCK	3
HIPK1 (Myak) HIPK2	-12 4
HIPK3 (YAK1)	-2
HIPK4	30
IGF1R	-9
IKBKB (IKK beta)	-1
IKBKE (IKK epsilon)	0
INSR INSRR (IRR)	1
IRAK1	-18
IRAK1 IRAK4	6
JAK1	-7 10
JAK2	10 19
JAK2 JH1 JH2	15
JAK2 JH1 JH2 V617F JAK3	3
JAK3 KDR (VEGFR2)	14
KIT	29
KIT T670I KIT V654A	0
KIT V654A	8
LCK LIMK1	7
LIMK2	4
LRRK2	35
LRRK2 G2019S	56
LTK (TYK1) LYN A LYN B	0
LYN B	-4
MAP2K1 (MEK1)	-3
MAP2K1 (MEK1) MAP2K1 (MEK1) S218D S222D	14 5
MAP2K2 (MEK2)	-6
MAP2K2 (MEK2) MAP2K2 (MEK2) MAP2K3 (MEK3)	10
MAP2K6 (MKK6)	-10
MAP2K6 (MKK6)	8
MAP2K6 (MKK6) S207E T211E	-7
MAP3K10 (MLK2) MAP3K11 (MLK3)	10 5
MAP3K14 (NIK)	ő
MAP3K2 (MEKK2)	-19
MAP3K3 (MEKK3) MAP3K5 (ASK1)	10
MAP3K7/MAP3K7IP1 (TAK1-TAB1)	-5 15
MAP3K8 (COT) MAP3K9 (MLK1)	-17
MAP3K9 (MLK1)	32
MAP4K2 (GCK) MAP4K4 (HGK)	8 11
MAP4K5 (KHS1)	10
MAPK1 (ERK2) MAPK10 (JNK3)	-2
MAPK10 (JNK3) MAPK10 (JNK3)	-5 29
MAPK11 (p38 beta)	8
MAPK12 (p38 gamma)	-5
MAPK13 (p38 delta)	-7 15
MAPK14 (p38 alpha) MAPK14 (p38 alpha) Direct	4
MAPK3 (ERK1)	-10
MAPK8 (JNK1)	14
MAPK8 (JNK1) MAPK9 (JNK2)	6
MAPK9 (JNK2) MAPKAPK2	18
MAPKAPK2 MAPKAPK3	2
MAPKAPK3 MAPKAPK5 (PRAK)	4 -6
MARK1 (MARK)	-8
MARK2	-19
MARK3 MARK4	-5 -15
MATK (HYL)	-15
MELK	11
MERTK (cMER)	1
MET (cMet) MET M1250T	20
MINK1	-3
MKNK1 (MNK1)	-7
MKNK2 (MNK2)	3
MLCK (MLCK2) MST1R (RON)	16 9
MST4	9
	-9
MUSK MYLK (MLCK)	2

	% Inhibition
Enzyme	by 10 µM A66
MYLK2 (skMLCK) NEK1	18
NEK2 NEK4	-3
NEK6	2
NEK7 NEK9	-6 -8
NLK NTRK4 (TRKA)	6
NTRK2 (TRKB)	2
NTRK3 (TRKC) NUAK1 (ARK5)	-18
PAK1	2
PAK2 (PAK65) PAK3	-1 10
PAK4	0
PAK6 PAK7 (KIAA1264)	10 11
PASK	1
PDGFRA (PDGFR alpha) PDGFRA D842V	11
PDGFRA T674I	3
PDGFRA V561D	4
PDGFRB (PDGFR beta) PDK1	-3 -1
PDK1 Direct	-1 4
PHKG1 PHKG2	-1
PI4KA (PI4K alpha) PI4KB (PI4K beta)	-19 98
PIK3C2A (PI3K-C2 alpha) PIK3C2B (PI3K-C2 beta)	-2
PIK3C2B (PI3K-C2 beta) PIK3C3 (hVPS34)	77 21
PIK3CA/PIK3R1 (p110 alpha/p85 alp	96
PIK3CD/PIK3R1 (p110 delta/p85 alp PIK3CG (p110 gamma)	91 86
PIM1	-4
PIM2 PKN1 (PRK1)	-4 -19
PLK1	-3
PLK2 PLK3	-24 3
PRKACA (PKA)	-2
PRKCA (PKC alpha) PRKCB1 (PKC beta I) PRKCB2 (PKC beta II) PRKCD (PKC delta)	3
PRKCB2 (PKC beta II)	-10
PRICE (PIC epsilon)	9
PRKCG (PKC gamma)	6 9
PRKCH (PKC eta) PRKCI (PKC iota)	9
PRKCN (PKD3) PRKCQ (PKC theta)	7 10
PRKCZ (PKC zeta)	3
PRKD1 (PKC mu) PRKD2 (PKD2) PRKG1	12 7
PRKG1 PRKG2 (PKG2)	-2 -5
PRKX	-3
PTK2 (FAK) PTK2B (FAK2)	4 10
PTK6 (Brk)	4
RAF1 (cRAF) Y340D Y341D RAF1 (cRAF) Y340D Y341D	-4 14
RET	0
RET V804L RET Y791F	-3 5
RIPK2 ROCK1 ROCK2	66
ROCK2	-17
ROS1 RPS6KA1 (RSK1)	-11 -1
RPS6KA2 (RSK3)	-4
RPS6KA3 (RSK2) RPS6KA4 (MSK2)	-10
RPS6KA5 (MSK1)	-6
RPS6KA6 (RSK4) RPS6KB1 (p70S6K)	0
SGK (SGK1)	-3
SGK2 SGKL (SGK3)	8
SLK	2 -5
SNF1LK2 SPHK1	10
SPHK2 SRC	-23 11
SRC N1	8
SRMS (Srm) SRPK1	8
SRPK2	0
STK16 (PKL12) STK17A (DRAK1)	-4 11
STK22B (TSSK2)	-12
STK22D (TSSK1) STK23 (MSSK1)	2
STK24 (MST3) STK25 (YSK1)	-2 -1
STK3 (MST2) STK33	12
STK33 STK4 (MST1)	-5 11
(morr)	

Enzyme	% Inhibition by 10 µM A66
SYK	8
TAOK2 (TAO1)	0
TAOK3 (JIK)	3
TBK1	-9
TEC	17
TEK (Tie2)	19
TGFBR1 (ALK5)	-2
TNK2 (ACK)	8
TTK	-10
TXK	1
TYK2	-8
TYRO3 (RSE)	5 6
WEE1	6
WNK2	10
YES1	9
ZAK	5
ZAP70	4
Leger	nd
< 40% Inhi	
40% - 80% Ir	hibition
≥ 80% Inhi	bition

Figure S2 Inhibition of kinases by A66



 $Figure \ S3 \quad Reprobes \ of \ blots \ in \ Figure \ 3 \ of \ the \ main \ paper \ with \ the \ total \ PKB \ antibody$

Ly, LY294002.

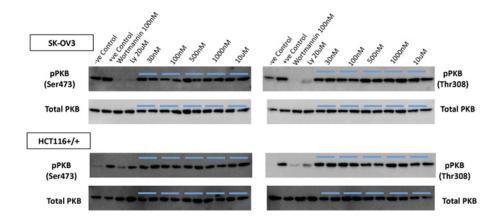


Figure S4 A66 R enantiomer does not block signalling to PKB in cells with the PIK3CA H1047R mutation

Experiments were performed as in Figure 3 of the main paper, except that the R form of A66 was used. Ly, LY294002.

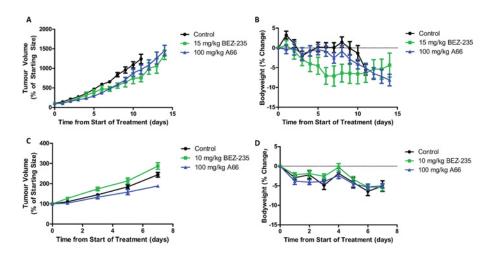


Figure S5 In vivo antitumour efficacy and body weight change following treatment with A66 and BEZ-235 in the U87MG and HCT-116 tumour xenograft models

(A) Average tumour volume and (B) body weight loss during QD \times 14 dosing with 100 mg of A66/kg of body weight and 15 mg of BEZ-235/kg of body weight in mice with U87MG tumours. (C) Average tumour volume and (D) body weight loss during QD \times 7 dosing with 100 mg of A66/kg of body weight and 10 mg of BEZ-235/kg of body weight in mice with HCT-116 tumours. Bars represent the means \pm S.E.M. for five to seven animals.

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