

Supplementary Figure Legends

Figure S1 **IC₅₀ analysis of ability of VPS34-IN1 to inhibit Vps34 kinase employing Life Technology assay.** (A) Recombinant human Vps34 was assayed by measuring phosphorylation of PtdIns in a ³²P-radioactive kinase assay by Selectscreen biochemical kinase profiling service at Life technology. The assay conditions are described at www.lifetechnologies.com/selectscreen. IC₅₀ graph was generated using prism software with non-linear regression analysis. Assays were undertaken in duplicates and data presented as mean ± SD and activity plotted relative to 100% activity in DMSO control.

Figure S2 Protein kinase profiling of the VPS34-IN1 at a single concentration of 1µM carried out against the ProKinase panel of 300 protein kinases. Results for each kinase are presented as the mean kinase activity ± SD for an assay undertaken in triplicate relative to a Control kinase assay in which inhibitor was omitted. Abbreviation used for each kinase and assay conditions utilised are defined at the (<http://www.proqinase.com>)

Figure S3 **IC₅₀ analysis of ability of VPS34-IN1 to inhibit lipid kinases employing ProKinase screen technology.** IC₅₀ graphs for PIK3C3, PIP5K1A and PIP5K1C were generated using Prism software with non-linear regression analysis. Abbreviation used for each kinase and assay conditions utilised are defined at the (<http://www.proqinase.com>)

Table S1

Results are presented as the percentage of kinase activity in DMSO control reactions. Protein kinases were assayed *in vitro* in the presence of 1µM VPS34-IN1 inhibitor as described on the International Centre for Kinase Profiling website (<http://www.kinase-screen.mrc.ac.uk/>), and the results are means ± S.D. for triplicate reactions. Abbreviations are as follows: ABL, Abelson tyrosine-protein kinase 1; AMPK, AMP-activated protein kinase; ASK, apoptosis signal-regulating kinase; BRK, breast tumour kinase; BRSK, brain-specific kinase; BTK, Bruton's tyrosine kinase; CaMK, calmodulin-dependent kinase; CaMKK, CaMK kinase; CDK, cyclin-dependent kinase; CHK, checkpoint kinase; CK, casein kinase; CLK, CDC-like kinase; CSK, C-terminal Src kinase; DAPK, death-associated protein kinase; DDR, discoidin domain receptor; DYRK, dual-specificity tyrosine-phosphorylated and regulated kinase; EF2K, elongation-factor-2 kinase; EIF2AK, eukaryotic translation initiation factor 2-alpha kinase; EPH, ephrin; ERK, extracellular signal-regulated kinase; FGF-R, fibroblast growth factor receptor; GSK, germinal centre kinase; GSK, glycogen synthase kinase; HER, human epidermal growth factor receptor; HIPK, homeodomain-interacting protein kinase; IGF1R, IGF1 receptor; IKK, inhibitory κB kinase; IR, insulin receptor; IRAK, interleukin-1 receptor-associated kinase; IRR, insulin-related receptor; JAK, Janus kinase; JNK, c-Jun N-terminal kinase; Lck, lymphocyte cell-specific protein tyrosine kinase; LKB1, liver kinase B1; MAPK, mitogen-activated protein kinase; MAPKAP-K, MAPK-activated protein kinase; MARK, microtubule-affinityregulating kinase; MEKK, MAP kinase kinase kinase; MELK, maternal

embryonic leucine zipper kinase; MINK, misshapen/NIK-related kinase; MKK, MAPK kinase; MLK, mixed lineage kinase; MNK, MAPK-integrating protein kinase; MPSK, myristoylated and palmitoylated serine/threonine-protein kinase; MSK, mitogen- and stress-activated protein kinase; MST, mammalian homologue Ste20-like kinase; NEK, NIMA (never in mitosis in *Aspergillus nidulans*)-related kinase; NUAK, novel (NUA) family SnF1-like kinase; OSR, oxidative stress-responsive kinase; PAK, p21-activated protein kinase; PDGFRA, platelet-derived growth factor receptor- α ; PDK, phosphoinositide-dependent kinase; PHK, phosphorylase kinase; PIM, provirus integration site for Moloney murine leukaemia virus; PINK (insect homologue), PTEN-induced kinase; PKA, cAMP-dependent protein kinase; PKB, protein kinase B; PKC, protein kinase C; PKD, protein kinase D; PLK, polo-like kinase; PRAK, p38-regulated activated kinase; PRK, protein kinase C-related kinase; RIPK, receptor-interacting protein kinase; ROCK, Rho-dependent protein kinase; RSK, ribosomal S6 kinase; S6K, p70 ribosomal S6 kinase; SGK, serum- and glucocorticoid-induced protein kinase; SIK, salt-induced kinase; smMLCK, smooth muscle myosin light-chain kinase; SRPK, serine/arginine protein kinase; STK, serine/threonine kinase; SYK, spleen tyrosine kinase; TAK, TGF β -activated kinase; TAO, thousand and one amino acid; TBK1, TANK-binding kinase 1; TESK, testis-specific protein kinase; TGFBR, TGF β receptor; TIE, tyrosine-protein kinase receptor; TLK, tousled-like kinase; TrkA, tropomyocin receptor kinase; TSSK, testis-specific serine/threonine-protein kinase; TTBK, tau-tubulin kinase; ULK, Unc-51-like kinase; VEGFR, vascular endothelial growth factor receptor; WNK, with no lysine; YES1, Yamaguchi sarcoma viral oncogene homologue 1; ZAP, ζ -chain-associated protein.

FIGURE S1

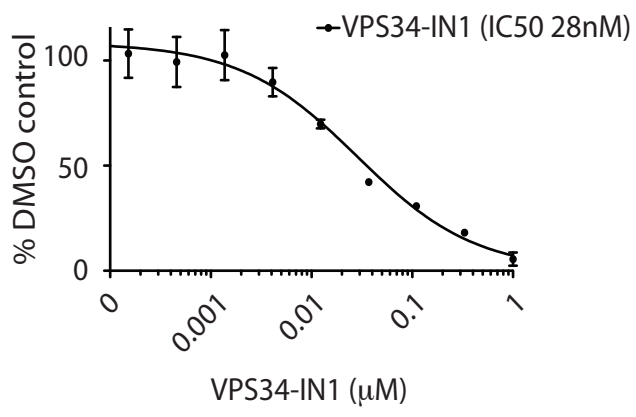
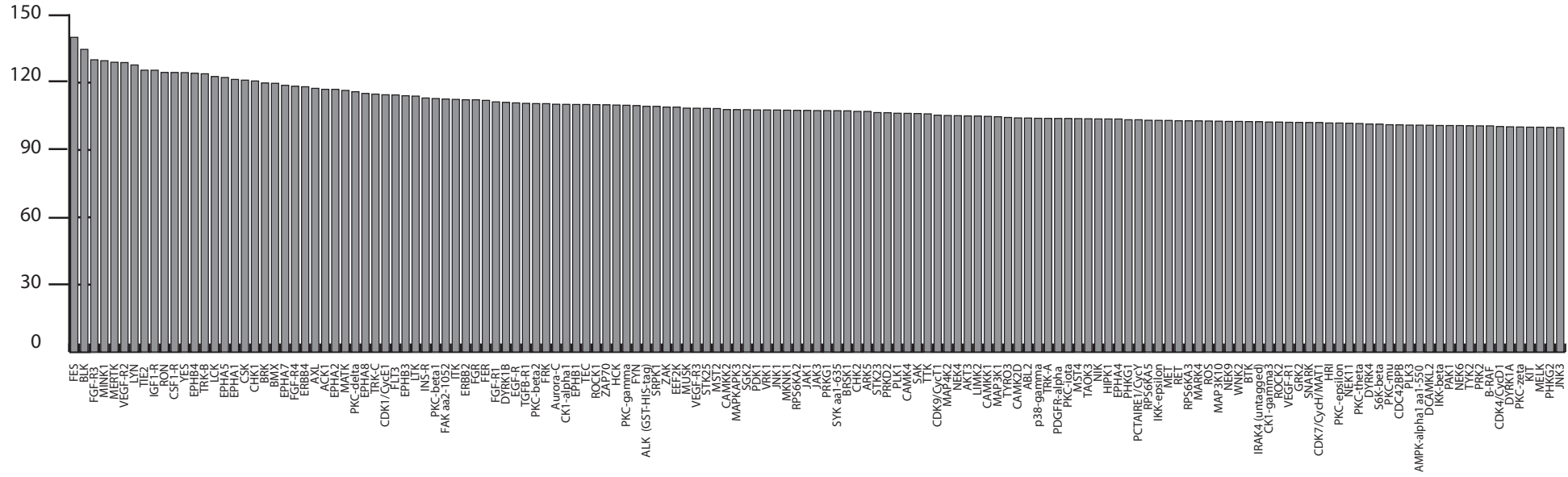


FIGURE S2

VPS34-IN1, 1 μ M (ProQinase panel)



VPS34-IN1, 1 μ M (ProQinase panel)

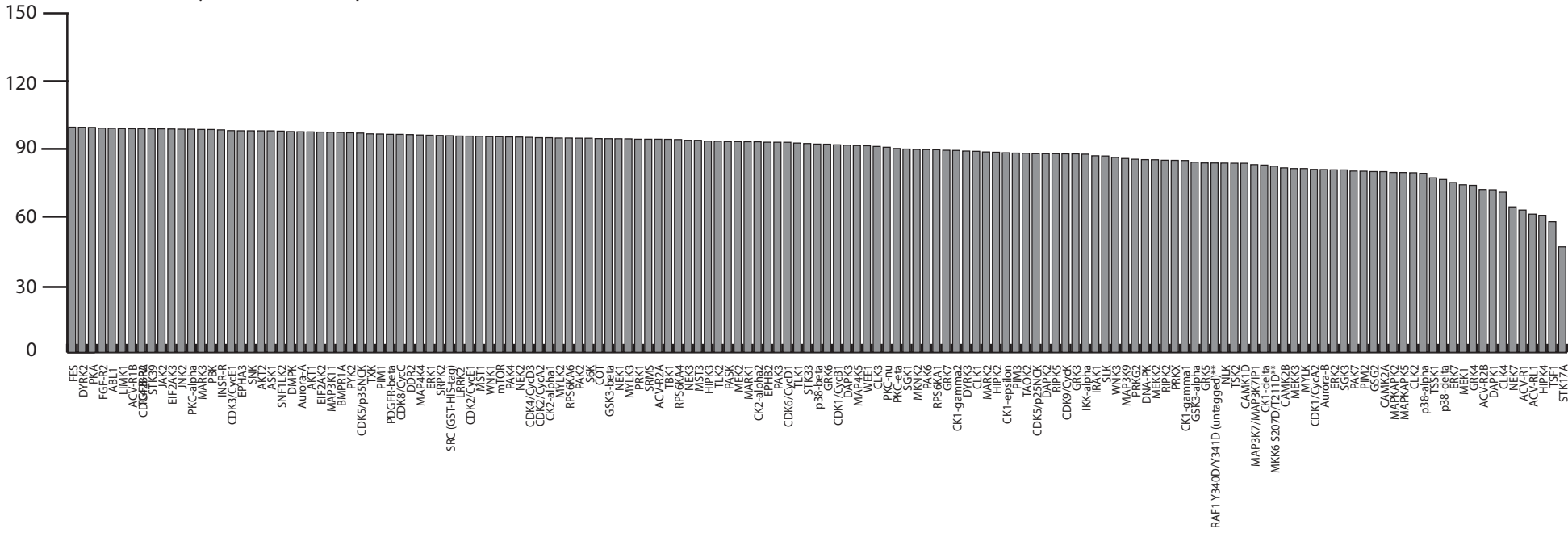


FIGURE S3

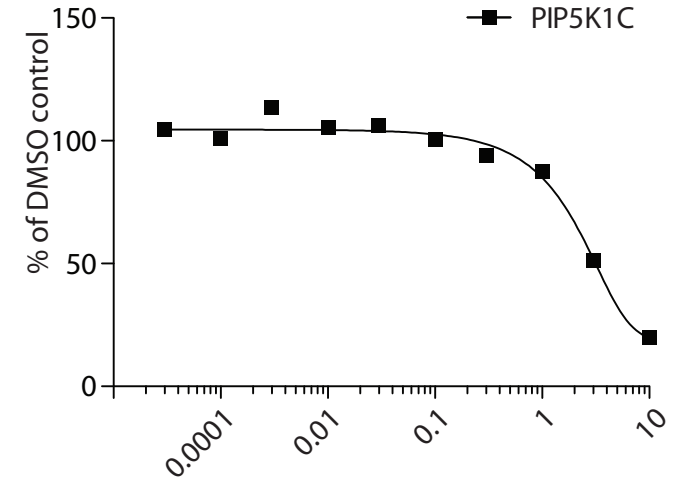
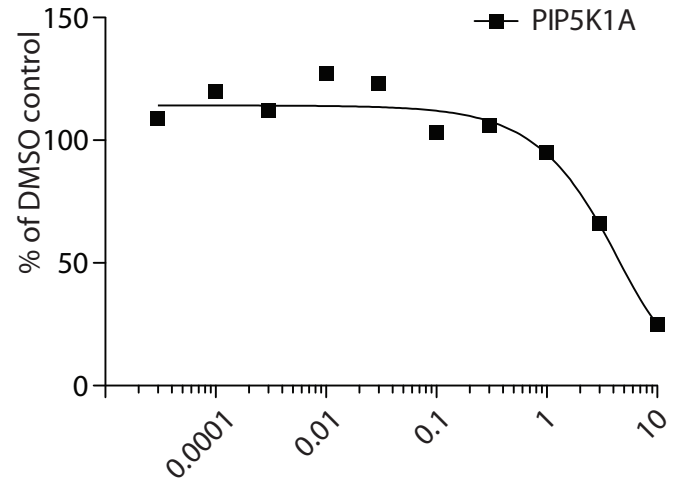
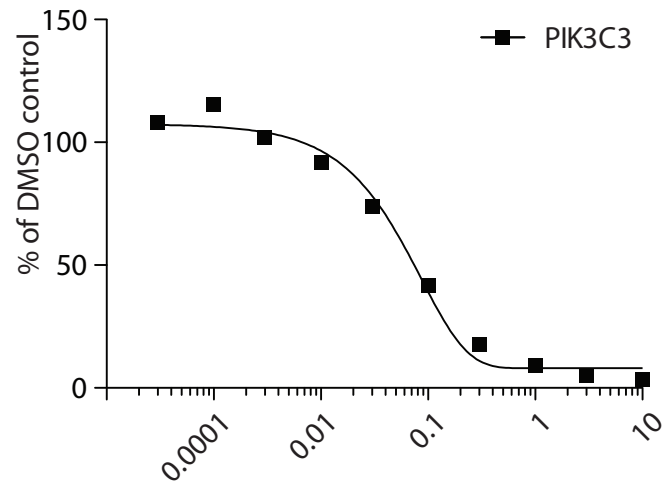


Table S1

p38g MAPK	133	NUAK1	112	PAK4	103
IRAK4	133	DYRK3	112	RSK2	103
CSK	132	SIK3	112	PKCz	103
MLK3	129	JNK1	112	CHK2	103
TBK1	125	p38d MAPK	111	NEK2a	103
p38a MAPK	125	MKK2	111	MINK1	103
EIF2AK3	125	EPH-B3	111	IKKe	103
ASK1	124	ROCK 2	111	BRK	103
MKK6	124	CK2	111	IGF-1R	101
STK33	124	SRPK1	111	EPH-A2	101
PKBb	123	DDR2	111	HER4	101
TGFBR1	123	PAK2	111	MNK2	100
MNK1	122	PKCy	111	TLK1	100
CK1γ2	122	MAPKAP-K2	110	RSK1	99
MKK1	122	Aurora A	110	EPH-B1	99
PDGFRA	121	ZAP70	110	NEK6	98
MST2	120	IR	109	ULK1	98
MLK1	119	MEKK1	109	BRSK2	98
PKCa	119	PINK	109	SmMLCK	97
MST3	118	MARK3	109	PAK6	97
ULK2	118	DYRK2	109	AMPK (hum)	96
MPSK1	118	EPH-B2	109	PAK5	96
TSSK1	118	BRSK1	109	DAPK1	96
CHK1	118	PIM1	108	HIPK2	96
HIPK3	117	TTK	108	JNK3	95
MAP4K3	117	CAMKKb	108	FGF-R1	95
PRK2	116	BTK	108	TESK1	95
CAMK1	116	MELK	108	TIE2	93
WNK1	116	MARK2	108	EPH-A4	93
S6K1	116	HIPK1	108	JAK2	93
PKBa	116	SGK1	108	Lck	92
ERK2	116	ERK1	108	SYK	91
MAPKAP-K3	115	MST4	108	CDK9-Cyclin T1	91
EF2K	115	LKB1	106	TTBK2	88
p38b MAPK	115	EPH-B4	106	CDK2-Cyclin A	88
MARK4	115	IKKb	106	ABL	87
PKD1	115	SIK2	106	Src	84
MARK1	114	TTBK1	106	Aurora B	83
PLK1	114	MAP4K5	105	CLK2	82
OSR1	114	PDK1	105	TAO1	80
PIM3	114	DYRK1A	105	RIPK2	79
JNK2	113	CK1δ	105	YES1	77
PIM2	113	MSK1	105	TrkA	70
VEG-FR	113	PHK	105	GSK3b	51
IRR	113	PRAK	105	TAK1	40
IRAK1	112	ERK5	104	ERK8	36
PKA	112	GCK	104		