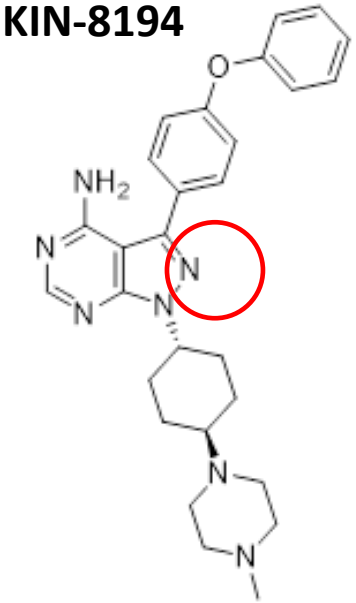
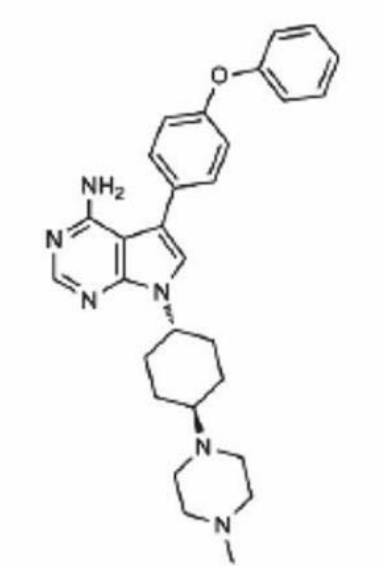
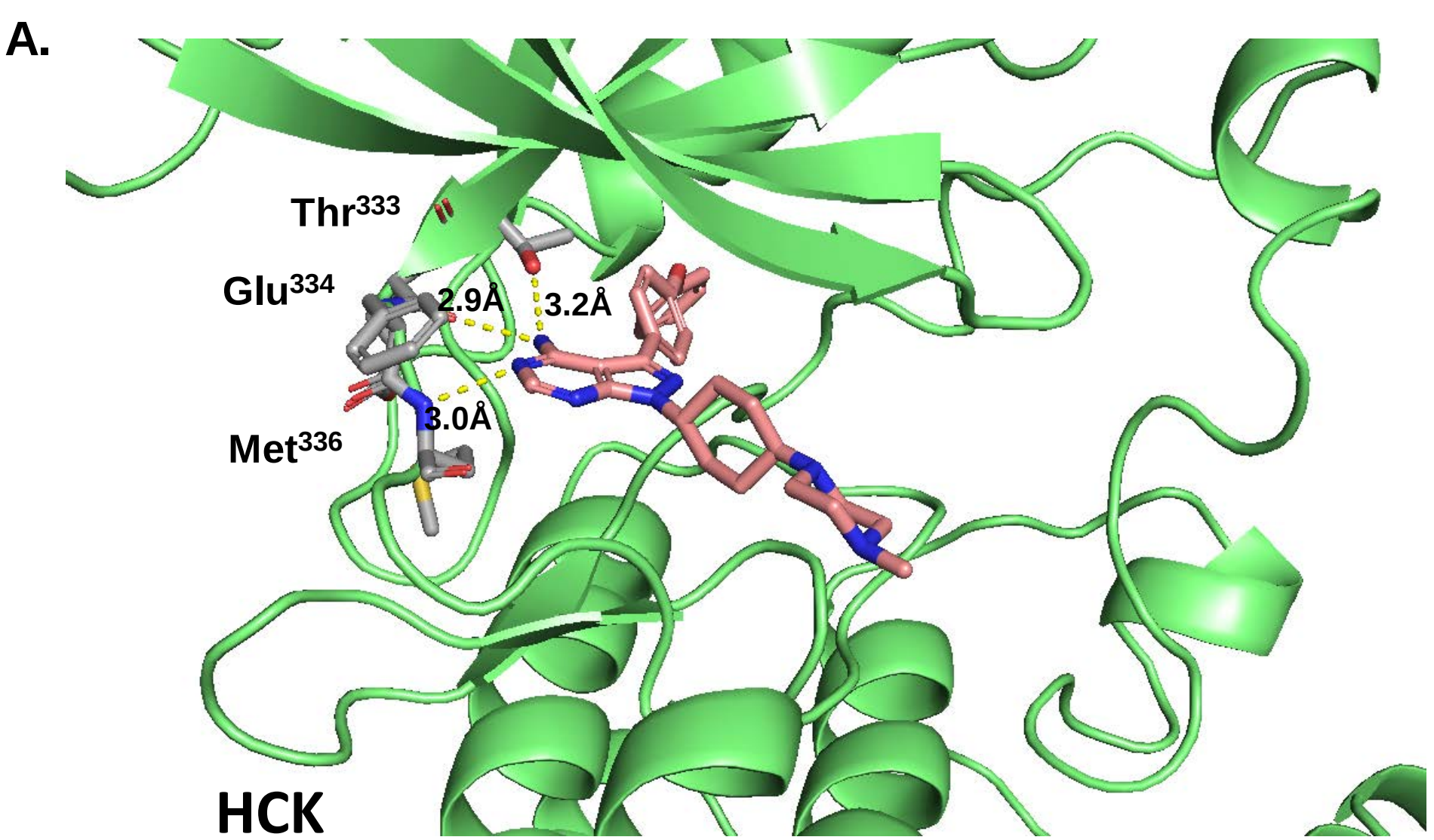
KIN-8194



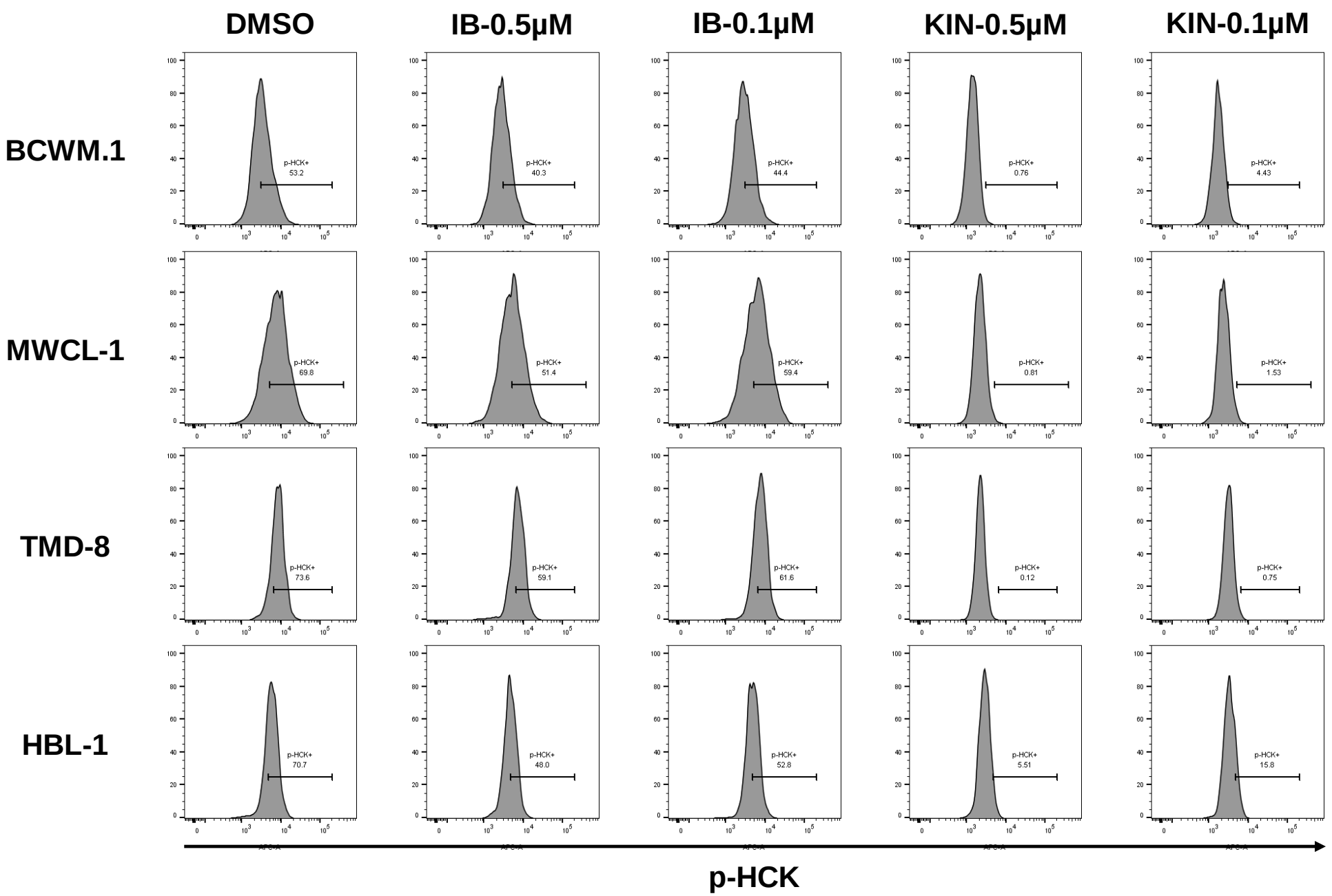
A419259/RK-20449



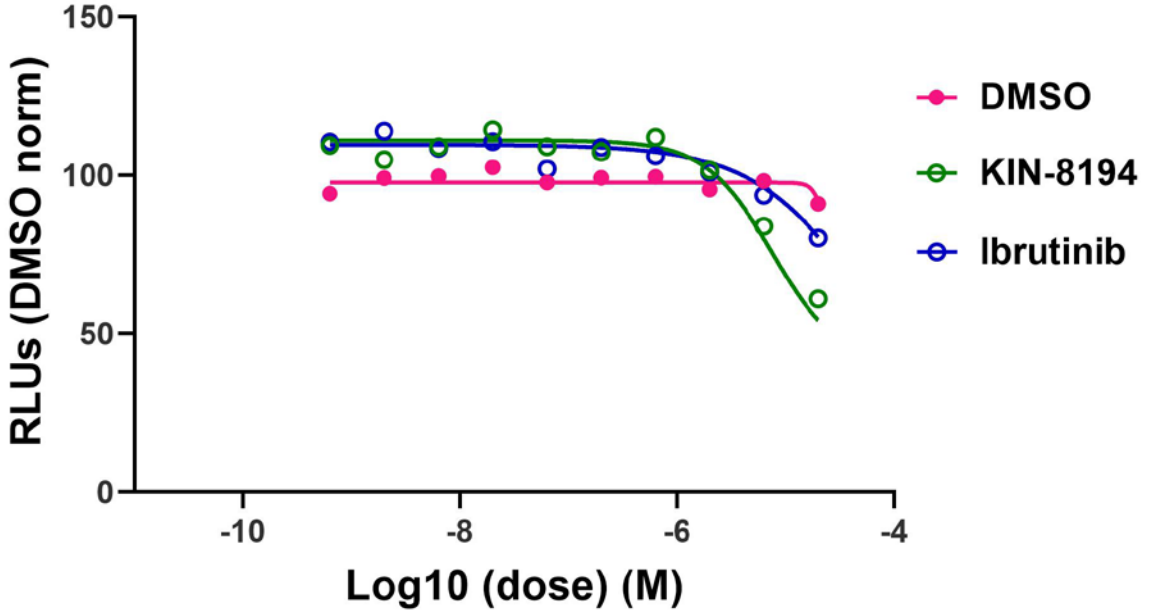
Supplemental Figure 1. Comparison of KIN-8194 and A419259 (RK20449) Chemical Structures.



Supplementary Figure 2. Docking study of KIN-8194 into the co-crystal structure of (A) HCK with A419259 (pdb:5zj6) and (B) BTK with Ibrutinib



Supplementary Figure 3. Changes in HCK activation by flow cytometry following treatment with either ibrutinib (IB) or KIN-8194 (KIN) in MYD88-mutated lymphoma cell lines at



Supplementary Figure 4. Comparative dose-response curves for ibrutinib and KIN-8194 in MYD88 and CARD11 mutated OCI-Ly3 ABC DLBCL cells. Experiment was performed in triplicate, and representative experiment is shown.

A419259

Microsome stability

Species	$t_{1/2}$ (min)
Mouse	76.8
Rat	69.9
Human	33.6

Plasma protein binding

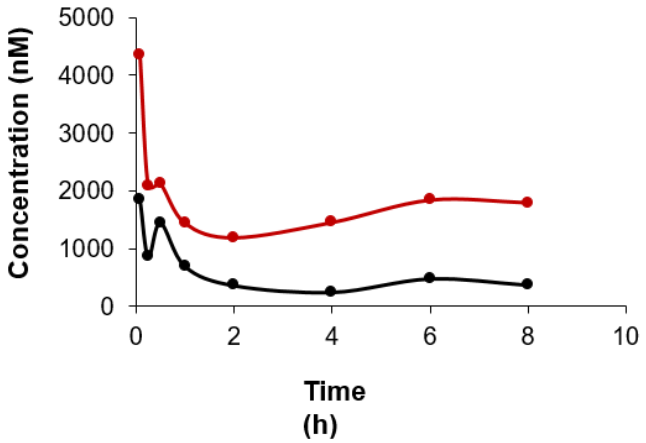
Species	%
Mouse	99.8%
Rat	99.7%
Dog	99.2%
Human	99.8%

PK parameters

$t_{1/2}$ = 5.7 h
Cl = 10.78 mL/min/kg
Vss = 4.9 L/kg
$t_{1/2}$ = 176.0 h
AUC = 13.0 µM•h
F= 65.5 %

Mouse pharmacokinetics

i.v.: 2 mg/kg, 0.2 mg/mL A419259•3HCl in saline
p.o.: 10mg/kg, 1 mg/mL A419259•3HCl in saline



KIN-8194

Microsome stability

Species	$t_{1/2}$ (min)
Mouse	106.4
Rat	>120
Human	49.5

Plasma protein binding

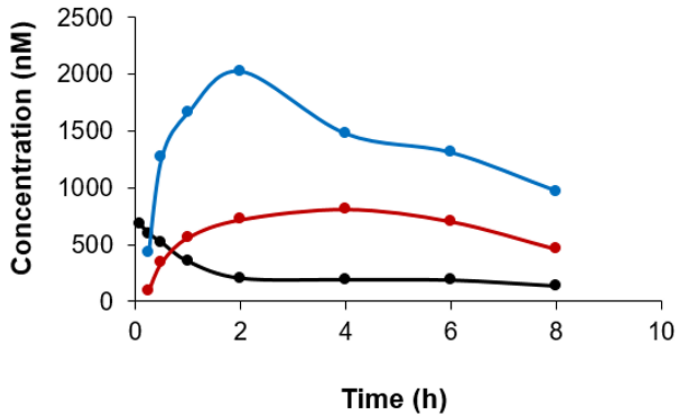
Species	%
Mouse	97.7
Rat	95.5
Dog	95.0
Human	95.7

PK parameters

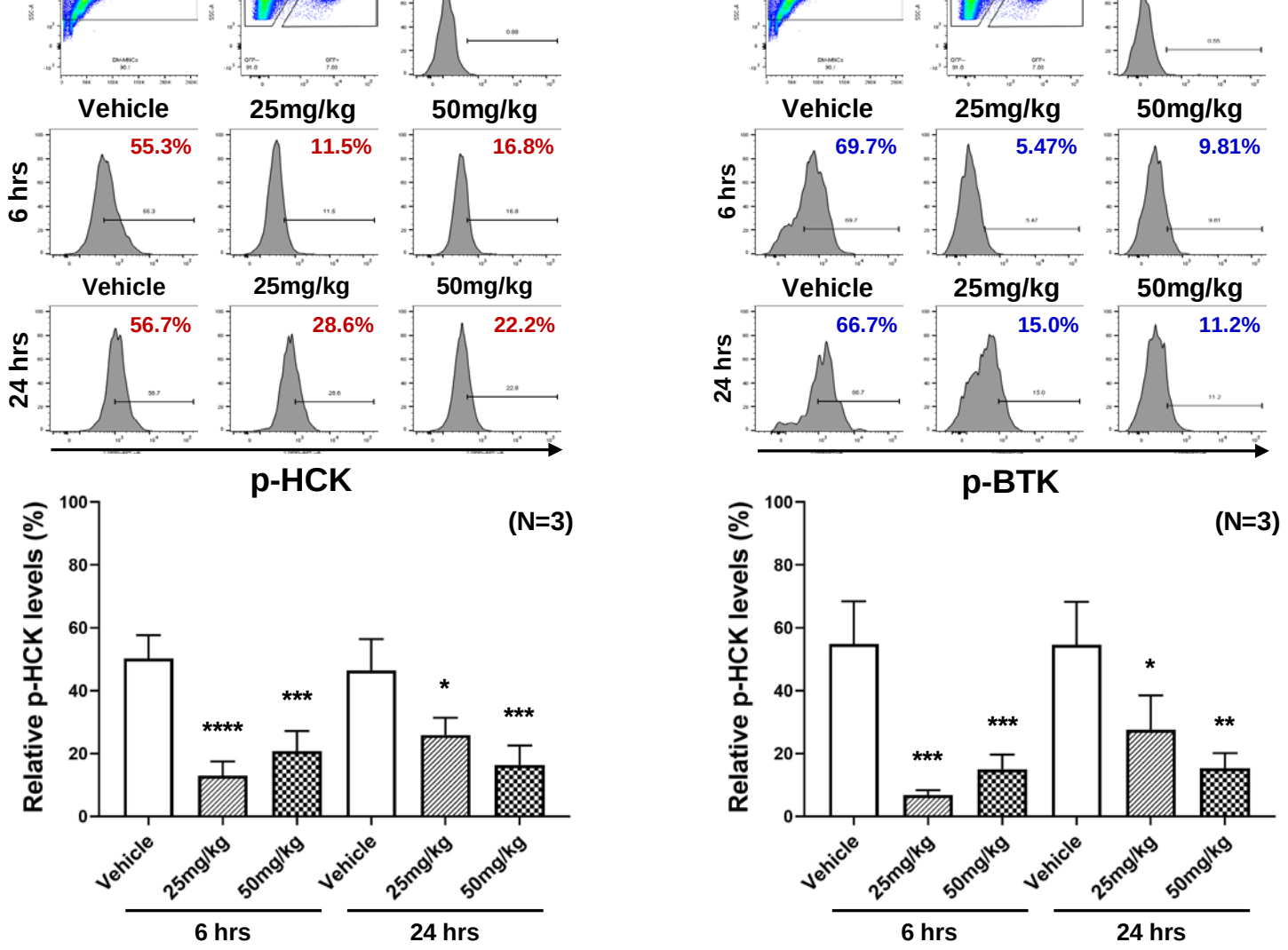
$t_{1/2}$ = 11.5 h
Cl = 17.4 mL/min/kg
Vss = 14.8 L/kg
$t_{1/2}$ = 15.1 h
AUC = 5.2 µM•h
F= 55%
$t_{1/2}$ = 16.9 h
AUC = 11.4 µM•h
F= 49%

Mouse pharmacokinetics

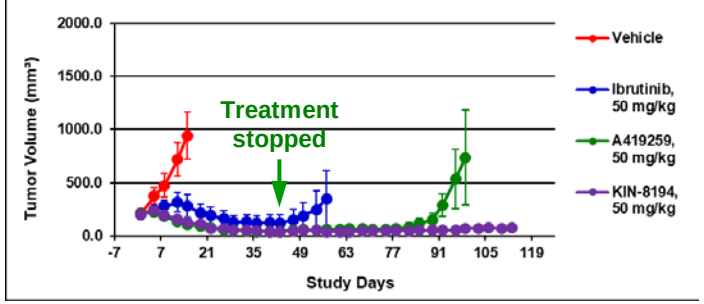
i.v.: 2 mg/kg, 0.2 mg/mL Compound (I) • 3 HCl in Saline
i.v.: 10 mg/kg, 1 mg/mL Compound (I) • 3 HCl in Saline
i.v.: 25 mg/kg, 2.5 mg/mL Compound (I) • 3 HCl in Saline

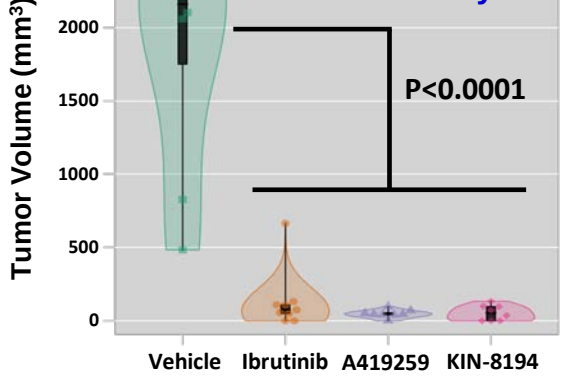


Supplementary Figure 5. Comparison of A419259 and KIN-8194 microsomal stability, protein binding, and pharmacokinetics. Arrows denote key differences in compound parameters.

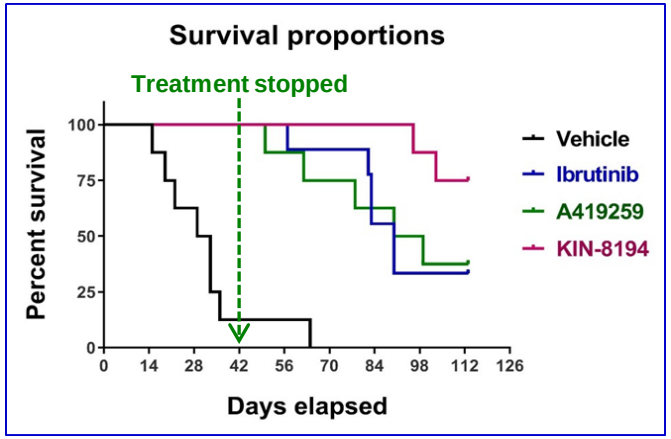


Supplemental Figure 6. Pharmacodynamic studies of KIN-8194 in ibrutinib sensitive BTK^{WT} expressing BCWM.1 WM xenografted mice. Pharmacodynamic study showing changes in the activity of $p\text{-}HCK^{Y410}$ and BTK^{Y223} following oral administration of KIN-8194 in NOD-SCID mice xenografted with ibrutinib sensitive BTK^{WT} BCWM.1 WM cells by intravenous injection. PhosFLow plots for $pHCK^{Y410}$ (**A**) and $pBTK^{Y223}$ (**B**) are shown of GFP^{+} gated BCWM.1 tumor cells obtained from mononuclear cells of mouse femurs at 6 and 24 hours following oral administration of KIN-8194 at the indicated doses (n=3 per group). *p<0.05; **p<0.01; ***p<0.005; ****p<0.0001.





C.



	Vehicle	Ibrutinib 50mg/kg	A419259 50mg/kg	KIN-8194 50mg/kg
Median Survival (days)	31	90	94.5	Undefined

Log-rank (Mantel-Cox) test, P<0.0001

Supplementary Figure 7. Efficacy studies of KIN-8194 and A419259 (RK20449) in ibrutinib sensitive BTK^{WT} TMD-8 ABC DLBCL xenografted mice. (C) Efficacy studies in NOD-SCID mice (n=8 per cohort) bearing ibrutinib sensitive BTKWT TMD-8 cells following daily oral administration of vehicle control, ibrutinib, A419259 or KIN-8194 at 50mg/kg. Tumor volume (mm3) was measured twice weekly and reported as the mean volume ± SEM. Treatment was stopped (indicated by green arrow) at day 42 and tumor volumes were monitored until day 113. (D) Tumor volume comparisons at day 33, p-values for cohort comparisons are shown. (E) Survival

A419259

Compound Name	DiscoveRx Gene Symbol	Entrez Gene Symbol	Percent Control
A419259	ABL1(F317I)-nonphosphorylated	ABL1	0
A419259	ABL1(F317L)-nonphosphorylated	ABL1	0
A419259	ABL1(Q252H)-nonphosphorylated	ABL1	0
A419259	ABL1-nonphosphorylated	ABL1	0
A419259	ERBB2	ERBB2	0
A419259	ERBB3	ERBB3	0
A419259	PDGFRB	PDGFRB	0
A419259	CSK	CSK	0.05
A419259	HCK	HCK	0.05
A419259	MEK5	MAP2K5	0.05
A419259	PFCDPK1(P.falciparum)	CDPK1	0.05
A419259	SRMS	SRMS	0.05
A419259	BLK	BLK	0.1
A419259	SRC	SRC	0.1
A419259	FLT3(K663Q)	FLT3	0.15
A419259	KIT(L576P)	KIT	0.15
A419259	ABL1(H396P)-nonphosphorylated	ABL1	0.2
A419259	FYN	FYN	0.2
A419259	YES	YES1	0.2
A419259	FLT3(D835V)	FLT3	0.25
A419259	BTK	BTK	0.35
A419259	EGFR	EGFR	0.45
A419259	LCK	LCK	0.55
A419259	FRK	FRK	0.65
A419259	BRK	PTK6	0.85
A419259	EGFR(T790M)	EGFR	0.9
A419259	ERBB4	ERBB4	1.3
A419259	FGR	FGR	1.3
A419259	FLT3	FLT3	2.6
A419259	KIT(V559D)	KIT	2.6
A419259	RET	RET	2.6
A419259	MEK1	MAP2K1	2.7
A419259	FLT3(N841I)	FLT3	3.1
A419259	RIPK2	RIPK2	3.2
A419259	FLT3(R834Q)	FLT3	3.5
A419259	EPHB6	EPHB6	3.9
A419259	CSNK1E	CSNK1E	4.2
A419259	MEK2	MAP2K2	4.8
A419259	TNK2	TNK2	5.2
A419259	EGFR(L861Q)	EGFR	5.4
A419259	PDGFRA	PDGFRA	6.1
A419259	LYN	LYN	6.6
A419259	RET(M918T)	RET	6.7
A419259	EGFR(G719C)	EGFR	8.2
A419259	KIT	KIT	8.7
A419259	ABL1(Q252H)-phosphorylated	ABL1	9.3
A419259	ABL1(F317L)-phosphorylated	ABL1	9.8

KIN-8194

Compound Name	DiscoveRx Gene Symbol	Entrez Gene Symbol	Percent Control
KIN-8194	ERBB2	ERBB2	0
KIN-8194	ERBB3	ERBB3	0
KIN-8194	LATS2	LATS2	0
KIN-8194	PFCDPK1(P.falciparum)	CDPK1	0
KIN-8194	SRMS	SRMS	0
KIN-8194	BLK	BLK	0.05
KIN-8194	BTK	BTK	0.15
KIN-8194	MEK5	MAP2K5	0.2
KIN-8194	SRC	SRC	0.2
KIN-8194	FYN	FYN	0.25
KIN-8194	YES	YES1	0.3
KIN-8194	CSK	CSK	0.4
KIN-8194	LCK	LCK	0.45
KIN-8194	ABL1-nonphosphorylated	ABL1	0.55
KIN-8194	HCK	HCK	0.65
KIN-8194	EGFR(T790M)	EGFR	0.7
KIN-8194	EGFR	EGFR	0.95
KIN-8194	FRK	FRK	0.95
KIN-8194	ABL1(F317I)-nonphosphorylated	ABL1	1.1
KIN-8194	ABL1(H396P)-nonphosphorylated	ABL1	1.2
KIN-8194	ABL1(F317L)-nonphosphorylated	ABL1	1.4
KIN-8194	BRK	PTK6	1.5
KIN-8194	FGR	FGR	1.5
KIN-8194	PDGFRB	PDGFRB	1.6
KIN-8194	FLT3(D835V)	FLT3	3.5
KIN-8194	ABL1(Q252H)-nonphosphorylated	ABL1	4.1
KIN-8194	ERBB4	ERBB4	4.5
KIN-8194	CSNK1E	CSNK1E	4.7
KIN-8194	LYN	LYN	5.2
KIN-8194	RIPK2	RIPK2	5.7
KIN-8194	MEK1	MAP2K1	6.6
KIN-8194	MEK2	MAP2K2	6.9
KIN-8194	TNK2	TNK2	8
KIN-8194	EGFR(L861Q)	EGFR	8.5

Supplementary Table 4. Comparison of KIN-8194 vs. A419259 (RK-20449) kinase inhibition (≥90%) by KINOMEscan at 100 nM.

Supplementary Table 1

Compound Name	DiscoveRx Gene Symbol	Entrez Gene Symbol	Percent Control	Compound Concentration (nM)
KIN-8194	AAK1	AAK1	90	1000
KIN-8194	ABL1(E255K)-phosphorylated	ABL1	1	1000
KIN-8194	ABL1(F317I)-nonphosphorylated	ABL1	2.5	1000
KIN-8194	ABL1(F317I)-phosphorylated	ABL1	8	1000
KIN-8194	ABL1(F317L)-nonphosphorylated	ABL1	11	1000
KIN-8194	ABL1(F317L)-phosphorylated	ABL1	2.9	1000
KIN-8194	ABL1(H396P)-nonphosphorylated	ABL1	1.2	1000
KIN-8194	ABL1(H396P)-phosphorylated	ABL1	2.3	1000
KIN-8194	ABL1(M351T)-phosphorylated	ABL1	4.3	1000
KIN-8194	ABL1(Q252H)-nonphosphorylated	ABL1	2.9	1000
KIN-8194	ABL1(Q252H)-phosphorylated	ABL1	2	1000
KIN-8194	ABL1(T315I)-nonphosphorylated	ABL1	56	1000
KIN-8194	ABL1(T315I)-phosphorylated	ABL1	65	1000
KIN-8194	ABL1(Y253F)-phosphorylated	ABL1	1	1000
KIN-8194	ABL1-nonphosphorylated	ABL1	0.3	1000
KIN-8194	ABL1-phosphorylated	ABL1	0.7	1000
KIN-8194	ABL2	ABL2	5	1000
KIN-8194	ACVR1	ACVR1	98	1000
KIN-8194	ACVR1B	ACVR1B	100	1000
KIN-8194	ACVR2A	ACVR2A	100	1000
KIN-8194	ACVR2B	ACVR2B	95	1000
KIN-8194	ACVRL1	ACVRL1	60	1000
KIN-8194	ADCK3	CABC1	92	1000
KIN-8194	ADCK4	ADCK4	96	1000
KIN-8194	AKT1	AKT1	94	1000
KIN-8194	AKT2	AKT2	65	1000
KIN-8194	AKT3	AKT3	83	1000
KIN-8194	ALK	ALK	48	1000
KIN-8194	ALK(C1156Y)	ALK	36	1000
KIN-8194	ALK(L1196M)	ALK	65	1000
KIN-8194	AMPK-alpha1	PRKAA1	34	1000
KIN-8194	AMPK-alpha2	PRKAA2	50	1000
KIN-8194	ANKK1	ANKK1	49	1000
KIN-8194	ARK5	NUAK1	64	1000
KIN-8194	ASK1	MAP3K5	79	1000
KIN-8194	ASK2	MAP3K6	77	1000
KIN-8194	AURKA	AURKA	4.8	1000
KIN-8194	AURKB	AURKB	94	1000
KIN-8194	AURKC	AURKC	79	1000
KIN-8194	AXL	AXL	23	1000
KIN-8194	BIKE	BMP2K	84	1000
KIN-8194	BLK	BLK	0.1	1000
KIN-8194	BMPR1A	BMPR1A	100	1000
KIN-8194	BMPR1B	BMPR1B	85	1000
KIN-8194	BMPR2	BMPR2	100	1000
KIN-8194	BMX	BMX	0.3	1000
KIN-8194	BRAF	BRAF	32	1000
KIN-8194	BRAF(V600E)	BRAF	18	1000
KIN-8194	BRK	PTK6	0.05	1000
KIN-8194	BRSK1	BRSK1	64	1000
KIN-8194	BRSK2	BRSK2	35	1000
KIN-8194	BTK	BTK	0	1000
KIN-8194	BUB1	BUB1	91	1000

KIN-8194	CAMK1	CAMK1	48	1000
KIN-8194	CAMK1B	PNCK	80	1000
KIN-8194	CAMK1D	CAMK1D	58	1000
KIN-8194	CAMK1G	CAMK1G	77	1000
KIN-8194	CAMK2A	CAMK2A	83	1000
KIN-8194	CAMK2B	CAMK2B	84	1000
KIN-8194	CAMK2D	CAMK2D	97	1000
KIN-8194	CAMK2G	CAMK2G	100	1000
KIN-8194	CAMK4	CAMK4	47	1000
KIN-8194	CAMKK1	CAMKK1	87	1000
KIN-8194	CAMKK2	CAMKK2	70	1000
KIN-8194	CASK	CASK	95	1000
KIN-8194	CDC2L1	CDK11B	72	1000
KIN-8194	CDC2L2	CDC2L2	70	1000
KIN-8194	CDC2L5	CDK13	98	1000
KIN-8194	CDK11	CDK19	4.5	1000
KIN-8194	CDK2	CDK2	97	1000
KIN-8194	CDK3	CDK3	100	1000
KIN-8194	CDK4	CDK4	98	1000
KIN-8194	CDK4-cyclinD1	CDK4	29	1000
KIN-8194	CDK4-cyclinD3	CDK4	79	1000
KIN-8194	CDK5	CDK5	92	1000
KIN-8194	CDK7	CDK7	53	1000
KIN-8194	CDK8	CDK8	14	1000
KIN-8194	CDK9	CDK9	86	1000
KIN-8194	CDKL1	CDKL1	78	1000
KIN-8194	CDKL2	CDKL2	99	1000
KIN-8194	CDKL3	CDKL3	100	1000
KIN-8194	CDKL5	CDKL5	60	1000
KIN-8194	CHEK1	CHEK1	91	1000
KIN-8194	CHEK2	CHEK2	28	1000
KIN-8194	CIT	CIT	75	1000
KIN-8194	CLK1	CLK1	98	1000
KIN-8194	CLK2	CLK2	71	1000
KIN-8194	CLK3	CLK3	84	1000
KIN-8194	CLK4	CLK4	97	1000
KIN-8194	CSF1R	CSF1R	31	1000
KIN-8194	CSF1R-autoinhibited	CSF1R	100	1000
KIN-8194	CSK	CSK	1	1000
KIN-8194	CSNK1A1	CSNK1A1	50	1000
KIN-8194	CSNK1A1L	CSNK1A1L	92	1000
KIN-8194	CSNK1D	CSNK1D	36	1000
KIN-8194	CSNK1E	CSNK1E	1.2	1000
KIN-8194	CSNK1G1	CSNK1G1	95	1000
KIN-8194	CSNK1G2	CSNK1G2	100	1000
KIN-8194	CSNK1G3	CSNK1G3	100	1000
KIN-8194	CSNK2A1	CSNK2A1	76	1000
KIN-8194	CSNK2A2	CSNK2A2	15	1000
KIN-8194	CTK	MATK	26	1000
KIN-8194	DAPK1	DAPK1	73	1000
KIN-8194	DAPK2	DAPK2	81	1000
KIN-8194	DAPK3	DAPK3	76	1000
KIN-8194	DCAMKL1	DCLK1	57	1000
KIN-8194	DCAMKL2	DCLK2	77	1000

KIN-8194	DCAMKL3	DCLK3	63	1000
KIN-8194	DDR1	DDR1	24	1000
KIN-8194	DDR2	DDR2	63	1000
KIN-8194	DLK	MAP3K12	58	1000
KIN-8194	DMPK	DMPK	94	1000
KIN-8194	DMPK2	CDC42BPG	4	1000
KIN-8194	DRAK1	STK17A	91	1000
KIN-8194	DRAK2	STK17B	82	1000
KIN-8194	DYRK1A	DYRK1A	66	1000
KIN-8194	DYRK1B	DYRK1B	100	1000
KIN-8194	DYRK2	DYRK2	83	1000
KIN-8194	EGFR	EGFR	0	1000
KIN-8194	EGFR(E746-A750del)	EGFR	71	1000
KIN-8194	EGFR(G719C)	EGFR	1.8	1000
KIN-8194	EGFR(G719S)	EGFR	1.9	1000
KIN-8194	EGFR(L747-E749del, A750P)	EGFR	10	1000
KIN-8194	EGFR(L747-S752del, P753S)	EGFR	83	1000
KIN-8194	EGFR(L747-T751del,Sins)	EGFR	12	1000
KIN-8194	EGFR(L858R)	EGFR	8.9	1000
KIN-8194	EGFR(L858R,T790M)	EGFR	21	1000
KIN-8194	EGFR(L861Q)	EGFR	0.75	1000
KIN-8194	EGFR(S752-I759del)	EGFR	5.2	1000
KIN-8194	EGFR(T790M)	EGFR	0.35	1000
KIN-8194	EIF2AK1	EIF2AK1	100	1000
KIN-8194	EPHA1	EPHA1	63	1000
KIN-8194	EPHA2	EPHA2	100	1000
KIN-8194	EPHA3	EPHA3	75	1000
KIN-8194	EPHA4	EPHA4	89	1000
KIN-8194	EPHA5	EPHA5	100	1000
KIN-8194	EPHA6	EPHA6	73	1000
KIN-8194	EPHA7	EPHA7	88	1000
KIN-8194	EPHA8	EPHA8	48	1000
KIN-8194	EPHB1	EPHB1	91	1000
KIN-8194	EPHB2	EPHB2	100	1000
KIN-8194	EPHB3	EPHB3	82	1000
KIN-8194	EPHB4	EPHB4	100	1000
KIN-8194	EPHB6	EPHB6	0	1000
KIN-8194	ERBB2	ERBB2	0	1000
KIN-8194	ERBB3	ERBB3	0	1000
KIN-8194	ERBB4	ERBB4	0.15	1000
KIN-8194	ERK1	MAPK3	89	1000
KIN-8194	ERK2	MAPK1	99	1000
KIN-8194	ERK3	MAPK6	90	1000
KIN-8194	ERK4	MAPK4	62	1000
KIN-8194	ERK5	MAPK7	82	1000
KIN-8194	ERK8	MAPK15	100	1000
KIN-8194	ERN1	ERN1	47	1000
KIN-8194	FAK	PTK2	93	1000
KIN-8194	FER	FER	83	1000
KIN-8194	FES	FES	98	1000
KIN-8194	FGFR1	FGFR1	13	1000
KIN-8194	FGFR2	FGFR2	29	1000
KIN-8194	FGFR3	FGFR3	36	1000
KIN-8194	FGFR3(G697C)	FGFR3	81	1000

KIN-8194	FGFR4	FGFR4	77	1000
KIN-8194	FGR	FGR	0	1000
KIN-8194	FLT1	FLT1	73	1000
KIN-8194	FLT3	FLT3	3.9	1000
KIN-8194	FLT3(D835H)	FLT3	8.5	1000
KIN-8194	FLT3(D835V)	FLT3	0	1000
KIN-8194	FLT3(D835Y)	FLT3	13	1000
KIN-8194	FLT3(ITD)	FLT3	9.9	1000
KIN-8194	FLT3(ITD,D835V)	FLT3	31	1000
KIN-8194	FLT3(ITD,F691L)	FLT3	82	1000
KIN-8194	FLT3(K663Q)	FLT3	7.7	1000
KIN-8194	FLT3(N841I)	FLT3	0	1000
KIN-8194	FLT3(R834Q)	FLT3	3	1000
KIN-8194	FLT3-autoinhibited	FLT3	8.8	1000
KIN-8194	FLT4	FLT4	42	1000
KIN-8194	FRK	FRK	0	1000
KIN-8194	FYN	FYN	0	1000
KIN-8194	GAK	GAK	76	1000
KIN-8194	GCN2(Kin.Dom.2,S808G)	EIF2AK4	80	1000
KIN-8194	GRK1	GRK1	74	1000
KIN-8194	GRK2	ADRBK1	93	1000
KIN-8194	GRK3	ADRBK2	97	1000
KIN-8194	GRK4	GRK4	67	1000
KIN-8194	GRK7	GRK7	100	1000
KIN-8194	GSK3A	GSK3A	91	1000
KIN-8194	GSK3B	GSK3B	75	1000
KIN-8194	HASPIN	GSG2	100	1000
KIN-8194	HCK	HCK	1.3	1000
KIN-8194	HIPK1	HIPK1	65	1000
KIN-8194	HIPK2	HIPK2	15	1000
KIN-8194	HIPK3	HIPK3	91	1000
KIN-8194	HIPK4	HIPK4	84	1000
KIN-8194	HPK1	MAP4K1	56	1000
KIN-8194	HUNK	HUNK	100	1000
KIN-8194	ICK	ICK	81	1000
KIN-8194	IGF1R	IGF1R	79	1000
KIN-8194	IKK-alpha	CHUK	99	1000
KIN-8194	IKK-beta	IKBKB	100	1000
KIN-8194	IKK-epsilon	IKBKE	78	1000
KIN-8194	INSR	INSR	77	1000
KIN-8194	INSRR	INSRR	65	1000
KIN-8194	IRAK1	IRAK1	67	1000
KIN-8194	IRAK3	IRAK3	55	1000
KIN-8194	IRAK4	IRAK4	75	1000
KIN-8194	ITK	ITK	16	1000
KIN-8194	JAK1(JH1domain-catalytic)	JAK1	100	1000
KIN-8194	JAK1(JH2domain-pseudokinase)	JAK1	82	1000
KIN-8194	JAK2(JH1domain-catalytic)	JAK2	100	1000
KIN-8194	JAK3(JH1domain-catalytic)	JAK3	100	1000
KIN-8194	JNK1	MAPK8	89	1000
KIN-8194	JNK2	MAPK9	81	1000
KIN-8194	JNK3	MAPK10	69	1000
KIN-8194	KIT	KIT	1.6	1000
KIN-8194	KIT(A829P)	KIT	8.2	1000

KIN-8194	KIT(D816H)	KIT	45	1000
KIN-8194	KIT(D816V)	KIT	96	1000
KIN-8194	KIT(L576P)	KIT	0.8	1000
KIN-8194	KIT(V559D)	KIT	0.3	1000
KIN-8194	KIT(V559D,T670I)	KIT	82	1000
KIN-8194	KIT(V559D,V654A)	KIT	67	1000
KIN-8194	KIT-autoinhibited	KIT	18	1000
KIN-8194	LATS1	LATS1	26	1000
KIN-8194	LATS2	LATS2	0	1000
KIN-8194	LCK	LCK	0.8	1000
KIN-8194	LIMK1	LIMK1	4.8	1000
KIN-8194	LIMK2	LIMK2	56	1000
KIN-8194	LKB1	STK11	100	1000
KIN-8194	LOK	STK10	24	1000
KIN-8194	LRRK2	LRRK2	96	1000
KIN-8194	LRRK2(G2019S)	LRRK2	99	1000
KIN-8194	LTK	LTK	47	1000
KIN-8194	LYN	LYN	2.4	1000
KIN-8194	LZK	MAP3K13	85	1000
KIN-8194	MAK	MAK	95	1000
KIN-8194	MAP3K1	MAP3K1	71	1000
KIN-8194	MAP3K15	MAP3K15	34	1000
KIN-8194	MAP3K2	MAP3K2	0.75	1000
KIN-8194	MAP3K3	MAP3K3	5.9	1000
KIN-8194	MAP3K4	MAP3K4	91	1000
KIN-8194	MAP4K2	MAP4K2	67	1000
KIN-8194	MAP4K3	MAP4K3	16	1000
KIN-8194	MAP4K4	MAP4K4	93	1000
KIN-8194	MAP4K5	MAP4K5	16	1000
KIN-8194	MAPKAPK2	MAPKAPK2	64	1000
KIN-8194	MAPKAPK5	MAPKAPK5	81	1000
KIN-8194	MARK1	MARK1	84	1000
KIN-8194	MARK2	MARK2	84	1000
KIN-8194	MARK3	MARK3	80	1000
KIN-8194	MARK4	MARK4	99	1000
KIN-8194	MAST1	MAST1	49	1000
KIN-8194	MEK1	MAP2K1	0.2	1000
KIN-8194	MEK2	MAP2K2	0.3	1000
KIN-8194	MEK3	MAP2K3	54	1000
KIN-8194	MEK4	MAP2K4	55	1000
KIN-8194	MEK5	MAP2K5	0	1000
KIN-8194	MEK6	MAP2K6	96	1000
KIN-8194	MELK	MELK	36	1000
KIN-8194	MERTK	MERTK	17	1000
KIN-8194	MET	MET	55	1000
KIN-8194	MET(M1250T)	MET	99	1000
KIN-8194	MET(Y1235D)	MET	84	1000
KIN-8194	MINK	MINK1	30	1000
KIN-8194	MKK7	MAP2K7	80	1000
KIN-8194	MKNK1	MKNK1	79	1000
KIN-8194	MKNK2	MKNK2	16	1000
KIN-8194	MLCK	MYLK3	100	1000
KIN-8194	MLK1	MAP3K9	89	1000
KIN-8194	MLK2	MAP3K10	98	1000

KIN-8194	MLK3	MAP3K11	97	1000
KIN-8194	MRCKA	CDC42BPA	73	1000
KIN-8194	MRCKB	CDC42BPB	65	1000
KIN-8194	MST1	STK4	32	1000
KIN-8194	MST1R	MST1R	98	1000
KIN-8194	MST2	STK3	42	1000
KIN-8194	MST3	STK24	3.1	1000
KIN-8194	MST4	MST4	2.8	1000
KIN-8194	MTOR	MTOR	16	1000
KIN-8194	MUSK	MUSK	88	1000
KIN-8194	MYLK	MYLK	92	1000
KIN-8194	MYLK2	MYLK2	98	1000
KIN-8194	MYLK4	MYLK4	95	1000
KIN-8194	MYO3A	MYO3A	2	1000
KIN-8194	MYO3B	MYO3B	31	1000
KIN-8194	NDR1	STK38	33	1000
KIN-8194	NDR2	STK38L	66	1000
KIN-8194	NEK1	NEK1	91	1000
KIN-8194	NEK10	NEK10	100	1000
KIN-8194	NEK11	NEK11	75	1000
KIN-8194	NEK2	NEK2	73	1000
KIN-8194	NEK3	NEK3	89	1000
KIN-8194	NEK4	NEK4	82	1000
KIN-8194	NEK5	NEK5	98	1000
KIN-8194	NEK6	NEK6	94	1000
KIN-8194	NEK7	NEK7	91	1000
KIN-8194	NEK9	NEK9	88	1000
KIN-8194	NIK	MAP3K14	67	1000
KIN-8194	NIM1	MGC42105	100	1000
KIN-8194	NLK	NLK	74	1000
KIN-8194	OSR1	OXSR1	60	1000
KIN-8194	p38-alpha	MAPK14	100	1000
KIN-8194	p38-beta	MAPK11	96	1000
KIN-8194	p38-delta	MAPK13	98	1000
KIN-8194	p38-gamma	MAPK12	96	1000
KIN-8194	PAK1	PAK1	24	1000
KIN-8194	PAK2	PAK2	46	1000
KIN-8194	PAK3	PAK3	41	1000
KIN-8194	PAK4	PAK4	68	1000
KIN-8194	PAK6	PAK6	71	1000
KIN-8194	PAK7	PAK7	52	1000
KIN-8194	PCTK1	CDK16	65	1000
KIN-8194	PCTK2	CDK17	88	1000
KIN-8194	PCTK3	CDK18	88	1000
KIN-8194	PDGFRA	PDGFRA	4.7	1000
KIN-8194	PDGFRB	PDGFRB	0	1000
KIN-8194	PDPK1	PDPK1	95	1000
KIN-8194	PFCDPK1(P.falciparum)	CDPK1	0	1000
KIN-8194	PFPK5(P.falciparum)	MAL13P1.279	92	1000
KIN-8194	PFTAIRE2	CDK15	85	1000
KIN-8194	PFTK1	CDK14	37	1000
KIN-8194	PHKG1	PHKG1	100	1000
KIN-8194	PHKG2	PHKG2	68	1000
KIN-8194	PIK3C2B	PIK3C2B	37	1000

KIN-8194	PIK3C2G	PIK3C2G	100	1000
KIN-8194	PIK3CA	PIK3CA	88	1000
KIN-8194	PIK3CA(C420R)	PIK3CA	81	1000
KIN-8194	PIK3CA(E542K)	PIK3CA	71	1000
KIN-8194	PIK3CA(E545A)	PIK3CA	67	1000
KIN-8194	PIK3CA(E545K)	PIK3CA	54	1000
KIN-8194	PIK3CA(H1047L)	PIK3CA	52	1000
KIN-8194	PIK3CA(H1047Y)	PIK3CA	63	1000
KIN-8194	PIK3CA(I800L)	PIK3CA	40	1000
KIN-8194	PIK3CA(M1043I)	PIK3CA	94	1000
KIN-8194	PIK3CA(Q546K)	PIK3CA	72	1000
KIN-8194	PIK3CB	PIK3CB	20	1000
KIN-8194	PIK3CD	PIK3CD	56	1000
KIN-8194	PIK3CG	PIK3CG	95	1000
KIN-8194	PIK4CB	PI4KB	73	1000
KIN-8194	PIKFYVE	PIKFYVE	70	1000
KIN-8194	PIM1	PIM1	88	1000
KIN-8194	PIM2	PIM2	99	1000
KIN-8194	PIM3	PIM3	69	1000
KIN-8194	PIP5K1A	PIP5K1A	100	1000
KIN-8194	PIP5K1C	PIP5K1C	85	1000
KIN-8194	PIP5K2B	PIP4K2B	74	1000
KIN-8194	PIP5K2C	PIP4K2C	91	1000
KIN-8194	PKAC-alpha	PRKACA	100	1000
KIN-8194	PKAC-beta	PRKACB	88	1000
KIN-8194	PKMYT1	PKMYT1	100	1000
KIN-8194	PKN1	PKN1	98	1000
KIN-8194	PKN2	PKN2	92	1000
KIN-8194	PKNB(M.tuberculosis)	pknB	62	1000
KIN-8194	PLK1	PLK1	100	1000
KIN-8194	PLK2	PLK2	91	1000
KIN-8194	PLK3	PLK3	93	1000
KIN-8194	PLK4	PLK4	66	1000
KIN-8194	PRKCD	PRKCD	91	1000
KIN-8194	PRKCE	PRKCE	66	1000
KIN-8194	PRKCH	PRKCH	71	1000
KIN-8194	PRKCI	PRKCI	43	1000
KIN-8194	PRKCQ	PRKCQ	92	1000
KIN-8194	PRKD1	PRKD1	50	1000
KIN-8194	PRKD2	PRKD2	52	1000
KIN-8194	PRKD3	PRKD3	29	1000
KIN-8194	PRKG1	PRKG1	93	1000
KIN-8194	PRKG2	PRKG2	100	1000
KIN-8194	PRKR	EIF2AK2	90	1000
KIN-8194	PRKX	PRKX	88	1000
KIN-8194	PRP4	PRPF4B	91	1000
KIN-8194	PYK2	PTK2B	91	1000
KIN-8194	QSK	KIAA0999	85	1000
KIN-8194	RAF1	RAF1	93	1000
KIN-8194	RET	RET	0.1	1000
KIN-8194	RET(M918T)	RET	0.35	1000
KIN-8194	RET(V804L)	RET	45	1000
KIN-8194	RET(V804M)	RET	53	1000
KIN-8194	RIOK1	RIOK1	100	1000

KIN-8194	RIOK2	RIOK2	68	1000
KIN-8194	RIOK3	RIOK3	85	1000
KIN-8194	RIPK1	RIPK1	99	1000
KIN-8194	RIPK2	RIPK2	0	1000
KIN-8194	RIPK4	RIPK4	80	1000
KIN-8194	RIPK5	DSTYK	13	1000
KIN-8194	ROCK1	ROCK1	88	1000
KIN-8194	ROCK2	ROCK2	80	1000
KIN-8194	ROS1	ROS1	86	1000
KIN-8194	RPS6KA4(Kin.Dom.1-N-terminal)	RPS6KA4	51	1000
KIN-8194	RPS6KA4(Kin.Dom.2-C-terminal)	RPS6KA4	73	1000
KIN-8194	RPS6KA5(Kin.Dom.1-N-terminal)	RPS6KA5	75	1000
KIN-8194	RPS6KA5(Kin.Dom.2-C-terminal)	RPS6KA5	92	1000
KIN-8194	RSK1(Kin.Dom.1-N-terminal)	RPS6KA1	49	1000
KIN-8194	RSK1(Kin.Dom.2-C-terminal)	RPS6KA1	75	1000
KIN-8194	RSK2(Kin.Dom.1-N-terminal)	RPS6KA3	26	1000
KIN-8194	RSK2(Kin.Dom.2-C-terminal)	RPS6KA3	91	1000
KIN-8194	RSK3(Kin.Dom.1-N-terminal)	RPS6KA2	41	1000
KIN-8194	RSK3(Kin.Dom.2-C-terminal)	RPS6KA2	2.1	1000
KIN-8194	RSK4(Kin.Dom.1-N-terminal)	RPS6KA6	69	1000
KIN-8194	RSK4(Kin.Dom.2-C-terminal)	RPS6KA6	3.6	1000
KIN-8194	S6K1	RPS6KB1	29	1000
KIN-8194	SBK1	SBK1	71	1000
KIN-8194	SGK	SGK1	100	1000
KIN-8194	SgK110	SgK110	98	1000
KIN-8194	SGK2	SGK2	100	1000
KIN-8194	SGK3	SGK3	52	1000
KIN-8194	SIK	SIK1	10	1000
KIN-8194	SIK2	SIK2	43	1000
KIN-8194	SLK	SLK	66	1000
KIN-8194	SNARK	NUAK2	18	1000
KIN-8194	SNRK	SNRK	99	1000
KIN-8194	SRC	SRC	0.05	1000
KIN-8194	SRMS	SRMS	0	1000
KIN-8194	SRPK1	SRPK1	78	1000
KIN-8194	SRPK2	SRPK2	100	1000
KIN-8194	SRPK3	SRPK3	74	1000
KIN-8194	STK16	STK16	80	1000
KIN-8194	STK33	STK33	33	1000
KIN-8194	STK35	STK35	6.4	1000
KIN-8194	STK36	STK36	6.2	1000
KIN-8194	STK39	STK39	82	1000
KIN-8194	SYK	SYK	100	1000
KIN-8194	TAK1	MAP3K7	97	1000
KIN-8194	TAOK1	TAOK1	88	1000
KIN-8194	TAOK2	TAOK2	75	1000
KIN-8194	TAOK3	TAOK3	91	1000
KIN-8194	TBK1	TBK1	60	1000
KIN-8194	TEC	TEC	1.9	1000
KIN-8194	TESK1	TESK1	99	1000
KIN-8194	TGFBR1	TGFBR1	100	1000
KIN-8194	TGFBR2	TGFBR2	76	1000
KIN-8194	TIE1	TIE1	52	1000
KIN-8194	TIE2	TEK	14	1000

KIN-8194	TLK1	TLK1	95	1000
KIN-8194	TLK2	TLK2	96	1000
KIN-8194	TNIK	TNIK	57	1000
KIN-8194	TNK1	TNK1	97	1000
KIN-8194	TNK2	TNK2	0.6	1000
KIN-8194	TNNI3K	TNNI3K	85	1000
KIN-8194	TRKA	NTRK1	35	1000
KIN-8194	TRKB	NTRK2	43	1000
KIN-8194	TRKC	NTRK3	66	1000
KIN-8194	TRPM6	TRPM6	53	1000
KIN-8194	TSSK1B	TSSK1B	87	1000
KIN-8194	TSSK3	TSSK3	100	1000
KIN-8194	TTK	TTK	32	1000
KIN-8194	TXK	TXK	11	1000
KIN-8194	TYK2(JH1domain-catalytic)	TYK2	88	1000
KIN-8194	TYK2(JH2domain-pseudokinase)	TYK2	87	1000
KIN-8194	TYRO3	TYRO3	44	1000
KIN-8194	ULK1	ULK1	65	1000
KIN-8194	ULK2	ULK2	78	1000
KIN-8194	ULK3	ULK3	55	1000
KIN-8194	VEGFR2	KDR	39	1000
KIN-8194	VPS34	PIK3C3	100	1000
KIN-8194	VRK2	VRK2	58	1000
KIN-8194	WEE1	WEE1	100	1000
KIN-8194	WEE2	WEE2	97	1000
KIN-8194	WNK1	WNK1	74	1000
KIN-8194	WNK2	WNK2	71	1000
KIN-8194	WNK3	WNK3	72	1000
KIN-8194	WNK4	WNK4	75	1000
KIN-8194	YANK1	STK32A	17	1000
KIN-8194	YANK2	STK32B	24	1000
KIN-8194	YANK3	STK32C	82	1000
KIN-8194	YES	YES1	0	1000
KIN-8194	YSK1	STK25	22	1000
KIN-8194	YSK4	MAP3K19	50	1000
KIN-8194	ZAK	ZAK	16	1000
KIN-8194	ZAP70	ZAP70	100	1000

Supplementary Table 2

Kinase	Reference	Sequence	Labeling Site	KIN-8194
HCK	**UniRef100_P08631**	**EGAKFPIKWTAPEAINFGSFTIK**	**Activation Loop**	**97.2**
LYN	UniRef100_P07948	EGAKFPIKWTAPEAINFGCFTIK	Activation Loop	97.0
HER2/**ErbB2**	UniRef100_P04626	LLDIDETEYHADGGKVPIK	Activation Loop	96.1
CSK	UniRef100_P41240	VSDFGLTKEASSTQDTGKLPVK	Activation Loop	95.9
HER2/ErbB2	UniRef100_P04626	GIWIPDGENVKIPVAIKVLR	Lys1	>95
ABL, ARG	UniRef100_P00519, UniRef100_P42684	LMTGDTYTAHAGAKFPIK	Activation Loop	94.4
BTK	**UniRef100_Q06187**	**YVLDDEYTSSVGSKFPVR**	**Activation Loop**	**94.1**
HCK	UniRef100_P08631	VAVKTMKPGSMSVEAFLAEANVMK	Lys1	**93.5**
ABL, ARG	UniRef100_P00519, UniRef100_P42684	YSLTVAVKTLKEDTMEVEEFLK	Lys1	90.7
BLK	UniRef100_P51451	IIDSEYTAQEGAKFPIK	Activation Loop	>90
FRK	UniRef100_P42685	HEIKLPVK	Activation Loop	85.7
MAP2K5	UniRef100_Q13163	DVKPSNMLVNTR	Lys2	84.5
CSK	UniRef100_P41240	VAVKCIK	Lys1	83.7
ACK	UniRef100_Q07912	KVPFAWCAPESLK	Activation Loop	81.6
RIPK3	UniRef100_Q9Y572	DLKPSNVLLDPELHVK	Lys2	66.9
DNAPK	UniRef100_P78527	KGGSWIQEINVAEK	ATP	66.2
DNAPK	UniRef100_P78527	EHPFLVKGGEDLR	ATP	53.7
ACK	UniRef100_Q07912	TVSVAVKCLKPDVLSQPEAMDDFIR	Lys1	51.5
LATS1	UniRef100_O95835	ALYATKTLR	Lys1	44.1
MST3	UniRef100_Q9Y6E0	DIKAANVLLSEHGEVK	Lys2	43.4
CDK11, CDK8	UniRef100_P49336, UniRef100_Q9BWU1	DLKPANILVMGEGPER	Lys2	39.2
CDK10	UniRef100_Q15131	DLKVSNLLMTDK	Lys2	34.0
MST4, YSK1	UniRef100_O00506, UniRef100_Q9P289	DIKAANVLLSEQGDVK	Lys2	31.7
STLK6	UniRef100_Q9C0K7	HTPTGTLVTIKITNLENCNEER	Lys1	31.7
AMPKa1, AMPKa2	UniRef100_P54646, UniRef100_Q96E92	DLKPENVLLDAHMNAK	Lys2	30.4
LATS1	UniRef100_O95835	DIKPDNILIDR	Lys2	29.0
IKKe, TBK1	UniRef100_Q14164, UniRef100_Q9UHD2	DIKPGNIMR	Lys2	28.6
MST1, MST2	UniRef100_Q13188, UniRef100_Q13043	DIKAGNILLNTEGHAK	Lys2	27.7
AGK	UniRef100_Q53H12	ATVFLNPAACKGK	ATP	27.0
PI4KA, PI4KAP2	UniRef100_A4QPH2, UniRef100_P42356	SGTPMQSAAKAPYLAK	ATP	26.9
CDC2	UniRef100_Q5H9N4	TTGQVVAMKK	Lys1	24.9
p38b	UniRef100_Q15759	QELNKTVWEVPQR	Other	24.7
MAP2K4	UniRef100_P45985	MVHKPSGQIMAVKR	Lys1	23.8
ZAK	UniRef100_Q9NYL2	WISQDKEVAVKK	Lys1	21.7
PEK	UniRef100_Q9NZJ5	DLKPSNIFFTMDDVVK	Lys2	21.2
ATR	UniRef100_Q13535	FYIMMCKPK	ATP	20.5
PIP4K2C	UniRef100_Q8TBX8	TLVIKEVSSEDIADMHSNLSNYHQYIVK	ATP	20.0
PITSLRE	UniRef100_P21127	DLKTSNLLLSHAGILK	Lys2	19.8
CDK7	UniRef100_P50613	DKNTNQIVAIKK	Lys1	19.3
ILK	UniRef100_Q13418	ISMADVKFSFQCPGR	Protein Kinase Domain	19.2
RAF1	UniRef100_P04049	DMKSNNIFLHEGLTVK	Lys2	19.1
p70S6Kb	UniRef100_Q9UBS0	IYAMKVLR	Lys1	17.9
LOK	UniRef100_O94804	DLKAGNVLMTLEGDIR	Lys2	17.1
MAP3K1	UniRef100_Q13233	DVKGANLLIDSTGQR	Lys2	17.1
GCK	UniRef100_Q12851, UniRef100_P35557	DIKGANLLLTLQGDVK	Lys2	16.7
LYN	UniRef100_P07948	VAVKTLKPGTMSVQAFLEEANLMK	Lys1	14.8
PIK3CD	UniRef100_O00329	VNWLAHNVSKDNRQ	ATP	14.6
AurB	UniRef100_Q96GD4	SHFIVALKVLFK	Lys1	14.5
SGK	UniRef100_O00141	HKAEEVFYAVKVLQK	Lys1	14.0
HPK1	UniRef100_Q92918	DKVSGDLVALKMVK	Lys1	13.9
MAP3K5	UniRef100_Q99683	DIKGDNVLINTYSGVLK	Lys2	13.8
MAP2K6	UniRef100_P52564, UniRef100_L5KNH7	HVPSGQIMAVKR	Lys1	13.5
NDR2	UniRef100_Q9Y2H1	DTGHIYAMKILR	Lys1	13.4
PKN1	UniRef100_Q16512	VLLSEFRPSGELFAIKALK	Lys1	13.0
Erk2	UniRef100_P28482	DLKPSNLLLNTTCDLK	Lys2	12.7
MAST1, MAST2	UniRef100_Q6P0Q8, UniRef100_Q9Y2H9	DLKPDNLLITSMGHIK	Lys2	12.5
FER	UniRef100_P16591	QEDGGVYSSSGLKQIPIK	Activation Loop	11.5
CASK	UniRef100_O14936	ETGQQFAVKIVDVAK	Lys1	11.3
JAK1 domain1	UniRef100_P23458	QLASALSYLEDKDLVHGNVCTKNLLLAR	Activation Loop	11.3
PKN1	UniRef100_Q16512	DLKLDNLLLDTEGYVK	Lys2	11.3
PKCd	UniRef100_Q05655	KPTMYPEWK	Other	11.2
NDR2	UniRef100_Q9Y2H1	DIKPDNLLLDAK	Lys2	11.1

Labeling Site Key

Lys1	Conserved Lysine 1
Lys2	Conserved Lysine 2
ATP Loop	ATP binding loop,
Activation Loop	Activation loop
ATP	ATP site in non-canonical kinase (e.g. lipid kinase)
Protein Kinase Domain	Other lysine within kinase domain, possibly not in ATP binding site
Other	Labeling of residue outside of the protein kinase domain, possibly not in ATP binding site

	>90% Inhibition
	75 - 90% Inhibition
	50 - 75% Inhibition
	35 - 50% Inhibition
	No change
	>100% increase in MS signal (>2 fold increase)
	Not determined

STK33	UniRef100_Q9BYT3	DLKLENIMVK	Lys2	10.9
PIK3CB	UniRef100_P42338	VFGEDSVGVIFKNGDDLRQDMLTLQMLR	ATP	10.7
AMPKa1, AMPKa2	UniRef100_P54646, UniRef100_Q96E92	VAVKILNR	Lys1	10.2
STLK5	UniRef100_Q7RTN6	SVKASHILISVDGK	Lys2	10.1
FAM20B	UniRef100_O75063	ETEPACADGDIMEGSVTLWLPDVWPLQKHR	ATP	10.0
ARAF	UniRef100_P10398	DLKSNNIFLHEGLTVK	Lys2	9.9
PIK3C3	UniRef100_Q8NEB9	TEDGGKYPVIFKHGDDLRQDQLILQIISLMDK	ATP	9.9
CaMKK2	UniRef100_Q96RR4	LAYNENDNTYYAMKVLSK	Lys1	9.6
NEK4	UniRef100_P51957	DLKTQNVFLTR	Lys2	9.5
AurA, AurB, AurC	UniRef100_O14965, UniRef100_Q9UQB9, Un	GKFGNVYLAR	ATP Loop	9.4
CaMK2g	UniRef100_Q13555	TSTQEYAAKIINTK	Lys1	9.4
MLK3	UniRef100_Q16584	DLKSNNILLLQPIESDDMEHK	Lys2	9.2
MSK2 domain1	UniRef100_O75676	LYAMKVLR	Lys1	9.0
Erk1	UniRef100_P27361	DLKPSNLLINTTCDLK	Lys2	8.5
HPK1	UniRef100_Q92918	DIKGANILINDAGEVR	Lys2	7.7
CaMK2a, CaMK2b, CaMI	UniRef100_Q53H78, UniRef100_Q13557, Un	DLKPENLLLASK	Lys2	7.2
p38a	UniRef100_Q16539	QELNKTIWEVPER	Other	7.1
TAO1, TAO3	UniRef100_Q9H2K8, UniRef100_Q7L7X3	DIKAGNILLTEPGQVK	Lys2	7.0
AurA	UniRef100_O14965	FILALKVLFK	Lys1	6.9
LRRK2	UniRef100_Q5S007	DLKPHNVLLFTLYPNAAIIAK	Lys2	6.8
TLK1	UniRef100_Q9UKI8	YAAVKIHQLNK	Lys1	6.8
MAP4K5	UniRef100_Q9Y4K4	DIKGANILLTDHGDVK	Lys2	6.5
PIK3C3	UniRef100_Q8NEB9	TEDGGKYPVIFKHGDDLR	ATP	6.3
p70S6Kb	UniRef100_Q9UBS0	DLKPENIMLSSQGHIK	Lys2	6.1
JAK3 domain2	UniRef100_P52333	LLPLDKDYYVVR	Activation Loop	6.1
NDR1, NDR2	UniRef100_Q9Y2H1, UniRef100_Q15208	LSDFGLCTGLKK	Activation Loop	6.1
CDK9	UniRef100_P50750	IGQGTFGEVFKAR	ATP Loop	6.0
CDK4	UniRef100_P11802	DLKPENILVTSGGTVK	Lys2	5.8
MAPKAPK2, MAPKAPK3	UniRef100_Q16644, UniRef100_P49137	DVKPENLLYTSK	Lys2	5.7
SLK	UniRef100_Q9H2G2	DLKAGNILFTLDGDIK	Lys2	5.5
PDK1	UniRef100_O15530	EYAIKILEK	Lys1	5.2
IRAK3	UniRef100_Q9Y616	SHLEHQSCTINMTSSSSKHLWYMPEEYIR	Protein Kinase Domain	4.9
MAP2K6	UniRef100_P52564, UniRef100_L5KNH7	DVKPSNVLINALGQVK	Lys2	4.9
JAK3 domain2	UniRef100_P52333	YDPLGDNTGALVAVKQLQHSGPDQQR	Lys1	4.9
NEK3	UniRef100_P51956	SKNIFLTQNGK	Activation Loop	4.7
MAP2K3	UniRef100_P46734	HAQSGTIMAVKR	Lys1	4.6
MARK2, MARK3	UniRef100_P27448, UniRef100_Q7KZI7	DLKAENLLLDADMNIK	Lys2	4.6
MAP3K4	UniRef100_Q9Y6R4	DIKGANIFLTSSGLIK	Lys2	4.4
HRI	UniRef100_Q9BQI3	IGDFGLACTDILQKNTDWTNR	Activation Loop	4.1
GSK3A	UniRef100_P49840	DIKPQNLLVDPDTAVLK	Lys2	4.0
NEK9	UniRef100_Q8TD19	RTEDDSLVVWKEVDLTR	Lys1	3.9
p38d, p38g	UniRef100_O15264, UniRef100_P53778	DLKPGNLAVNEDCELK	Lys2	3.6
JAK2 domain2	UniRef100_O60674	IGDFGLTKVLPQDKEYYK	Activation Loop	3.6
p38a	UniRef100_Q16539	DLKPSNLAVNEDCELK	Lys2	3.6
PI4KB	UniRef100_Q9UBF8	LLSVIVKCGDDLRQELLAFQVLK	ATP	3.3
TAO2	UniRef100_Q9UL54	DVKAGNILLSEPGLVK	Lys2	3.2
JAK3 domain2	UniRef100_P52333	IADFGLAKLLPLDKDYYVVR	Activation Loop	3.2
PAN3	UniRef100_Q58A45	VMDPTKILITGK	ATP	2.7
RSK3 domain1	UniRef100_Q15349	DLKPENILLDEEGHIKITDFGLSK	Lys2	2.6
NDR1	UniRef100_Q15208	DTGHVYAMKILR	Lys1	2.3
CaMK2d	UniRef100_Q13557	IPTGQEYAAKIINTKK	Lys1	2.2
TBK1	UniRef100_Q9UHD2	TGDLFAIKVFNNISFLRPVDVQMR	Lys1	1.9
RSK2 domain1	UniRef100_P51812	QLYAMKVLK	Lys1	1.8
CaMKK1	UniRef100_Q8N5S9	DIKPSNLLLGDDGHVK	Lys2	1.8
RSK1 domain1, RSK2 do	UniRef100_Q15418, UniRef100_P51812, Uni	DLKPENILLDEEGHIK	Lys2	1.0
CDK6	UniRef100_Q00534	DLKPQNILVTSSGQIK	Lys2	0.9
CK1g1, CK1g2, CK1g3	UniRef100_Q9Y6M4, UniRef100_P78368, Un	KIGCGNFGELR	ATP Loop	0.7
TLK1	UniRef100_Q9UKI8	YLNEIKPPIIHYDLKPGNILLVDGTACGEIK	Lys2	0.4
Wnk1, Wnk2, Wnk3	UniRef100_Q9Y3S1, UniRef100_Q9BYP7, Uni	DLKCDNIFITGPTGSVK	Lys2	0.4
GSK3B	UniRef100_P49841	DIKPQNLLLDPDTAVLK	Lys2	0.0
IKKa	UniRef100_O15111	DLKPENIVLQDVGGK	Lys2	-0.4
ULK3	UniRef100_D3DW67	EVVAIKCVAK	Lys1	-0.8
IRE1	UniRef100_O75460	DLKPHNILISMPNAHGK	Lys2	-1.4

IRAK4	UniRef100_Q9NWZ3	GYVNNTTVAVKK	Lys1	-1.5
CDK9	UniRef100_P50750	DMKAANVLITR	Lys2	-1.6
IRAK4	UniRef100_Q9NWZ3	DIKSANILLDEAFTAK	Lys2	-1.9
NDR1	UniRef100_Q15208	DIKPDNLLLDSK	Lys2	-2.0
CDK2	UniRef100_P24941	LTGEVVALKK	Lys1	-2.1
NEK8	UniRef100_Q86SG6	DLKTQNILLDK	Lys2	-2.5
PIP4K2C	UniRef100_Q8TBX8	VKELPTLKDMDFLNK	ATP	-2.6
CaMK4	UniRef100_Q16566	DLKPENLLYATPAPDAPLK	Lys2	-2.6
ULK1	UniRef100_O75385	DLKPQNILLSNPAGR	Lys2	-2.9
MAP3K4	UniRef100_Q9Y6R4	VYTCISVDTGELMAMKEIR	Lys1	-3.0
PKCa, PKCg	UniRef100_P17252, UniRef100_P05129	NLIPMDPNGLSDPYVKLK	Other	-3.1
CDK2	UniRef100_P24941	DLKPQNLLINTEGAIK	Lys2	-3.2
RSK2 domain1	UniRef100_P51812	LTDFGLSKESIDHEKK	Activation Loop	-3.4
LKB1	UniRef100_Q15831	DIKPGNLLLTTGGTLK	Lys2	-3.4
CDK7	UniRef100_P50613	DLKPNNLLLDENGVLK	Lys2	-3.4
LOK	UniRef100_O94804	NKETGALAAAKVIETK	Lys1	-3.6
CDC2	UniRef100_Q5H9N4	DLKPQNLLIDDK	Lys2	-3.7
TLK2	UniRef100_Q86UE8	YLNEIKPPIIHYDLKPGNILLVNGTACGEIK	Lys2	-3.7
PFTAIRE2	UniRef100_Q96Q40	DLKPQNLLISHLGELK	Lys2	-5.1
STLK5	UniRef100_Q7RTN6	YSVKVLPWLSPEVLQQNLQGYDAK	Activation Loop	-5.3
CaMK1a	UniRef100_Q14012	LVAIKCIAK	Lys1	-5.5
MAP2K3	UniRef100_P46734	DVKPSNVLINK	Lys2	-5.6
PFTAIRE1	UniRef100_O94921	DLKPQNLLISDTGELK	Lys2	-5.7
eEF2K	UniRef100_O00418	YIKYNSNSGFVR	ATP	-5.7
MARK4	UniRef100_Q96L34	DLKAENLLLDAEANIK	Lys2	-5.8
p70S6K	UniRef100_P23443	DLKPENIMLNHQGHVK	Lys2	-6.0
NLK	UniRef100_Q9UBE8	DIKPGNLLVNSNCVLK	Lys2	-6.1
CLK3	UniRef100_P49761	YEIVGNLGEGTFGKVVECLDHAR	ATP Loop	-6.2
NEK9	UniRef100_Q8TD19	LGDYGLAKK	Activation Loop	-6.4
DGKA	UniRef100_P23743	IDPVPNTHPLLVFVNPKSGGK	ATP	-6.7
AurA	UniRef100_O14965	DIKPENLLLGSAGELK	Lys2	-7.1
PIP5K3	UniRef100_Q9Y2I7	GGKSGAAFYATEDDRFILK	ATP	-7.4
MLKL	UniRef100_Q8NB16	APVAIKVFK	Lys1	-7.8
JNK1, JNK2, JNK3	UniRef100_P45983, UniRef100_P53779, Unif	DLKPSNIVVK	Lys2	-8.0
MST1	UniRef100_Q13043	ETGQIVAIKQVPVESDLQEIIK	Lys1	-8.4
CaMKK2	UniRef100_Q96RR4	DIKPSNLLVGEDGHIK	Lys2	-8.5
IKKe	UniRef100_Q14164	SGELVAVKVFNTTSYLRPR	Lys1	-8.6
TLK2	UniRef100_Q86UE8	YVAVKIHQLNK	Lys1	-8.7
MAST3	UniRef100_O60307	DLKPDNLLITSLGHIK	Lys2	-8.7
MSK2 domain1	UniRef100_O75676	DLKLENVLLDSEGHIVLTDFGLSK	Lys2	-8.8
MLK4	UniRef100_Q5TCX8	DLKSSNILLLEK	Lys2	-8.8
MSK1 domain1	UniRef100_O75582	DIKLENILLDSNGHVVLTDFGLSK	Lys2	-9.0
CK2a1	UniRef100_P68400	GGPNIITLADIVKDPVSR	Protein Kinase Domain	-9.2
MAP3K2	UniRef100_Q9Y2U5	ELAVKQVQFDPDSPETSKEVNALECEIQLLK	Lys1	-9.9
MAP2K1, MAP2K2	UniRef100_P36507, UniRef100_Q02750	DVKPSNILVNSR	Lys2	-10.0
MAP2K7	UniRef100_O14733	DVKPSNILLDER	Lys2	-10.3
ZC1/HGK, ZC2/TNIK, ZC3	UniRef100_O95819, UniRef100_Q9UKE5, Uni	DIKGQNVLLTENAEVK	Lys2	-10.5
RSK1 domain1	UniRef100_Q15418	LTDFGLSKEAIDHEKK	Activation Loop	-10.5
MARK4	UniRef100_Q96L34	EVAIKIIDKTQLNPSSLQK	Lys1	-10.7
GCN2 domain2	UniRef100_Q9P2K8	LDGCCYAVKR	Lys1	-10.8
MASTL	UniRef100_Q96GX5	LYAVKVVK	Lys1	-11.2
CaMK1d	UniRef100_Q8IU85	DLKPENLLYYSQDEESK	Lys2	-11.2
PIP4K2B	UniRef100_P78356	AKDLPTFKDNDFLNEGQK	ATP	-11.5
MST2	UniRef100_Q13188	ESGQVVAIKQVPVESDLQEIIK	Lys1	-11.7
CaMK1d	UniRef100_Q8IU85	LFAVKCIPK	Lys1	-11.8
PI4KB	UniRef100_Q9UBF8	VPHTQAVVLNSKDK	ATP	-12.2
GCK	UniRef100_Q12851, UniRef100_P35557	DTVTSELAAVKIVK	Lys1	-12.2
ILK	UniRef100_Q13418	WQGNDIVVKVLK	Lys1	-12.6
PKR	UniRef100_P19525	DLKPSNIFLVDTK	Lys2	-12.8
MARK3, MARK4	UniRef100_Q96L34, UniRef100_P27448	EVAIKIIDK	Lys1	-13.2
MAP4K5	UniRef100_Q9Y4K4	NVHTGELAAVKIIK	Lys1	-13.4
MAPKAPK3	UniRef100_Q16644	QVLGLGVNGKVLECFHR	ATP Loop	-13.8
ROCK1	UniRef100_Q13464	KLQLELNQER	Other	-14.1

KSR1, KSR2	UniRef100_Q6VAB6, UniRef100_Q8IVT5	SKNVFYDNGK	Activation Loop	-14.3
FRAP	UniRef100_P42345	IQSIAPSLQVITSKQRPR	ATP	-15.3
NEK9	UniRef100_Q8TD19	DIKTLNIFLTK	Lys2	-15.6
SGK3	UniRef100_Q96BR1	FYAVKVLQK	Lys1	-16.3
AKT1	UniRef100_P31749	GTFGKVILVK	ATP Loop	-16.4
PCTAIRE1	UniRef100_Q00536	SKLTDNLVALKEIR	Lys1	-16.4
IKKb	UniRef100_O14920	DLKPENIVLQQGEQR	Lys2	-16.9
SMG1	UniRef100_Q96Q15	DTVTIHSVGGTITILPTKTKPK	ATP	-17.1
PIK3CG	UniRef100_P48736	KKPLWLEFK	ATP	-17.2
PLK1	UniRef100_P53350	DLKLGNLFLNEDLEVK	Lys2	-17.2
MAP3K2, MAP3K3	UniRef100_Q9Y2U5, UniRef100_Q99759	DIKGANILR	Lys2	-17.6
MST3, MST4, YSK1	UniRef100_O00506, UniRef100_Q9P289, Uni	LADFGVAGQLTDTQIKR	Activation Loop	-17.6
MARK2	UniRef100_Q7KZI7	EVAVKIIDKTQLNSSSLQK	Lys1	-18.4
BRAF	UniRef100_P15056	DLKSNNIFLHEDLTVK	Lys2	-18.5
FER	UniRef100_P16591	TSVAVKTCKEDLPQELK	Lys1	-18.6
Erk5	UniRef100_Q13164	DLKPSNLLVNENCELK	Lys2	-18.8
NEK1	UniRef100_Q96PY6	DIKSQNIFLTK	Lys2	-19.1
PCTAIRE1, PCTAIRE3	UniRef100_Q00536, UniRef100_Q07002	DLKPQNLLINER	Lys2	-19.2
SMG1	UniRef100_Q96Q15	SYPYLFKGLEDLHLDER	ATP	-19.5
PFTAIRE1	UniRef100_O94921	LVALKVIR	Lys1	-19.6
TAK1	UniRef100_O43318	DLKPPNLLLVAGGTVLK	Lys2	-19.8
Wnk1, Wnk2	UniRef100_Q9Y3S1, UniRef100_Q9H4A3	GSFKTVYK	ATP Loop	-20.1
FES	UniRef100_P07332	LRADNTLVAVKSCR	Lys1	-20.2
NEK7	UniRef100_Q8TDX7	AACLLDGVPVALKK	Lys1	-21.0
CHK2	UniRef100_O96017	VAIKIISK	Lys1	-21.2
SNRK	UniRef100_Q9NRH2	DLKPENVVFFEK	Lys2	-21.2
MSK1 domain1, MSK2 d	UniRef100_O75676, UniRef100_O75582	VLGTGAYGKVFLVR	ATP Loop	-21.2
IRAK1	UniRef100_P51617	AIQFLHQDSPSLIHGDIKSSNVLLDER	Lys2	-21.4
JAK1 domain2	UniRef100_P23458	IGDFGLTKAIETDKEYYTVK	Activation Loop	-21.5
SYK	UniRef100_P43405	ISDFGLSKALR	Activation Loop	-21.6
PKD3	UniRef100_O94806	NIVHCDLKPENVLLASAEPFPQVK	Lys2	-22.2
PLK1	UniRef100_P53350	CFEISDADTKEVFAGKIVPK	Lys1	-23.1
RSK2 domain2	UniRef100_P51812	DLKPSNILYVDESGNPESIR	Lys2	-25.0
MELK	UniRef100_Q14680	DLKPENLLFDEYHK	Lys2	-25.4
PKR	UniRef100_P19525	IGDFGLVTSLKNDGKR	Activation Loop	-25.8
MAP2K4	UniRef100_P45985	DIKPSNILLDR	Lys2	-26.2
CDK5	UniRef100_Q00535	NRETHEIVALKR	Lys1	-26.4
NuaK2	UniRef100_Q9H093	LVAIKSIR	Lys1	-26.6
MAP3K15, MAP3K5, MA	UniRef100_Q99683, UniRef100_O95382, Uni	IAIKEIPER	Lys1	-27.7
MARK3	UniRef100_P27448	EVAIKIIDKTQLNPTSLQK	Lys1	-28.6
BARK1	UniRef100_P25098	DLKPANILLDEHGHVR	Lys2	-28.7
CDK5	UniRef100_Q00535	DLKPQNLLINR	Lys2	-29.2
PIP4K2A	UniRef100_P48426	AKELPTLKDNDFINEGQK	ATP	-30.1
DGKH	UniRef100_Q86XP1	ATFSFCVSPLLVFVNSKSGDNQGVK	ATP	-31.5
CHK2	UniRef100_O96017	DLKPENVLLSSQEEDCLIK	Lys2	-33.0
GCN2 domain2	UniRef100_Q9P2K8	DLKPVNIFLDSDDHVK	Lys2	-33.6
Wnk1, Wnk2, Wnk4	UniRef100_Q9Y3S1, UniRef100_Q96J92, Unif	IGDLGLATLKR	Activation Loop	-33.9
SIK	UniRef100_P57059	TQVAIKIIDK	Lys1	-35.2
MYO3A, MYO3B	UniRef100_Q8NEV4, UniRef100_Q8WXR4	DVKGNNILLTTEGGVK	Lys2	-36.7
PCTAIRE2, PCTAIRE3	UniRef100_Q00537, UniRef100_Q07002	SKLTENLVALKEIR	Lys1	-38.0
RSK1 domain2	UniRef100_Q15418	DLKPSNILYVDESGNPECLR	Lys2	-41.3
PAK2	UniRef100_Q13177	IGQGASGTVFTATDVALGQEVAIKQINLQK	Lys1	-41.5
JAK1 domain2	UniRef100_P23458	YDPEGDNTGEQVAVKSLKPESGGNHIADLKK	Lys1	-41.8
AKT1, AKT3	UniRef100_P31749, UniRef100_Q9Y243	DLKLENLMLDKDGHIK	Lys2	-42.4
SYK	UniRef100_P43405	TVAVKILK	Lys1	-44.3
MAP4K3	UniRef100_Q8IVH8	DIKGANILLTDNGHVK	Lys2	-50.6

EC50 (M)	KIN-8194	Ibrutinib
BCWM.1	4.83E-09	6.81E-07
MWCL-1	6.64E-09	7.79E-07
TMD8	5.41E-09	4.06E-09
HBL-1	7.09E-08	2.58E-08
OCI-Ly7	1.07E-07	1.75E-06
OCI-Ly19	8.26E-07	9.25E-06
Ramos	8.72E-06	5.07E-06
RPMI-8226	1.17E-04	1.45E-05
BCWM.1 - Vector	1.69E-08	1.12E-06
BCWM.1 - HCK^{WT}	8.87E-08	6.33E-07
BCWM.1 - HCK^{T333M}	2.02E-06	1.42E-05
MWCL-1 - Vector	1.12E-09	2.95E-06
MWCL-1 - HCK^{WT}	3.86E-09	9.82E-07
MWCL-1 - HCK^{T333M}	8.13E-07	4.00E-06
BCWM.1 - Vector	2.32E-08	5.73E-07
BCWM.1 - BTK^{WT}	2.50E-08	4.43E-07
BCWM.1 - BTK^{C481S}	4.01E-08	2.21E-06
TMD8 - Vector	1.27E-08	1.48E-09
TMD8 - BTK^{WT}	1.59E-08	4.10E-09
TMD8 - BTK^{C481S}	1.46E-08	7.17E-07