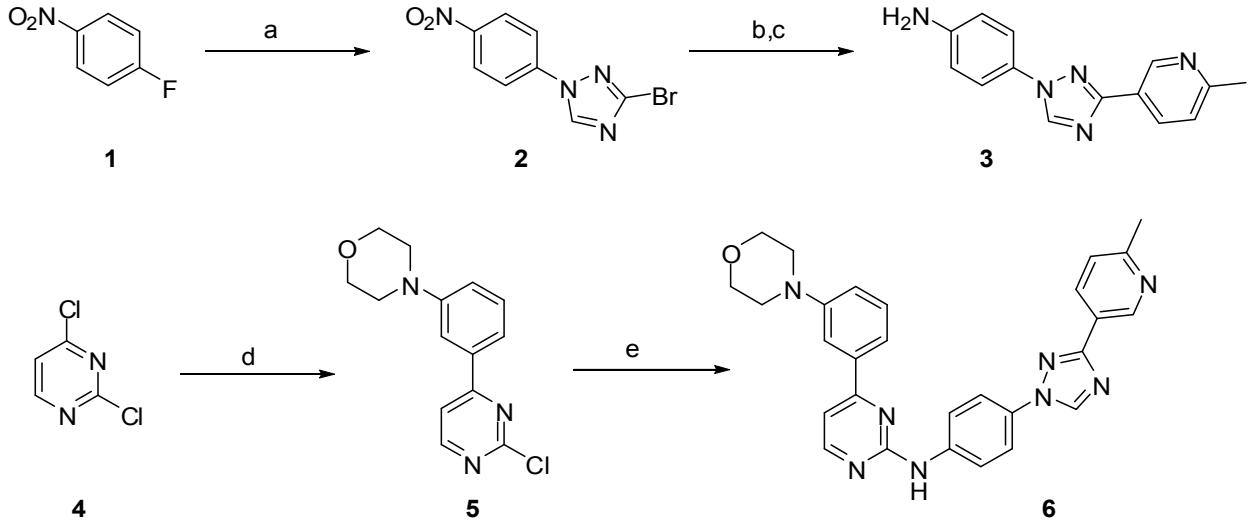
Supplemental Figure 1

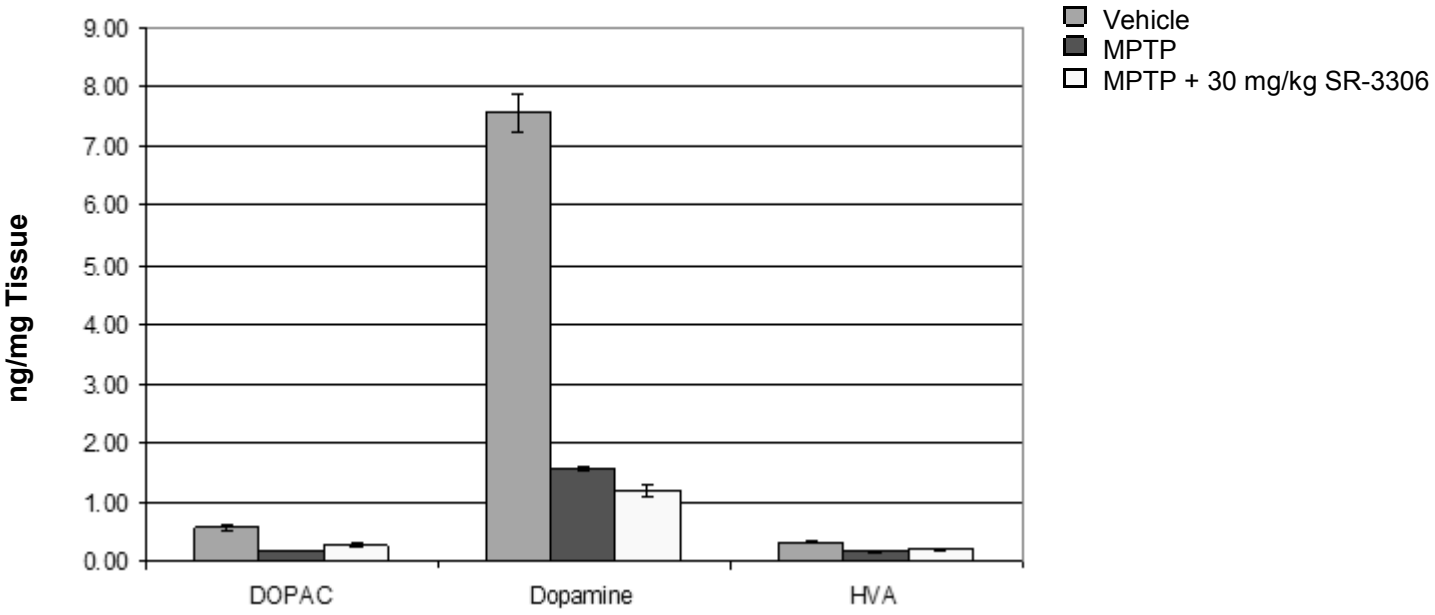
Treatment of 4-fluoro-1-nitrobenzene (**1**) with bromo-triazole resulted in clean conversion to substitution products (**2**). Suzuki coupling with pyridine boronic acid followed by hydrogenation of the nitro group to amino gave aniline **3**. Suzuki coupling of morpholino-substituted phenyl boronate ester with dichloropyrimidine afforded coupled product (**5**), which was then condensed with aniline **3** to provide SR-3306.

Scheme 1. Synthesis of SR-3306



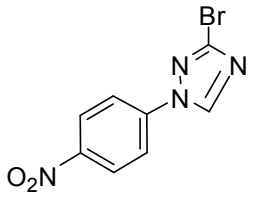
Reagents and Conditions: a. 3-bromo-1H-1,2,4-triazole, K_2CO_3, DMF, 70C; b. 6-methylpyridin-3-ylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, toluene/MeOH, 100C; c. Pt/C, EtOH, H_2; d. 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)morpholine, K_2CO_3, $Pd(PPh_3)_4$, DME/H_20, 90C; e. compound **3**, 2-ethoxyethanol, 190C.

Supplemental Figure 2. Striatal Catecholamine Levels 7-days after MPTP treatment



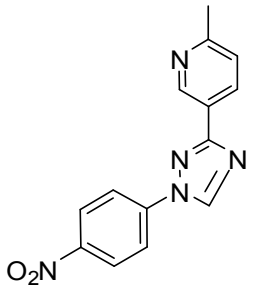
Supplemental Figure 3

3-Bromo-1-(4-nitrophenyl)-1H-1,2,4-triazole



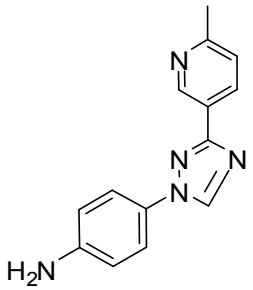
A mixture of 4-fluoro-1-nitrobenzene (28.2 g, 0.20 mol), 3-bromo-1H-1,2,4-triazole (32.3 g, 0.218 mol) and K_2CO_3 (55.3 g, 0.40 mol) in DMF (200 mL) was heated at 70 °C for 16 hrs. The reaction mixture was cooled down to room temperature, diluted with water (800 mL), stirred for 10 min. The resulting suspension was filtered and rinsed with water, dried under air to provide 3-bromo-1-(4-nitrophenyl)-1H-1,2,4-triazole as a beige solid, 53.0 g, 99% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.60 (s, 1H), 8.44 (d, 2H), 7.91 (d, 2H).

2-Methyl-5-(1-(4-nitrophenyl)-1H-1,2,4-triazol-3-yl)pyridine



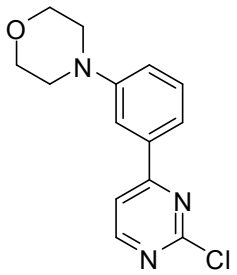
A mixture of 3-bromo-1-(4-nitrophenyl)-1H-1,2,4-triazole (5.92 g, 22.0 mmol), 6-methylpyridin-3-ylboronic acid monohydrate (4.09 g, 26.4 mmol), K_2CO_3 (6.08 g, 44.0 mmol) and $Pd(PPh_3)_4$ (1.27 g, 1.10 mmol) in 110 mL toluene/MeOH (10:1, v/v) was purged with argon for 5 min, then refluxed for 24 hrs. The reaction mixture was cooled down to room temperature, diluted with water (50 mL) and sat. $NaHCO_3$ (aq., 100 mL), extracted with EtOAc (4 x 100 mL). The combined organic solution was washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to remove the solvent, then triturated with Et_2O (30 mL) to provide 2-methyl-5-(1-(4-nitrophenyl)-1H-1,2,4-triazol-3-yl)pyridine as a pale brown solid, 4.15 g, 67% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.34 (s, 1H), 8.76 (s, 1H), 8.46 (d, 2H), 8.37 (dd, 1H), 8.01 (d, 2H), 7.33 (d, 1H), 2.67 (s, 3H).

4-(3-(6-Methylpyridin-3-yl)-1H-1,2,4-triazol-1-yl)aniline



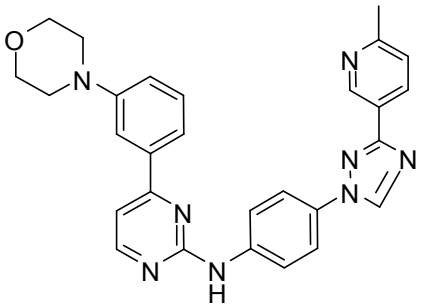
A mixture of 2-methyl-5-(1-(4-nitrophenyl)-1H-1,2,4-triazol-3-yl)pyridine (4.87 g, 17.3 mmol) and 5% Pt/C (0.50 g) in EtOH (170 mL) was stirred at room temperature under a H_2 balloon for 16 hrs. The reaction mixture was filtered through Celite and concentrated *in vacuo* to provide 4-(3-(6-methylpyridin-3-yl)-1H-1,2,4-triazol-1-yl)aniline as a beige solid, 4.00 g, 92% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.29 (s, 1H), 8.44 (s, 1H), 8.33 (dd, 1H), 7.49 (d, 2H), 7.25 (d, 1H), 6.80 (d, 2H), 3.88 (br s, 2H), 2.63 (s, 3H).

4-(3-(2-Chloropyrimidin-4-yl)phenyl)morpholine



A mixture of 4-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)morpholine (4.0 g, 13.8 mmol), 2,4-dichloropyrimidine (2.47 g, 16.6 mmol), $Pd(PPh_3)_4$ (0.80 g, 0.69 mmol), 2 M K_2CO_3 (aq., 21 mL) and DME (42 mL) was purged with argon for 10 min, then heated in a sealed tube at 90°C overnight. The reaction mixture was cooled down to room temperature, extracted with EtOAc (2 x 30 mL). The combined organic solution was dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to give an oil, which was purified by column chromatography on silica gel (0~20% EtOAc in hexane) to provide 4-(3-(2-chloropyrimidin-4-yl)phenyl)morpholine as a yellowish green solid, 3.54 g, 93% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (d, 1H), 7.70 (s, 1H), 7.64 (d, 1H), 7.51–7.47 (m, 1H), 7.41 (t, 1H), 7.10–7.08 (m, 1H), 3.92–3.90 (m, 4H), 3.29–3.26 (m, 4H). MS (ESI) 276.16 (M+H).

N-(4-(3-(6-Methylpyridin-3-yl)-1H-1,2,4-triazol-1-yl)phenyl)-4-(3-morpholinophenyl)pyrimidin-2-amine



A mixture of 4-(3-(2-chloropyrimidin-4-yl)phenyl)morpholine (0.99 g, 3.60 mmol) 4-(3-(6-methylpyridin-3-yl)-1H-1,2,4-triazol-1-yl)aniline (0.91 g, 3.60 mmol) in 2-ethoxyethanol (5 mL) was heated in a sealed tube at 190°C for 24 hrs. The reaction mixture was cooled down to room temperature, diluted with 1 M HCl (aq., 50 mL) and washed with EtOAc (3 x 50 mL). The remaining aqueous solution was added with 6 M NaOH (aq.) until pH~6 and the resulting precipitate was filtered. The solid collected was purified by column chromatography on silica gel (0~5% MeOH in EtOAc) to provide N-(4-(3-(6-methylpyridin-3-yl)-1H-1,2,4-triazol-1-yl)phenyl)-4-(3-morpholinophenyl)pyrimidin-2-amine as a beige solid, 1.20 g, 68% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.24 (s, 1H), 8.47 (s, 1H), 8.42

(d, 1H), 8.27 (dd, 1H), 7.82 (d, 2H), 7.63 (m, 3H), 7.47 (d, 1H), 7.42 (s, 1H), 7.35 (t, 1H), 7.21 (d, 1H), 7.14 (d, 1H), 7.01 (dd, 1H), 3.84 (m, 4H), 3.20 (m, 4H), 2.55 (s, 3H). MS (ESI) 491.34 (M+H).

Supplemental Table 1: Kinase Counterscreening Panel for SR-3306

Compound Name	Ambit Gene Symbol	Percent Control	Compound Concentration (nM)
SR-3306	AAK1	25	3000
SR-3306	ABL1	No hit	3000
SR-3306	ABL1(E255K)	No hit	3000
SR-3306	ABL1(F317I)	No hit	3000
SR-3306	ABL1(F317L)	No hit	3000
SR-3306	ABL1(H396P)	No hit	3000
SR-3306	ABL1(M351T)	No hit	3000
SR-3306	ABL1(Q252H)	No hit	3000
SR-3306	ABL1(T315I)	No hit	3000
SR-3306	ABL1(Y253F)	No hit	3000
SR-3306	ABL2	No hit	3000
SR-3306	ACVR1	No hit	3000
SR-3306	ACVR1B	No hit	3000
SR-3306	ACVR2A	No hit	3000
SR-3306	ACVR2B	No hit	3000
SR-3306	ACVRL1	No hit	3000
SR-3306	ADCK3	No hit	3000
SR-3306	ADCK4	19	3000
SR-3306	AKT1	No hit	3000
SR-3306	AKT2	No hit	3000
SR-3306	AKT3	No hit	3000
SR-3306	ALK	No hit	3000
SR-3306	AMPK-alpha1	No hit	3000
SR-3306	AMPK-alpha2	No hit	3000
SR-3306	ANKK1	No hit	3000
SR-3306	ARK5	No hit	3000
SR-3306	AURKA	No hit	3000
SR-3306	AURKB	No hit	3000
SR-3306	AURKC	No hit	3000
SR-3306	AXL	No hit	3000
SR-3306	BIKE	5.9	3000
SR-3306	BLK	No hit	3000
SR-3306	BMPR1A	No hit	3000
SR-3306	BMPR1B	No hit	3000
SR-3306	BMPR2	No hit	3000
SR-3306	BMX	No hit	3000
SR-3306	BRAF	No hit	3000
SR-3306	BRAF(V600E)	No hit	3000
SR-3306	BRSK1	No hit	3000
SR-3306	BRSK2	No hit	3000
SR-3306	BTK	No hit	3000
SR-3306	CAMK1	No hit	3000
SR-3306	CAMK1D	No hit	3000
SR-3306	CAMK1G	No hit	3000
SR-3306	CAMK2A	No hit	3000
SR-3306	CAMK2B	No hit	3000
SR-3306	CAMK2D	No hit	3000

SR-3306	CAMK2G	No hit	3000
SR-3306	CAMK4	No hit	3000
SR-3306	CAMKK1	No hit	3000
SR-3306	CAMKK2	No hit	3000
SR-3306	CDC2L1	No hit	3000
Compound Name	**Ambit Gene Symbol**	**Percent Control**	**Compound Concentration (nM)**
SR-3306	CDC2L2	No hit	3000
SR-3306	CDK11	No hit	3000
SR-3306	CDK2	No hit	3000
SR-3306	CDK3	No hit	3000
SR-3306	CDK5	No hit	3000
SR-3306	CDK7	8.5	3000
SR-3306	CDK8	No hit	3000
SR-3306	CDK9	4.1	3000
SR-3306	CDKL2	20	3000
SR-3306	CHEK1	No hit	3000
SR-3306	CHEK2	No hit	3000
SR-3306	CIT	No hit	3000
SR-3306	CLK1	33	3000
SR-3306	CLK2	No hit	3000
SR-3306	CLK3	No hit	3000
SR-3306	CLK4	34	3000
SR-3306	CSF1R	No hit	3000
SR-3306	CSK	No hit	3000
SR-3306	CSNK1A1L	No hit	3000
SR-3306	CSNK1D	No hit	3000
SR-3306	CSNK1E	No hit	3000
SR-3306	CSNK1G1	No hit	3000
SR-3306	CSNK1G2	No hit	3000
SR-3306	CSNK1G3	No hit	3000
SR-3306	CSNK2A1	No hit	3000
SR-3306	CSNK2A2	32	3000
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SR-3306	DAPK2	No hit	3000
SR-3306	DAPK3	No hit	3000
SR-3306	DCAMKL1	No hit	3000
SR-3306	DCAMKL2	No hit	3000
SR-3306	DCAMKL3	No hit	3000
SR-3306	DDR1	No hit	3000
SR-3306	DDR2	No hit	3000
SR-3306	DLK	No hit	3000
SR-3306	DMPK	No hit	3000
SR-3306	DMPK2	No hit	3000
SR-3306	DRAK1	No hit	3000
SR-3306	DRAK2	No hit	3000
SR-3306	DYRK1B	No hit	3000
SR-3306	EGFR	No hit	3000
SR-3306	EGFR(E746-A750del)	No hit	3000
SR-3306	EGFR(G719C)	No hit	3000
SR-3306	EGFR(G719S)	No hit	3000
SR-3306	EGFR(L747-E749del, A750P)	No hit	3000
SR-3306	EGFR(L747-S752del, P753S)	No hit	3000
SR-3306	EGFR(L747-T751del,Sins)	No hit	3000
SR-3306	EGFR(L858R)	No hit	3000
SR-3306	EGFR(L861Q)	No hit	3000

SR-3306	EGFR(S752-I759del)	No hit	3000
SR-3306	EPHA1	No hit	3000
SR-3306	EPHA2	No hit	3000
SR-3306	EPHA3	No hit	3000
SR-3306	EPHA4	No hit	3000
Compound Name	**Ambit Gene Symbol**	**Percent Control**	**Compound Concentration (nM)**
SR-3306	EPHA5	No hit	3000
SR-3306	EPHA6	No hit	3000
SR-3306	EPHA7	No hit	3000
SR-3306	EPHA8	No hit	3000
SR-3306	EPHB1	No hit	3000
SR-3306	EPHB2	No hit	3000
SR-3306	EPHB3	No hit	3000
SR-3306	EPHB4	No hit	3000
SR-3306	ERBB2	No hit	3000
SR-3306	ERBB4	No hit	3000
SR-3306	ERK1	No hit	3000
SR-3306	ERK2	No hit	3000
SR-3306	ERK3	No hit	3000
SR-3306	ERK4	No hit	3000
SR-3306	ERK5	No hit	3000
SR-3306	ERK8	14	3000
SR-3306	FER	No hit	3000
SR-3306	FES	No hit	3000
SR-3306	FGFR1	No hit	3000
SR-3306	FGFR2	No hit	3000
SR-3306	FGFR3	No hit	3000
SR-3306	FGFR3(G697C)	No hit	3000
SR-3306	FGFR4	No hit	3000
SR-3306	FGR	No hit	3000
SR-3306	FLT1	No hit	3000
SR-3306	FLT3	19	3000
SR-3306	FLT3(D835H)	No hit	3000
SR-3306	FLT3(D835Y)	No hit	3000
SR-3306	FLT3(ITD)	No hit	3000
SR-3306	FLT3(K663Q)	24	3000
SR-3306	FLT3(N841I)	17	3000
SR-3306	FLT4	No hit	3000
SR-3306	FRK	No hit	3000
SR-3306	FYN	No hit	3000
SR-3306	GAK	No hit	3000
SR-3306	GCN2(Kin.Dom.2,S808G)	No hit	3000
SR-3306	GSK3A	11	3000
SR-3306	GSK3B	No hit	3000
SR-3306	HCK	No hit	3000
SR-3306	HIPK1	No hit	3000
SR-3306	IGF1R	No hit	3000
SR-3306	IKK-alpha	No hit	3000
SR-3306	IKK-beta	No hit	3000
SR-3306	IKK-epsilon	No hit	3000
SR-3306	INSR	No hit	3000
SR-3306	INSRR	No hit	3000
SR-3306	IRAK3	33	3000
SR-3306	ITK	No hit	3000
SR-3306	JAK1(Kin.Dom.1)	No hit	3000

SR-3306	JAK1(Kin.Dom.2)	No hit	3000
SR-3306	JAK2(Kin.Dom.2)	25	3000
SR-3306	JAK3(Kin.Dom.2)	No hit	3000
SR-3306	JNK1	1	3000
SR-3306	JNK2	No hit	3000
Compound Name	**Ambit Gene Symbol**	**Percent Control**	**Compound Concentration (nM)**
SR-3306	JNK3	18	3000
SR-3306	KIT	0	3000
SR-3306	KIT(D816V)	No hit	3000
SR-3306	KIT(V559D)	0.1	3000
SR-3306	KIT(V559D,T670I)	No hit	3000
SR-3306	KIT(V559D,V654A)	20	3000
SR-3306	LATS1	No hit	3000
SR-3306	LATS2	No hit	3000
SR-3306	LCK	No hit	3000
SR-3306	LIMK1	No hit	3000
SR-3306	LIMK2	No hit	3000
SR-3306	LKB1	No hit	3000
SR-3306	LOK	No hit	3000
SR-3306	LTK	No hit	3000
SR-3306	LYN	No hit	3000
SR-3306	MAP3K3	No hit	3000
SR-3306	MAP3K4	No hit	3000
SR-3306	MAP3K5	No hit	3000
SR-3306	MAP4K1	No hit	3000
SR-3306	MAP4K2	No hit	3000
SR-3306	MAP4K3	No hit	3000
SR-3306	MAP4K4	No hit	3000
SR-3306	MAP4K5	No hit	3000
SR-3306	MAPKAPK2	No hit	3000
SR-3306	MAPKAPK5	No hit	3000
SR-3306	MARK1	No hit	3000
SR-3306	MARK2	No hit	3000
SR-3306	MARK3	No hit	3000
SR-3306	MARK4	No hit	3000
SR-3306	MEK1	No hit	3000
SR-3306	MEK2	No hit	3000
SR-3306	MEK3	No hit	3000
SR-3306	MEK4	No hit	3000
SR-3306	MEK6	No hit	3000
SR-3306	MELK	No hit	3000
SR-3306	MERTK	No hit	3000
SR-3306	MET	No hit	3000
SR-3306	MINK	No hit	3000
SR-3306	MKNK1	No hit	3000
SR-3306	MKNK2	No hit	3000
SR-3306	MLCK	No hit	3000
SR-3306	MLK1	No hit	3000
SR-3306	MLK2	No hit	3000
SR-3306	MLK3	No hit	3000
SR-3306	MRCKA	No hit	3000
SR-3306	MRCKB	No hit	3000
SR-3306	MST1	No hit	3000
SR-3306	MST1R	No hit	3000
SR-3306	MST2	No hit	3000

SR-3306	MST3	No hit	3000
SR-3306	MST4	No hit	3000
SR-3306	MUSK	No hit	3000
SR-3306	MYLK	No hit	3000
SR-3306	MYLK2	No hit	3000
Compound Name	**Ambit Gene Symbol**	**Percent Control**	**Compound Concentration (nM)**
SR-3306	MYO3A	No hit	3000
SR-3306	MYO3B	No hit	3000
SR-3306	NDR2	No hit	3000
SR-3306	NEK1	No hit	3000
SR-3306	NEK2	No hit	3000
SR-3306	NEK5	No hit	3000
SR-3306	NEK6	No hit	3000
SR-3306	NEK7	No hit	3000
SR-3306	NEK9	No hit	3000
SR-3306	NLK	No hit	3000
SR-3306	p38-alpha	No hit	3000
SR-3306	p38-beta	No hit	3000
SR-3306	p38-delta	No hit	3000
SR-3306	p38-gamma	No hit	3000
SR-3306	PAK1	No hit	3000
SR-3306	PAK2	No hit	3000
SR-3306	PAK3	No hit	3000
SR-3306	PAK4	No hit	3000
SR-3306	PAK6	No hit	3000
SR-3306	PAK7/PAK5	No hit	3000
SR-3306	PCTK1	24	3000
SR-3306	PCTK2	No hit	3000
SR-3306	PCTK3	No hit	3000
SR-3306	PDGFRA	0.65	3000
SR-3306	PDGFRB	1	3000
SR-3306	PDPK1	No hit	3000
SR-3306	PFTAIRE2	No hit	3000
SR-3306	PFTK1	No hit	3000
SR-3306	PHKG1	No hit	3000
SR-3306	PHKG2	No hit	3000
SR-3306	PIK3C2B	No hit	3000
SR-3306	PIK3CA	No hit	3000
SR-3306	PIK3CA(E545K)	No hit	3000
SR-3306	PIK3CB	No hit	3000
SR-3306	PIK3CD	No hit	3000
SR-3306	PIK3CG	18	3000
SR-3306	PIM1	No hit	3000
SR-3306	PIM2	No hit	3000
SR-3306	PIM3	No hit	3000
SR-3306	PIP5K1A	33	3000
SR-3306	PIP5K2B	25	3000
SR-3306	PKAC-alpha	No hit	3000
SR-3306	PKAC-beta	No hit	3000
SR-3306	PKMYT1	No hit	3000
SR-3306	PKN1	No hit	3000
SR-3306	PKN2	No hit	3000
SR-3306	PLK1	No hit	3000
SR-3306	PLK3	No hit	3000
SR-3306	PLK4	No hit	3000

SR-3306	PRKCD	No hit	3000
SR-3306	PRKCE	No hit	3000
SR-3306	PRKCH	No hit	3000
SR-3306	PRKCQ	No hit	3000
SR-3306	PRKD1	No hit	3000
Compound Name	**Ambit Gene Symbol**	**Percent Control**	**Compound Concentration (nM)**
SR-3306	PRKD2	No hit	3000
SR-3306	PRKD3	No hit	3000
SR-3306	PRKG1	No hit	3000
SR-3306	PRKG2	No hit	3000
SR-3306	PRKR	No hit	3000
SR-3306	PRKX	No hit	3000
SR-3306	PTK2	No hit	3000
SR-3306	PTK2B	No hit	3000
SR-3306	PTK6	No hit	3000
SR-3306	RAF1	No hit	3000
SR-3306	RET	No hit	3000
SR-3306	RET(M918T)	No hit	3000
SR-3306	RET(V804L)	No hit	3000
SR-3306	RET(V804M)	No hit	3000
SR-3306	RIOK1	12	3000
SR-3306	RIOK2	No hit	3000
SR-3306	RIOK3	18	3000
SR-3306	RIPK1	No hit	3000
SR-3306	RIPK2	No hit	3000
SR-3306	RIPK4	No hit	3000
SR-3306	ROCK2	No hit	3000
SR-3306	ROS1	No hit	3000
SR-3306	RPS6KA1(Kin.Dom.1)	No hit	3000
SR-3306	RPS6KA1(Kin.Dom.2)	No hit	3000
SR-3306	RPS6KA2(Kin.Dom.1)	No hit	3000
SR-3306	RPS6KA2(Kin.Dom.2)	No hit	3000
SR-3306	RPS6KA3(Kin.Dom.1)	No hit	3000
SR-3306	RPS6KA4(Kin.Dom.1)	No hit	3000
SR-3306	RPS6KA4(Kin.Dom.2)	No hit	3000
SR-3306	RPS6KA5(Kin.Dom.1)	No hit	3000
SR-3306	RPS6KA5(Kin.Dom.2)	No hit	3000
SR-3306	RPS6KA6(Kin.Dom.1)	No hit	3000
SR-3306	RPS6KA6(Kin.Dom.2)	No hit	3000
SR-3306	SgK085	No hit	3000
SR-3306	SgK110	No hit	3000
SR-3306	SLK	No hit	3000
SR-3306	SNARK	No hit	3000
SR-3306	SNF1LK	No hit	3000
SR-3306	SNF1LK2	No hit	3000
SR-3306	SRC	No hit	3000
SR-3306	SRMS	No hit	3000
SR-3306	SRPK1	No hit	3000
SR-3306	SRPK2	No hit	3000
SR-3306	SRPK3	26	3000
SR-3306	STK16	9.4	3000
SR-3306	STK33	No hit	3000
SR-3306	STK35	No hit	3000
SR-3306	STK36	No hit	3000
SR-3306	SYK	No hit	3000

SR-3306	TAK1	No hit	3000
SR-3306	TAOK1	No hit	3000
SR-3306	TAOK3	No hit	3000
SR-3306	TEC	No hit	3000
SR-3306	TESK1	24	3000
Compound Name	**Ambit Gene Symbol**	**Percent Control**	**Compound Concentration (nM)**
SR-3306	TGFBR1	No hit	3000
SR-3306	TGFBR2	No hit	3000
SR-3306	TIE1	No hit	3000
SR-3306	TIE2	No hit	3000
SR-3306	TLK1	No hit	3000
SR-3306	TLK2	No hit	3000
SR-3306	TNIK	No hit	3000
SR-3306	TNK1	No hit	3000
SR-3306	TNK2	No hit	3000
SR-3306	TNNI3K	No hit	3000
SR-3306	TRKA	23	3000
SR-3306	TRKB	No hit	3000
SR-3306	TRKC	No hit	3000
SR-3306	TSSK1	No hit	3000
SR-3306	TTK	No hit	3000
SR-3306	TXK	No hit	3000
SR-3306	TYK2(Kin.Dom.1)	1.8	3000
SR-3306	TYK2(Kin.Dom.2)	30	3000
SR-3306	TYRO3	No hit	3000
SR-3306	ULK1	No hit	3000
SR-3306	ULK2	No hit	3000
SR-3306	ULK3	No hit	3000
SR-3306	VEGFR2	No hit	3000
SR-3306	WEE1	No hit	3000
SR-3306	WEE2	No hit	3000
SR-3306	YANK2	No hit	3000
SR-3306	YANK3	No hit	3000
SR-3306	YES	No hit	3000
SR-3306	YSK1	No hit	3000
SR-3306	ZAK	34	3000
SR-3306	ZAP70	No hit	3000

Supplemental Table 2: MDS Pharma Lead Profiling Panel Counterscreen for SR-2502

Target	SPP.	n=	CONC.	%	% INHIBITION -100 ↓ -50 ↓ 0 ↓ 50 ↓ 100 ↓
Adenosine A_1	hum	2	3μM	25	
Adenosine A_{2A}	hum	2	3μM	55	
Adenosine A_3	hum	2	3μM	93	
Adrenergic α_{1A}	rat	2	3μM	5	
Adrenergic α_{1B}	Rat	2	3μM	4	
Adrenergic α_{1D}	hum	2	3μM	1	
Adrenergic α_{2A}	hum	2	3μM	2	
Adrenergic β_1	hum	2	3μM	6	
Adrenergic β_2	hum	2	3μM	-3	
Androgen (Testosterone) AR	Rat	2	3μM	11	
Bradykinin B_1	Hum	2	3μM	-8	
Bradykinin B_2	Hum	2	3μM	27	
Calcium Channel L-Type, Benzothianzepine	Rat	2	3μM	-3	
Calcium Channel L-Type, Dihydropyridine	Rat	2	3μM	7	
Calcium Channel N-Type	Rat	2	3μM	-1	
Dopamine D_1	Hum	2	3μM	-11	
Dopamine D_{25}	hum	2	3μM	12	
Dopamine D_3	Hum	2	3μM	-13	
Dopamine $D_{4.2}$	Hum	2	3μM	-3	
Endothelin ET_A	Hum	2	3μM	-4	
Endothelin ET_B	Hum	2	3μM	-10	
Epidermal growth Factor (EGF)	Hum	2	3μM	-18	
Estrogen ERα	Hum	2	3μM	0	
G Protein-Coupled Receptor GPR103	Hum	2	3μM	-14	
$GABA_{A,}$ Flunitrazepam, Central	Rat	2	3μM	7	
$GABA_{A,}$ Muscimol, Central	Rat	2	3μM	-2	
$GABA_{B1A}$	Hum	2	3μM	4	
Glutamate, Kainate	Rat	2	3μM	16	
Glutamate, MNDA, Agonism	Rat	2	3μM	-2	
Glutamate, MNDA, Glycine	Rat	2	3μM	11	
Glutamate, MNDA, Phencyclidine	Rat	2	3μM	-3	
Histamine H_1	Hum	2	3μM	0	
Histamine H_2	Hum	2	3μM	-4	
Histamine H_3	Hum	2	3μM	-10	
Imidazoline $I_{2,}$ Central	Rat	2	3μM	10	
Interleukin IL-1	Mouse	2	3μM	-5	
Leukotriene, Cysteinyl $CysLT_1$	Hum	2	3μM	8	
Melatonin MT_1	Hum	2	3μM	10	
Muscarinic M_1	Hum	2	3μM	10	
Muscarinic M_2	Hum	2	3μM	-9	
Muscarinic M_3	Hum	2	3μM	1	
Neuropeptide Y Y_1	Hum	2	3μM	-0	
Neuropeptide Y Y_2	Hum	2	3μM	7	
Nicotinic Acetylcholine	Hum	2	3μM	0	
Nicotinic Acetylcholine α1, Bungarotoxin	Hum	2	3μM	-10	
Opiate δ (OP1, DOP)	Hum	2	3μM	0	
Opiate $_K$ (OP2, KOP)	Hum	2	3μM	0	
Opiate $_\mu$ (OP3, MOP)	Hum	2	3μM	-4	
Phorbol Ester	Mouse	2	3μM	10	
Platelet Activating Factor (PAF)	Hum	2	3μM	20	
Potassium Channel [K_{ATP}]	Ham	2	3μM	-19	
Potassium Channel HERG	Hum	2	3μM	2	
Prostanoid EP_4	Hum	2	3μM	1	
Purinergic P_{2X}	Rabbit	2	3μM	4	
Purinergic P_{2Y}	Rat	2	3μM	3	
Rolipram	Rat	2	3μM	1	
Seratonin (5-Hydroxytrptamine) 5-HT_{1A}	Hum	2	3μM	28	
Seratonin (5-Hydroxytrptamine) 5-HT_3	Hum	2	3μM	5	
Sigma σ_1	Hum	2	3μM	-1	
Sigma σ_2	Rat	2	3μM	7	
Sodium channel, site 2	Rat	2	3μM	-4	
Tachykinin NK1	Hum	2	3μM	4	
Thyroid Hormone	Rat	2	3μM	-4	
Transporter, Dopamine (DAT)	Hum	2	3μM	6	
Transporter, GABA	Rat	2	3μM	-8	
Transporter, Norepinephrine (NET)	Hum	2	3μM	-16	
Transporter, Serotonin (5-Hydroxytryptamine) (SERT)	Hum	2	3μM	-4	

Supplemental Table 3. Drug Metabolism and Rat Pharmacokinetics for SR-3306

Compound	Cl_p (mL/min/kg)	$t_{½}$ (h)	Vd (L/Kg)	Oral AUC (μM*h)	Oral C_{max} (μM)	%F	Microsomal Stability [b] (min) Mouse / Rat / Human
SR-3306	14	2.3	2.3	1.5	0.2	31	26 / 30 / 28

[a] 1 mg/kg i.v.; 2 mg/kg p.o. [b] 2 mg/mL mouse, rat, or human liver microsomes were used in the stability studies.