Dual screening of BPTF and Brd4 using protein-observed fluorine NMR uncovers new bromodomain probe molecules.

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Protein Expression and Molecular Biology Materials:

For *E. coli* growth, LB agar, LB media, defined media components including unlabeled amino acids, uracil, thiamine-HCl, nicotinic acid, biotin and buffer components were purchased from RPI corp. Thymine, cytosine, guanosine were purchased from Alfa Aesar. Magnesium chloride, manganese sulfate, succinic acid, calcium chloride and 5-fluoroindole were purchased from Sigma-Aldrich. Miniprep plasmid purification kit was purchased from Clontech.

Methods:

Unlabeled Brd4 and BPTF Protein Expression:

The pNIC28-BSA4 plasmid containing the first bromodomain of Brd4 and BPTF genes were kind gifts from the laboratory of Stefan Knapp. For protein expression, either the *E. coli* Rosetta (DE3) strain (Novagen) was first transformed with the respective expression plasmid or the BL21(DE3) strain was cotransformed along with the pRARE (Novagen) plasmid and plated onto agar plates containing kanamycin (100 mg/L) and chloramphenicol (35 mg/L). Following overnight incubation at 37 °C, a single colony was selected from the agar plate and inoculated in 50 mL of LB media containing kanamycin (100 mg/L) and chloramphenicol (35 mg/L). The primary culture was grown overnight at 25 °C while shaking at 250 rpm. For secondary culture growth, 1 L of LB media containing kanamycin (100 mg/L) was inoculated with the primary culture and cultured at 37 °C while shaking at 250 rpm. When the O.D. of culture at 600 nm reached 0.6, the shaker temperature was reduced to 20 °C. After 30 minutes, the expression was induced with 1 mM IPTG overnight for 12-16 h. Cells were harvested by centrifugation and stored at -20 °C.

Bromodomain Purification:

To purify fluorinated and unlabeled Brd4, the cell pellet was thawed at room temperature followed by the addition of lysis buffer (50 mM Phosphate pH 7.4, 300 mM NaCl) containing protease inhibitor PMSF (5 mM) as well as the Halt protease inhibitor. Cells were lysed by sonication and the cell lysate was centrifuged at 7500 g for 30 minutes followed by supernatant filtration through Whatman filter paper. Filtrate containing the histidine-tagged Brd4 was loaded on to a nickel-NTA affinity column and eluted with an imidazole gradient on an AKTA FPLC system monitoring the absorbance at 280 nm. Imidazole was removed from the buffer using a HiPrep column (GE) for buffer exchange into 50 mM Tris pH 7.4, 100 mM NaCl. Purified and buffer exchanged protein was treated with TEV protease for either 2 hours at room temperature or alternatively at 4 °C overnight on a rotating carrousel. The cleaved His-tag, TEV protease and uncleaved Brd4 were removed using nickel-NTA affinity resin.

Protein Mass Spectral Analysis

Product molecular weight was confirmed by electrospray ionization mass spectrometry (ESI-MS) using a Thermo Scientific Orbitrap Velos LC-MS, reported previously. To determine the percent incorporation for fluorinated proteins the integration values of the different deconvoluted mass peaks are entered into the following equation to determine the relative incorporation e.g, FWBrd4:

$$\%_{incorporation} = \frac{(0FWBrd4)*0+(1FWBrd4)*1+(2FWBrd4)*2+(FWBrd4)*3}{(0FWBrd4)*3+(1FWBrd4)*3+(2FWBrd4)*3+(FWBrd4)*3} * 100$$

0FWBrd4 is 5FWBrd4 with no fluorine substitutions, 1FWBrd4 is 5FWBrd4 with one fluorine substitution, 2FWBrd4 has two fluorines substituted and FWBrd4 has 3 fluorines substituted.

Circular Dichroism:

To check the secondary structural content, far-UV CD spectra (200-260 nm) of unlabeled and labeled proteins were collected using a peltier equipped temperature controlled Jasco J-815 spectropolarimeter at 25 °C. For all measurements, 20 μM (50 mM Tris buffer pH 7.4 containing 100 mM NaCl) of protein and a 1 mm cuvette path-length were used. Spectral data was collected at a scan rate of 50 nm/min with averaging of 10 spectra. Processed data was baseline corrected against spectra taken with buffer alone.

Thermal Melting:

Thermal stabilities of labeled and unlabeled proteins were measured by the change in ellipticity at 222 nm with the increase in temperature from 20 °C to 80 °C at the scan rate of 60 degrees/h.

K_d estimation of AU1 by NMR:

The upper limit of k_{off} can be determined by the following equation:

$$\boldsymbol{\tau_{coalescense} = (\sqrt{2}\pi\Delta\upsilon)^{-1} = k^{-1}}$$

Where $\Delta\upsilon$ is the energy difference between the two resonances corresponding to the bound and unbound state in Hz and $k^1 = k_{off}$. The k_{on} rate can be estimated as diffusion controlled (1.0×10^8 M^{-1}/s). The following equation can then be used to estimate an upper limit to the K_d:

$$K_d = \frac{k_{off}}{k_{on}}$$

The energy difference between the bound and unbound resonance of 5FW-BPTF when binding with AU1 is a difference of 171 Hz, which results in an upper limit K_d of 8 μM

Docking Studies of AU1 with Brd4 and BPTF:

Brd4 (PDB ID: 3UVW) and BPTF (PDB ID: 3QZT) were prepared using the Protein Preparation Wizard workflow as follows: adding hydrogen, assigning partial charges using the OPLS-2005 force field, and assigning protonation states. AU1 was prepared using the Ligprep module, generating protonation states from pH range 6.2-8.2. The docking grid was generated by removing the bound peptides and analyzing the protein for binding sites using SiteMap with more restricted notion of hydrophobicity and fine grid. The known acetylated-lysine binding site was selected as the binding site to generate the grid. All tyrosines were allowed to rotate during the docking process. AU1 was then docked using QM/MM ligand polarized docking with initial docking being Glide XP with ligand-van der waals scaling of 0.8. The partial charges of the ligand atoms were calculated using B3LYP with 6-31G*/LACVP* basis set with Ultra-fine SCF accuracy level. AU1 was then redocked using Glide XP and sorted by gscore. Gscores were favorable for AU1 binding to both BPTF and Brd4, so predictions based upon the Gscore are unlikely to be helpful. The docking study was primarily used to suggest binding poses for further analysis. One such pose (**Fig. S11**) showed the methyl ester of AU1 hydrogen bonding with asparagine 2881 and a π–π interaction of the aryl ring with phenylalanine 2887.

Pharmacophore modeling studies:

Pharmacophore modeling was carried out using the PHASE (version 3.9, 2014) module of the Schrödinger suite implemented in Maestro (Maestro 2014-2) molecular modeling package. PHASE identifies the spatial arrangement of functional groups that are common and essential for the biological activity of the compounds. The structures of compounds were prepared using LigPrep (version 3.0, 2014). Conformers were generated using ConfGen by applying OPLS-2005 force field. Four features/sites were considered in generating pharmacophore variants: hydrogen bond acceptor (A), hydrogen bond donor (D), hydrophobic group (H) and aromatic ring (R). The maximum number of sites was set to 7 and minimum to 3. Common pharmacophores were required in all 5 of the active compounds with a final box size of 1 Å and minimum intersite distance of 2 Å. Resulting

pharmacophore hypotheses were then scored using default weights of scoring parameters for both active (survival score) and inactive ones (survival-inactive scores). Many of the pharmacophore sites generated in the hypotheses were consistent across many of the developed models due to the similarity of the various aryl-urea compounds analyzed, but location of the aryl ring with a hydrogen-bond acceptor present at the carbonyl seemed to correlate heavily with binding.

Cell Viability Experiments in HEK 293T cells.

A cell viability assay of HEK 293T cells was done by using a resazurine dye based CellTiter-Blue® from Promega assay. HEK 293T cells were plated in a 96 well plate and grew until 80% confluency. Desired confluent cells were treated with the 0, 1, 3 and 10 μM AU1 for 24 and 48 hours in 5% CO_2 (n=6 for 24 hours and n=5 for 48 hours treatment, per condition). After the desired time point of treatment 20 μL of CellTiter-Blue® was added to the each well and incubated for 2.5 h at 37 ^{o}C. The fluorescence of the reduced dye, resofurin was measured at 580 excitation and 590 emission wavelengths by using an omega plate reader. The presented data in **Fig. S13** is normalized with the control (DMSO treated), error bars are depicting the standard error of the mean.

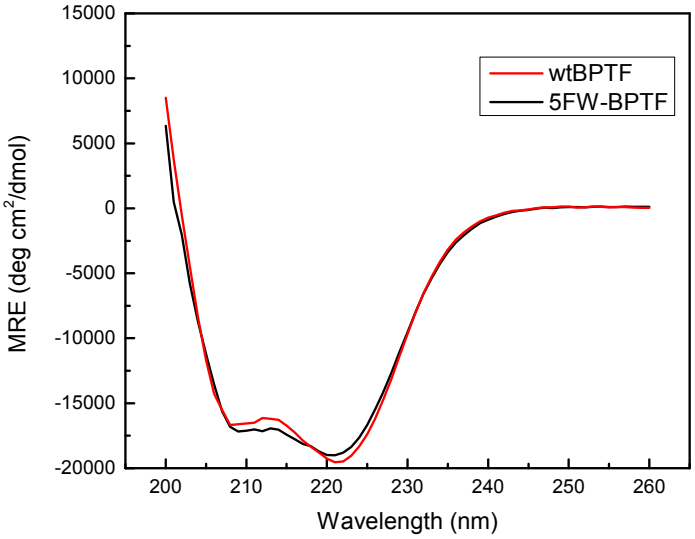


Fig S1. Secondary structure circular dichroism experiments indicate that fluorinating the tryptophan of BPTF only modestly perturbs the secondary structure.

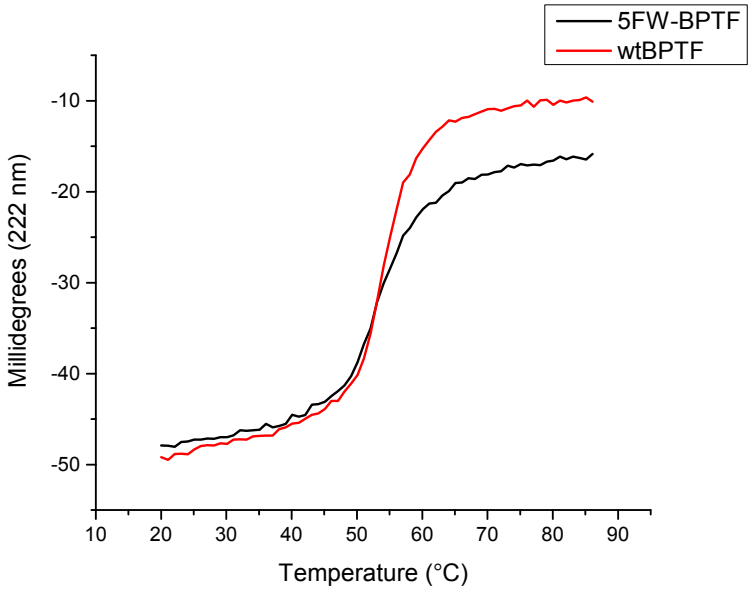


Fig S2. Thermal melting experiments at 222 nm result in negligible differences in melting temperatures (T_m = 53 °C in both cases)

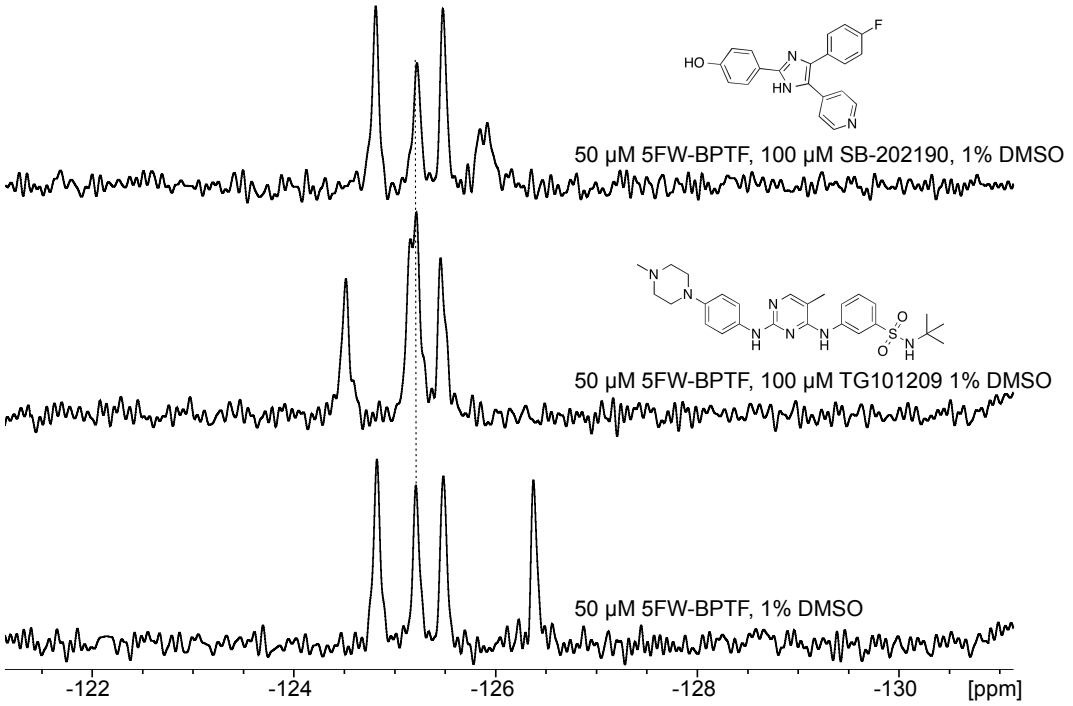


Fig. S3. PrOF NMR experiments to assess screening conditions with known Brd4 binders.

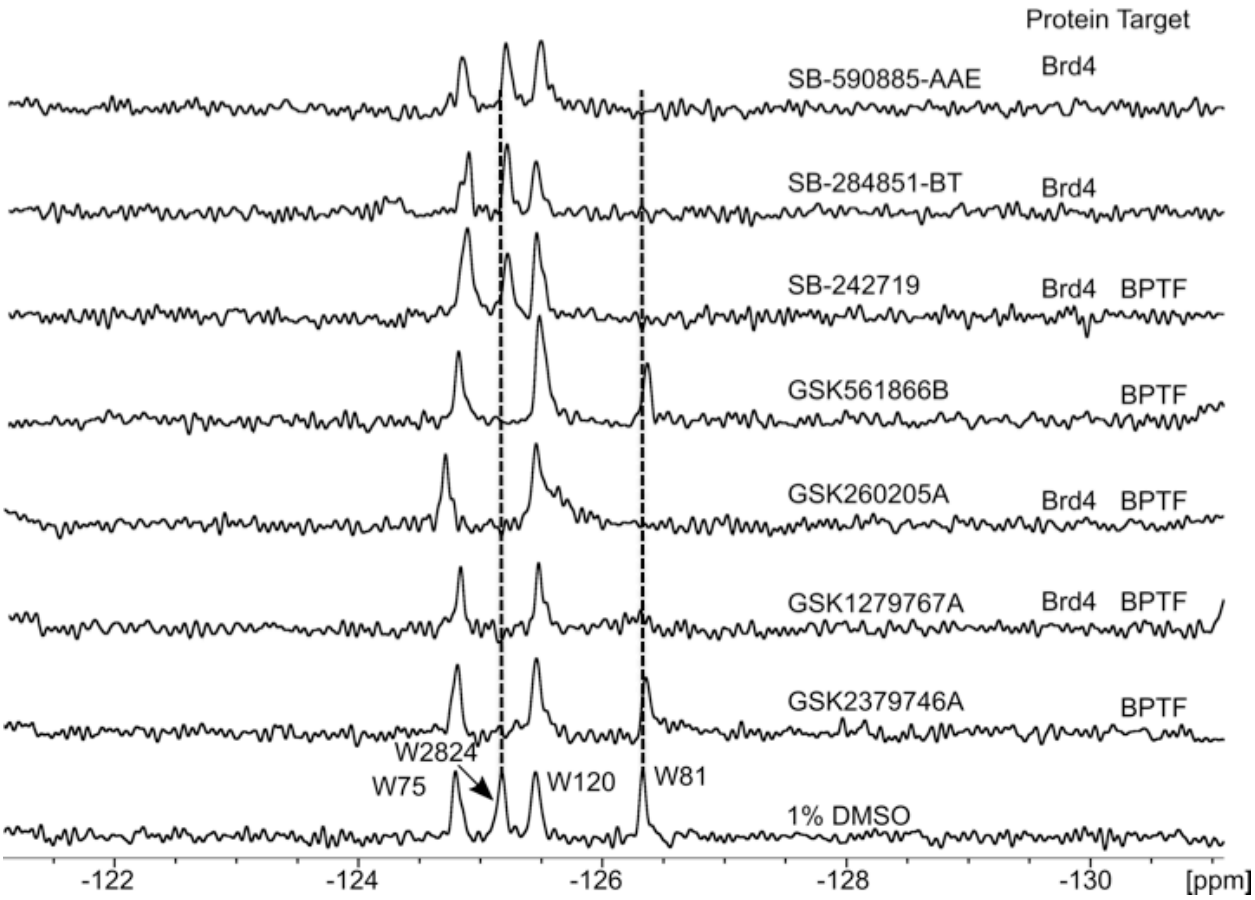
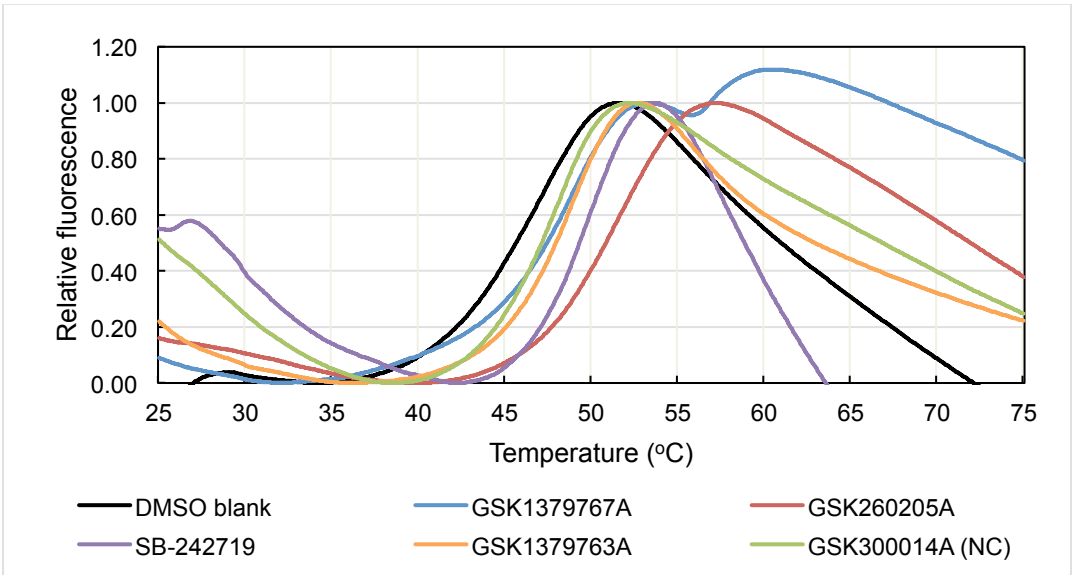


Fig. S4. A selection of NMR spectra from the dual bromodomain screen. There are spectra indicative of nonselective binders as well as ligands that selectively target Brd4 or BPTF. The protein target is indicated on the right of each spectrum.



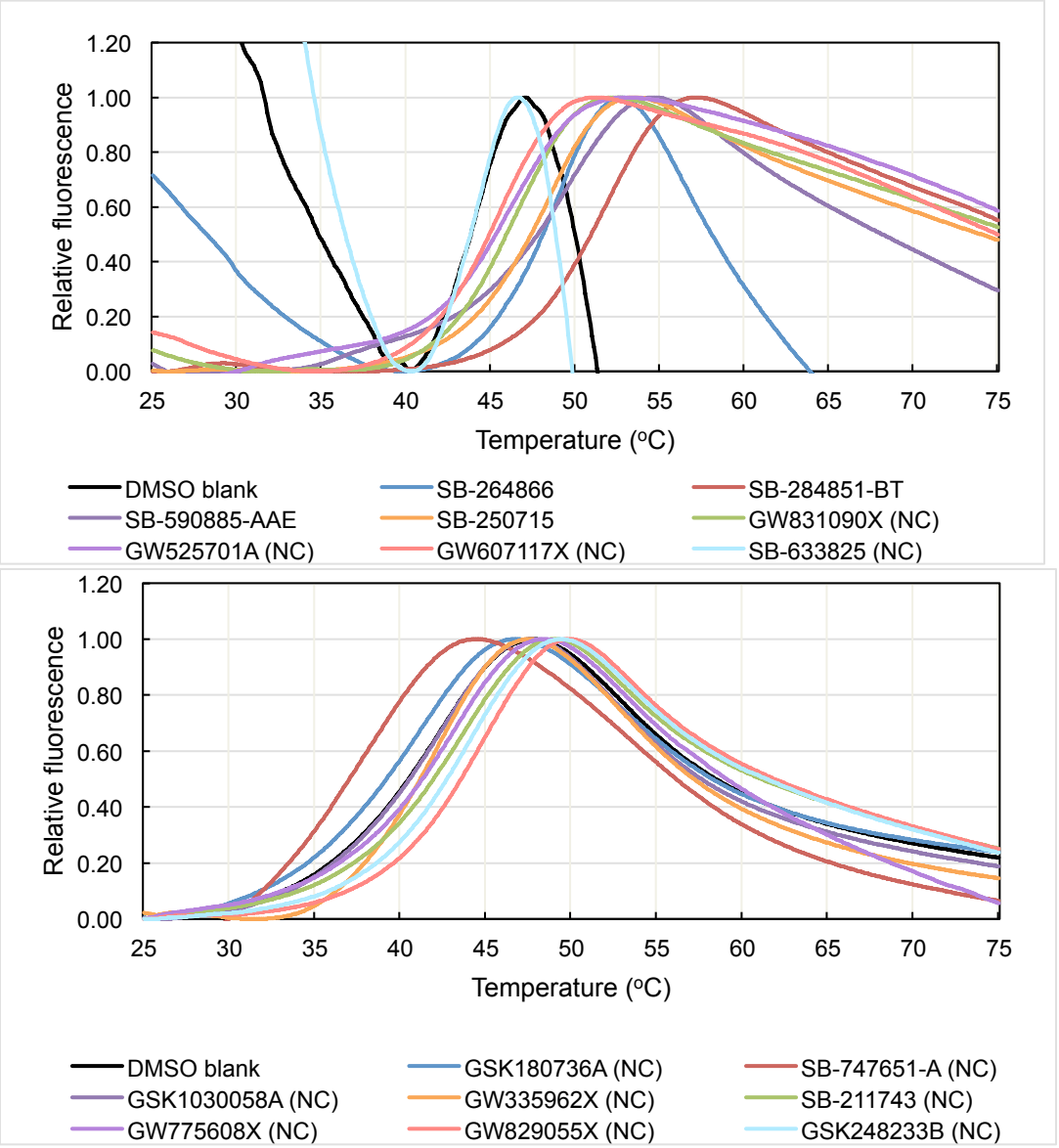


Fig. S5. Thermal shift data from Brd4 with various ligands identified from the NMR screen. Compounds that were not detected as hits in the NMR screen are labeled as negative controls (NC).

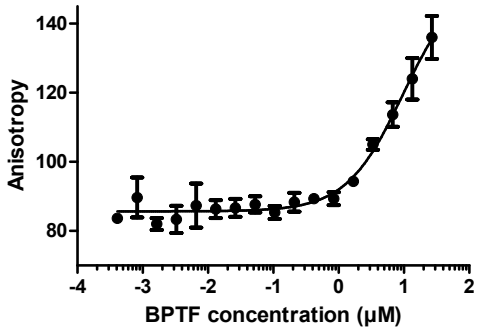


Fig. S6. Direct binding fluorescence anisotropy experiments between BODIPY-BI2536 and varying concentrations of BPTF were used to determine the dissociation constant (K_d = 67 μM +/- 21).

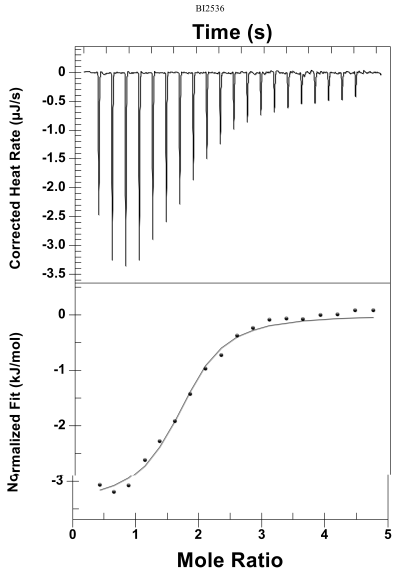


Fig. S7. ITC binding isotherm for BI2536 (0.5 mM) titrated with the bromodomain of BPTF (7 mM), K_d = 37 μM, n =1.66.

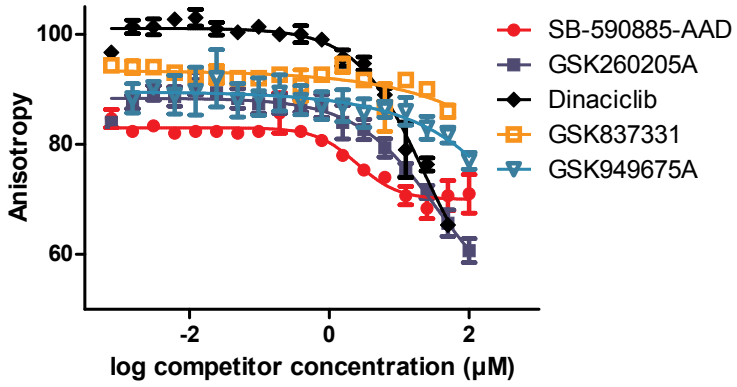


Fig. S8. Determination of K_i of Brd4 binders by fluorescence anisotropy competition assay. Fluorescence anisotropy signal is shown for several Brd4 binders, including dinaciclib (black diamonds, K_i=41 μM), GSK260205A (mauve squares, K_i=6.7 μM), and SB-590885-AAD (red circles, K_i= 0.39 μM), GSK837331 (orange unfilled squares, 18% inhibition at 100 μM), and GSK949675A (aqua unfilled triangles, 60% inhibition at 100 μM).

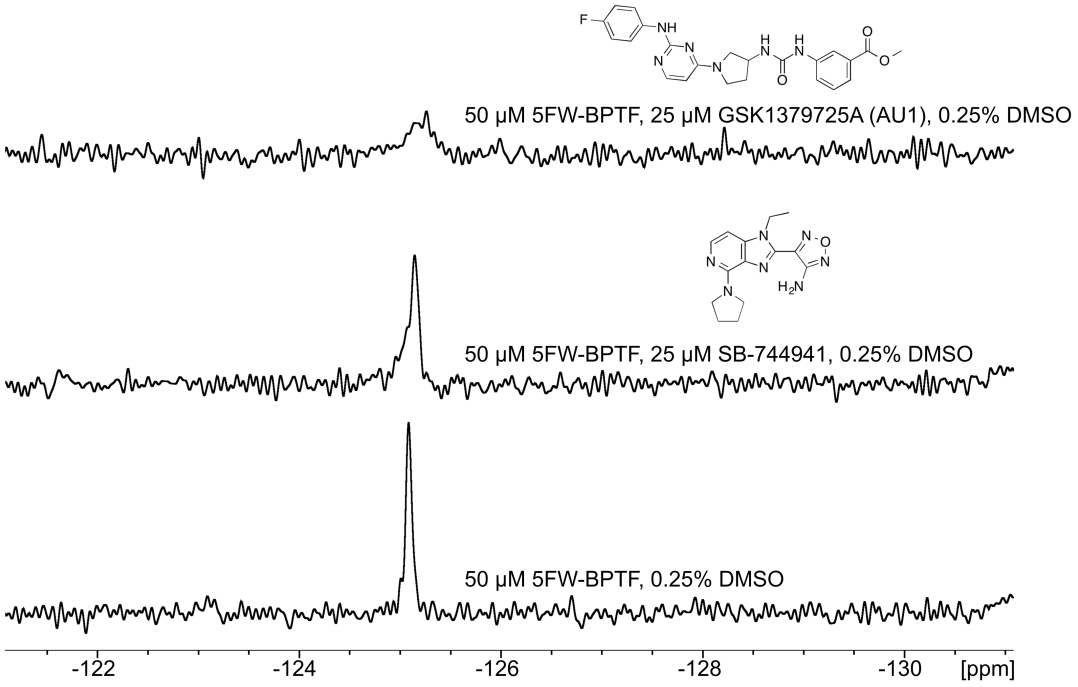


Fig. S9. The strongest selective binders were added into 5FW-BPTF at ¼ the concentration of the screen to rank-order the compounds. The rapid broadening of AU1 suggests a lower dissociation constant than the slight broadening of SB-744941.

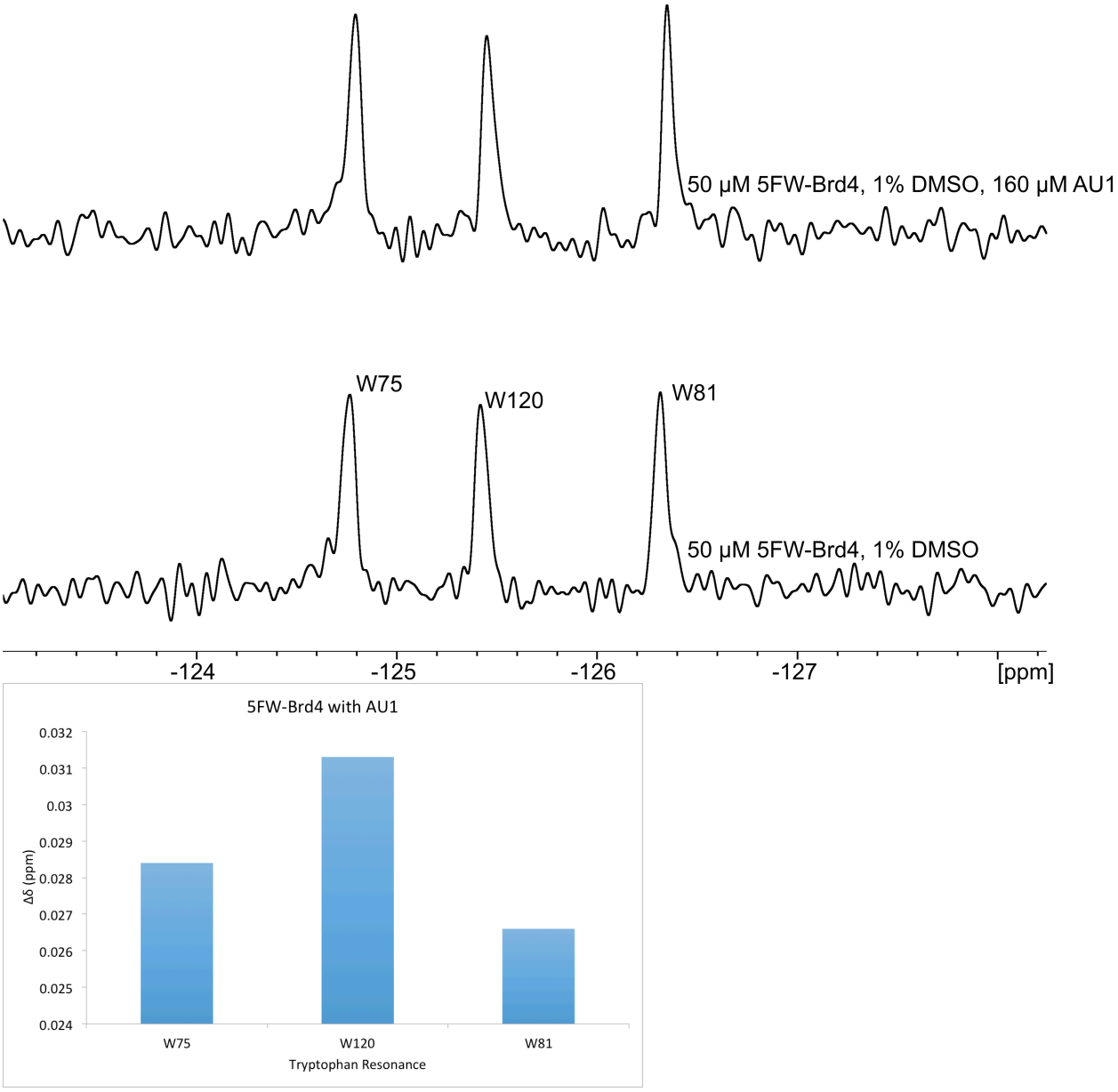


Fig. S10. Fluorine NMR spectra analyzing 5FW-Brd4 with AU1, and an accompanying graph showing absolute chemical shift perturbation of each resonance. The low chemical shift perturbations as well as no significant broadening indicate minimal interaction of AU1 with 5FW-Brd4.

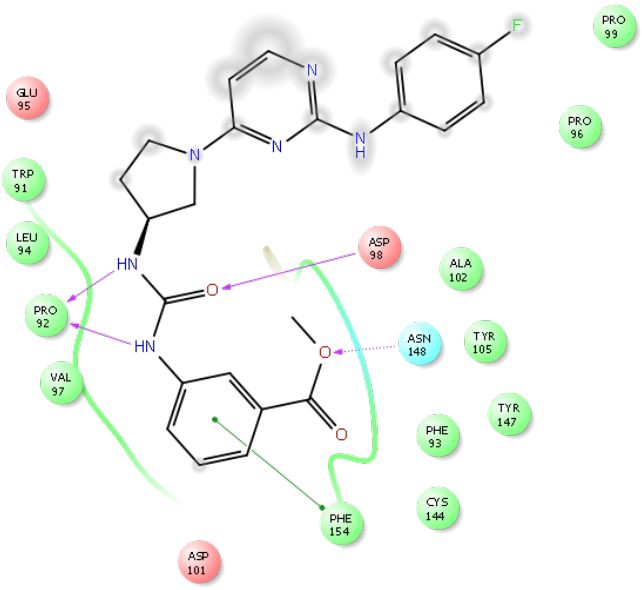


Fig S11. A per-residue interaction map of AU1 with BPTF developed from QM/MM docking studies in Glide. Please note that the residue numbers do not correspond to standard numbering for BPTF. The phenylalanine engaging in the pi-pi interaction is F2887 and the asparagine hydrogen bonding to the oxygen of AU1 is N2881. While (S)-AU1 is shown here, the SAR of the different stereoisomers has yet to be elucidated.

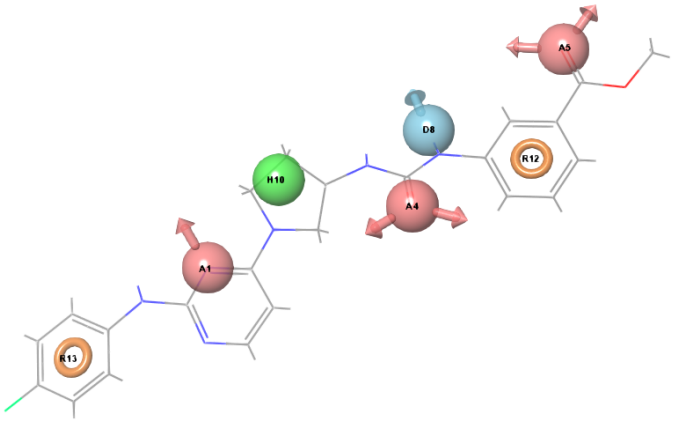


Fig. S12. A pharmacophore model of the aryl-urea compounds generated using Phase. Of particular interest are R12 and A5, both of which seem to correlate heavily with binding.

Table S1: A list of arylurea compounds used for the phase analysis, and their required activity by the generated pharmacophore model.

Name	Pharm Set
GSK1379706A	inactive
GSK1379710A	inactive
GSK1379712A	inactive
GSK1379714A	inactive
GSK1379717A	inactive
GSK1379720A	inactive
GSK1379721A	inactive
GSK1379722A	inactive
GSK1379723A	inactive
GSK1379724A	inactive
GSK1379725A	inactive
GSK1379727A	inactive
GSK1379731A	inactive
GSK1379741A	inactive
GSK1379742A	inactive
GSK1379745A	inactive
GSK1379746A	inactive
GSK1379748A	inactive
GSK1379753A	active
GSK1379762A	inactive
GSK1379763A	active
GSK1379765A	active
GSK1379766A	active
GSK1379767A	active

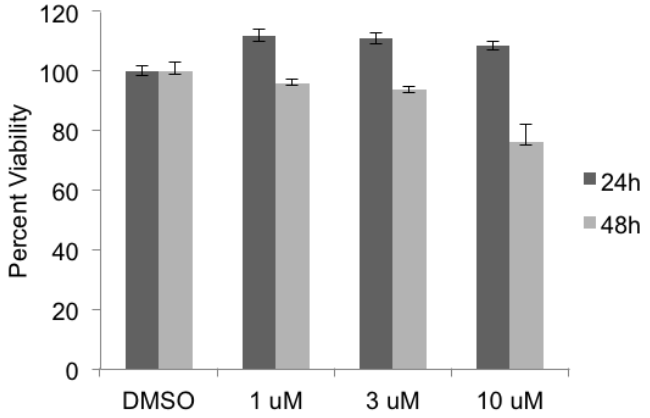


Fig. S13. HEK 293T cells were plated in 96-well plates. 24h post plating, cells were treated with DMSO or AU1 (1 μM, 3 μM and 10 μM) for 24 (n=6, per treatment) and 48h (n=5, per treatment). Cell viability was assessed by using a CellTiter Blue Viability kit from Promega.

Table S2. Summary of NMR screening data including change of Chemical Shift and line broadening upon ligand addition for Brd4 resonances and BPTF

	W75				W2824				W120				W81			
Compound Regno	Δδ	SD	Δlinewidth	SD	Δδ	SD	Δlinewidth	SD	Δδ	SD	Δlinewidth	SD	Δδ	SD	Δlinewidth	SD
GSK260205A	0.0928	2	-0.0194	-1	N/A	2	N/A	2	-0.0033	0	0.0483	2	N/A	2	N/A	2
GSK1379767A	-0.0104	0	-0.0273	-2	N/A	2	N/A	2	-0.0007	0	-0.0076	0	N/A	2	N/A	2
SKF-106164-A2	-0.0177	0	0.0052	0	N/A	2	N/A	2	0.0275	2	0.0406	2	N/A	2	N/A	2
GSK1379753A	-0.0101	0	-0.0005	0	N/A	2	N/A	2	0.0067	0	-0.0107	0	N/A	2	N/A	2
GSK1379710A	-0.0005	0	-0.0078	0	N/A	2	N/A	2	-0.007	-1	-0.0034	0	-0.0511	0	0.0255	1
GSK1379731A	-0.0062	0	-0.0025	0	N/A	2	N/A	2	-0.0002	0	0.0151	1	-0.058	0	0.0292	2
SB-744941	-0.0004	0	0.0006	0	N/A	2	N/A	2	0.0085	1	0.0337	2	0.0014	0	0.0037	0
GSK1379746A	-0.015	0	0.0061	0	N/A	2	N/A	2	-0.0028	0	-0.0026	0	-0.0244	0	0.0086	0
GSK1379725A	0.0006	0	0.003	0	N/A	2	N/A	2	0.0013	0	0.0064	0	-0.0092	0	0.0096	0
GSK1379765A	-0.0585	-2	0.0187	1	-0.1275	-2	0.0104	0	-0.0061	-1	-0.0126	-1	N/A	2	N/A	2
SB-738004	-0.0385	-1	0.0399	2	0.0098	0	-0.0212	-2	0.0199	2	0.0256	2	N/A	2	N/A	2
SKF-86055	-0.0043	0	0.0069	0	-0.1329	-2	0.0635	2	0.0072	0	-0.0047	0	N/A	2	N/A	2
GW876790X	0.0007	0	0.0325	2	-0.0468	0	0.0393	2	0.0019	0	0.0377	2	0.0049	0	0.0417	2
GSK949675A	0.0024	0	-0.0046	0	-0.1232	-2	0.0113	0	-0.0049	0	0.0111	0	0.0186	0	0.0313	2
GSK711701A	-0.0716	-2	0.0211	1	0.1324	2	0.0146	1	0.0171	2	-0.0073	0	0.0656	0	-0.009	-1
SB-732881	-0.038	-1	-0.0039	0	-0.1668	-2	0.0252	1	-0.0081	-1	0.0061	0	-0.0589	0	0.037	2
GSK1007102A	-0.015	0	-0.0055	0	-0.1787	-2	0.014	0	0.0062	0	0.0151	1	0.1039	0	-0.0016	0
GSK619487A	0.0005	0	0.0073	0	-0.1237	-2	0.0125	0	-0.0042	0	-0.0142	-1	0.0189	0	-0.0087	0
GW301789X	0.0009	0	0.0148	1	-0.0361	0	0.0304	2	-0.0098	-1	-0.0137	-1	0.0049	0	-0.0018	0
GSK507274A	0.0033	0	-0.0148	-1	-0.1481	-2	0.0313	2	0	0	0.0132	1	0.0177	0	-0.0008	0

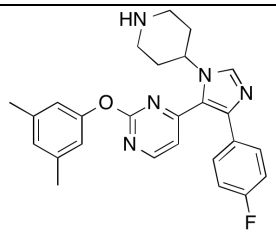
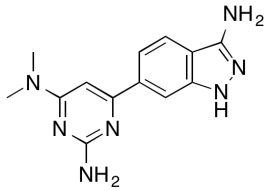
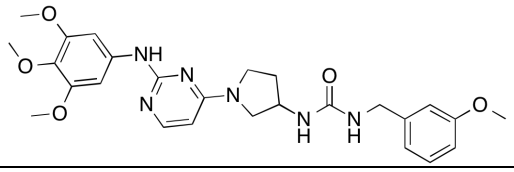
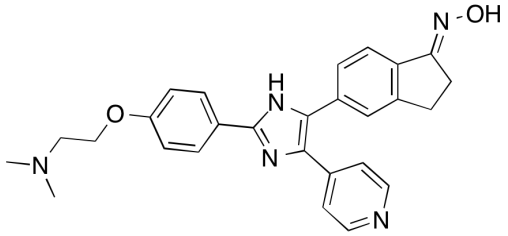
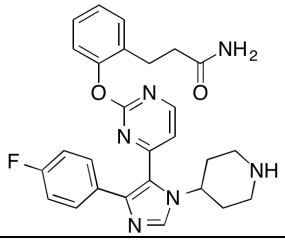
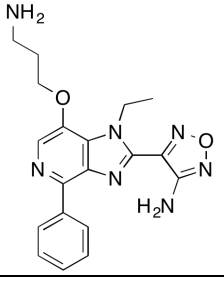
GSK902056A	-0.0022	0	-0.0197	-1	-0.162	-2	0.0279	2	-0.0015	0	0.0071	0	0.011	0	0.0125	0
GSK561866B	0.0047	0	0.002	0	-0.3035	-2	0.0405	2	-0.0073	-1	0.0312	2	0.0066	0	0.0008	0
GW445017X	-0.0105	0	0.0047	0	-0.0577	0	0.0395	2	0.0007	0	-0.0129	-1	0.0095	0	0.0099	0
SB-736290	-0.0072	0	-0.0049	0	-0.0313	0	-0.0224	-2	-0.007	-1	0.0047	0	0.0059	0	0.0067	0
GSK943949A	-0.0084	0	-0.0079	0	-0.1467	-2	0.0217	1	-0.0033	0	0.0103	0	0.0569	0	0.0131	0
GW679662X	0.0377	2	-0.0159	-1	0.0481	1	0.0038	0	0.0223	2	-0.0099	0	N/A	2	N/A	2
SB-242719	-0.0727	-2	0.0343	2	-0.0176	0	0.0175	1	0.0145	1	0.0148	1	N/A	2	N/A	2
GSK2219329A	-0.0552	-2	0.018	1	-0.057	0	0.0234	1	-0.0029	0	0.0009	0	N/A	2	N/A	2
SB-253228	-0.0378	-1	0.0131	1	-0.0156	0	-0.0107	-1	0.0074	0	-0.025	-2	N/A	2	N/A	2
GSK1379763A	-0.0438	-1	0.0042	0	-0.0832	-1	0.0036	0	-0.0075	-1	-0.0173	-1	N/A	2	N/A	2
GSK620503A	-0.0456	-1	0.0176	1	0.0653	1	0.0313	2	0.0069	0	-0.0023	0	N/A	2	N/A	2
GW684941X	-0.0434	-1	0.0006	0	-0.0908	-1	0.0267	2	0.0017	0	0.0115	0	N/A	2	N/A	2
GSK1379766A	-0.0169	0	0.0059	0	-0.0739	-1	-0.0032	0	-0.0073	-1	-0.0051	0	N/A	2	N/A	2
SB-251527	-0.0177	0	-0.0064	0	-0.0045	0	-0.0082	-1	0.0054	0	0.0067	0	N/A	2	N/A	2
GSK312948A	-0.0676	-2	0.0269	2	0.0453	1	-0.0055	0	0.0029	0	-0.001	0	0.1733	0	0.0003	0
GW873004X	0.0009	0	-0.0008	0	-0.0216	0	0.0167	1	0.0007	0	0.0244	1	0.0174	0	0.0324	2
SB-708998	0.007	0	-0.0307	-2	-0.0066	0	0.0154	1	0.0002	0	-0.0052	0	-0.0312	0	0.0047	0
SB-708999	0.0544	2	-0.0093	0	0.0018	0	-0.0093	-1	0.0051	0	-0.0056	0	0.1249	0	0.0052	0
GSK2297542A	-0.0338	-1	0.0012	0	0.0524	1	-0.0012	0	0.0166	2	-0.0035	0	0.1581	0	0.0136	0
GSK1379748A	-0.0446	-1	0.0093	0	-0.0904	-1	0.0226	1	-0.0058	-1	-0.0089	0	0.1348	0	0.0568	2
GW782907X	-0.0141	0	0.0151	1	0.0592	1	0.0127	0	0.0141	1	-0.0248	-2	0.0212	0	-0.0156	-1
SB-711805	-0.0435	-1	-0.0162	-1	-0.0926	-1	0.0061	0	0.0019	0	0.0003	0	0.1369	0	0.004	0
SB-390527	-0.0097	0	0.0125	1	-0.0301	0	0.0189	1	0.007	0	0.0103	0	0.0294	0	-0.0101	-1
GW305178X	-0.0018	0	-0.0029	0	-0.0795	-1	0.0065	0	-0.0219	-2	-0.008	0	0.1015	0	-0.0064	0
SB-751148	-0.0135	0	0.0102	0	-0.0631	-1	0.0169	1	0.0063	0	-0.0255	-2	0.1431	0	-0.007	0
GW620972X	0.0057	0	-0.0046	0	-0.0268	0	0.0173	1	-0.0062	-1	0.013	1	0.0024	0	-0.0089	-1
SB-698596-AC	-0.0199	0	-0.0023	0	-0.0769	-1	0.0027	0	-0.0089	-1	0.0134	1	0.0197	0	-0.0086	0
GW784307A	0.0046	0	0.0037	0	-0.0227	0	0.0165	1	0.0009	0	-0.02	-1	0.0128	0	-0.0147	-1
GW786460X	-0.0174	0	-0.0009	0	-0.0097	0	-0.0116	-1	-0.0018	0	0.0009	0	0.026	0	-0.0102	-1
SB-360741	-0.0153	0	-0.0033	0	-0.001	0	0.0201	1	0.0016	0	0.0099	0	0.0192	0	-0.0085	0
GW276655X	-0.0086	0	-0.0013	0	-0.0116	0	-0.0118	-1	0.0019	0	-0.0046	0	0.0205	0	-0.0087	0
GW694077X	-0.0002	0	-0.002	0	-0.0738	-1	0.0003	0	0.0063	0	0.0086	0	0.0926	0	-0.0093	-1
SB-707548-A	-0.1039	-2	0.0316	2	-0.0095	0	-0.0093	-1	0.0091	1	-0.0065	0	0.0826	0	0.0005	0
GSK1379723A	-0.0086	0	-0.0188	-1	-0.0186	0	-0.0093	-1	-0.0013	0	-0.0177	-1	0.0351	0	0.0013	0
GSK2297099A	-0.0416	-1	0.0053	0	0.0542	1	-0.0046	0	0.0105	1	-0.0073	0	0.0464	0	0.0054	0
GW781483X	0.0154	1	0.0065	0	-0.0872	-1	0.0154	1	-0.0028	0	0.0127	1	0.0743	0	-0.0027	0
GSK192082A	0.0013	0	0.0118	1	-0.0129	0	0.0154	1	0.0009	0	-0.023	-1	0.0094	0	-0.0049	0
SB-747651-A	0.0018	0	0.0165	1	-0.0652	-1	0.0003	0	-0.0016	0	0.0035	0	0.0128	0	0.0038	0
GW796410X	-0.0108	0	-0.0088	0	-0.006	0	-0.0084	-1	0.0082	0	0.0272	2	-0.0056	0	0.0022	0
GSK1379714A	-0.0101	0	-0.0045	0	-0.0311	0	-0.0093	-1	-0.0043	0	-0.0179	-1	0.0147	0	-0.0041	0
GSK1379720A	-0.0219	0	-0.0014	0	0.0329	1	0.0018	0	-0.0021	0	-0.0147	-1	0.0139	0	0.0019	0
GSK1535721A	-0.0244	0	0.0055	0	-0.0952	-1	0.0045	0	0.0106	1	-0.0029	0	0.0407	0	-0.0079	0
GW778894X	-0.0187	0	0.0111	0	0.036	1	0.0051	0	0.0107	1	-0.0002	0	0.0352	0	0.0028	0

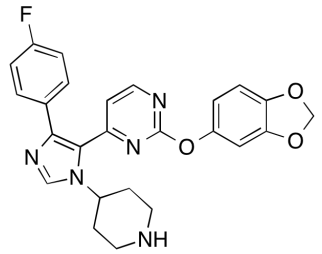
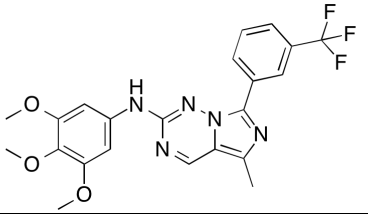
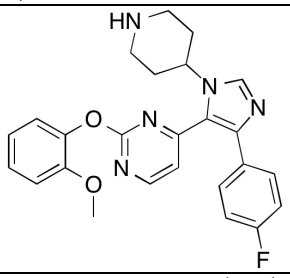
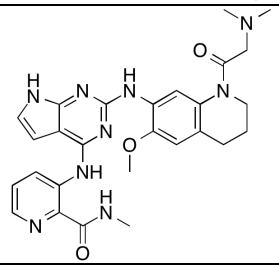
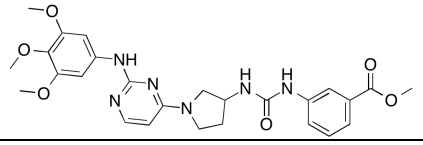
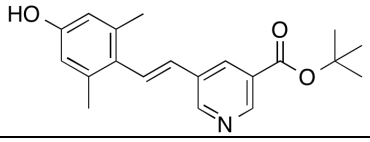
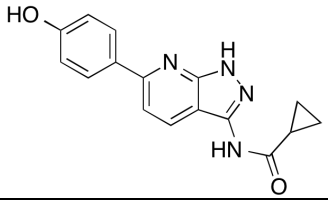
GSK614526A	0.0031	0	0.0037	0	-0.1008	-1	-0.006	0	-0.005	0	0.0221	1	0.0186	0	0.0024	0
GW300660X	-0.0141	0	-0.0016	0	-0.0757	-1	0.0097	0	-0.0036	0	-0.0082	0	0.0457	0	0.0122	0
GW811761X	0.0011	0	-0.0031	0	-0.0033	0	-0.0109	-1	0.0008	0	-0.0067	0	0.0069	0	0.0084	0
GW827105X	-0.0035	0	-0.0031	0	0.0052	0	0.0209	1	0.0011	0	0.0069	0	0.032	0	0.0142	0
GW810372X	-0.0055	0	0	0	-0.0068	0	-0.0099	-1	-0.0043	0	0.006	0	0.004	0	-0.007	0
SKF-104365	-0.0018	0	-0.0073	0	-0.0145	0	0.0246	1	-0.0016	0	-0.0029	0	0.0009	0	0.008	0
GSK1030058A	0.01	0	0.0073	0	-0.0239	0	-0.0087	-1	0.0005	0	0.0007	0	-0.0114	0	-0.0049	0
GW440137A	-0.0239	0	-0.0095	0	-0.0117	0	0.0161	1	-0.0041	0	-0.0073	0	0.0575	0	0.0034	0
GW709213X	-0.0059	0	0.0013	0	0.0019	0	-0.0111	-1	0.0018	0	-0.0044	0	0.0761	0	0.0121	0
GW693481X	-0.0056	0	0.0032	0	-0.0165	0	0.016	1	0.0036	0	-0.007	0	0.0676	0	0.0056	0
SB-400868-A	-0.0047	0	0.0031	0	-0.0056	0	0.0201	1	0.0071	0	0.0017	0	-0.001	0	0.0085	0
SB-772077-B	-0.0168	0	0.0075	0	0.029	1	0.0024	0	0.0075	0	-0.0119	-1	0.0376	0	0.0005	0
SB-750140	-0.0011	0	-0.0088	0	-0.0072	0	-0.0139	-1	-0.0014	0	0.0021	0	0.0313	0	0.0072	0
SB-751399-B	0.003	0	-0.0023	0	0.0076	0	-0.0171	-1	0.0015	0	-0.0071	0	0.0139	0	-0.0025	0
GW439255X	N/A	2	N/A	2	-0.0137	0	0.0029	0	0.0007	0	0.0119	0	N/A	2	N/A	2
SB-264866	-0.0717	-2	0.0281	2	-0.0124	0	-0.0002	0	0.0075	0	0.0251	2	N/A	2	N/A	2
SB-284851-BT	-0.0779	-2	-0.0229	-2	-0.0195	0	0.0042	0	0.02	2	0.0107	0	N/A	2	N/A	2
GW837331X	-0.0686	-2	0.017	1	-0.0591	0	0.0056	0	0.0018	0	-0.0055	0	N/A	2	N/A	2
SB-358518	-0.072	-2	0.0104	0	-0.0176	0	0.0117	0	0.0026	0	-0.005	0	N/A	2	N/A	2
SB-590885-AAE	-0.0401	-1	0.0098	0	-0.0037	0	0.0122	0	-0.0146	-2	0.0252	2	N/A	2	N/A	2
SB-250715	-0.041	-1	0.0096	0	-0.0396	0	0.0037	0	0.0028	0	0.0249	2	N/A	2	N/A	2
GW622475X	-0.0389	-1	0.0037	0	-0.033	0	0.0065	0	0.0142	1	0.0086	0	N/A	2	N/A	2
GSK317354A	-0.0444	-1	0.0006	0	0	0	0.0079	0	-0.0067	-1	-0.0106	0	N/A	2	N/A	2
GW407323A	-0.0415	-1	0.0234	2	0.0197	0	0.0003	0	0.0037	0	-0.0135	-1	N/A	2	N/A	2
GSK2220400A	0.0311	1	0.0017	0	-0.0098	0	-0.002	0	0.0002	0	0.0017	0	N/A	2	N/A	2
GSK1023156A	-0.0324	-1	0.0115	1	0.011	0	-0.0066	0	0.0078	0	-0.0116	0	N/A	2	N/A	2
SB-254169	-0.0186	0	0.0068	0	-0.0225	0	0.0061	0	0.013	1	0.0034	0	N/A	2	N/A	2
SB-223133	-0.0024	0	0.0017	0	-0.0048	0	0.0058	0	-0.004	0	-0.0079	0	N/A	2	N/A	2
GW702865X	-0.0093	0	0.0081	0	0.0062	0	-0.0053	0	-0.0003	0	-0.0075	0	N/A	2	N/A	2
GSK1321565A	-0.0537	-2	0.0024	0	-0.0186	0	-0.0061	0	0.0053	0	-0.0041	0	-0.2799	0	0.0237	1
SB-217360	0.0177	1	-0.008	0	-0.0019	0	-0.0067	0	0.0245	2	-0.0046	0	0.3748	0	0.0054	0
SB-732941	-0.0144	0	0.0144	1	-0.0159	0	0.0102	0	-0.0058	-1	-0.008	0	0.1942	0	-0.0076	0
SB-710363	0.0262	1	0.0126	1	-0.0553	0	-0.0021	0	-0.0039	0	-0.0011	0	0.377	0	-0.0001	0
GW824645A	0.0005	0	-0.0005	0	0.0162	0	-0.0028	0	-0.0009	0	-0.0128	-1	0.1708	0	0	0
GW493036X	-0.0299	0	-0.0014	0	0.0155	0	-0.0055	0	0.0096	1	-0.0047	0	0.2674	0	0.0277	1
GSK1173862A	0.0034	0	0.006	0	0.0068	0	-0.0072	0	-0.0038	0	-0.0105	0	0.0661	0	0.0328	2
GW57482A	0.0009	0	0.016	1	0.0069	0	-0.0025	0	0.0073	0	-0.0259	-2	0.009	0	-0.0104	-1
SB-226605	-0.0041	0	-0.017	-1	0.0013	0	-0.0032	0	0.0115	1	-0.002	0	0.1069	0	0.0029	0
GW335962X	0.0034	0	0.0157	1	-0.0552	0	-0.0035	0	-0.0077	-1	0.0088	0	0.0105	0	-0.0088	0
GW831090X	-0.0336	-1	-0.012	-1	-0.0239	0	-0.0064	0	0.0014	0	-0.0014	0	-0.0476	0	0.042	2
GSK1653539A	0.0105	0	-0.013	-1	-0.0051	0	-0.0013	0	-0.0035	0	-0.0013	0	0.0213	0	0.0215	1
SB-814597	0.0093	0	0.0078	0	-0.0322	0	0.0032	0	-0.0196	-2	-0.014	-1	-0.0026	0	0.022	1
GW583373A	0.0015	0	-0.0077	0	-0.0048	0	-0.0057	0	-0.0088	-1	-0.0038	0	0.0145	0	0.017	1

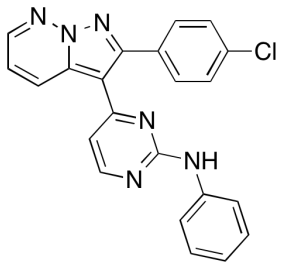
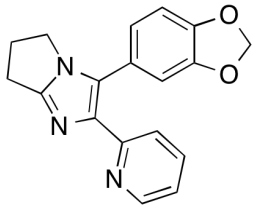
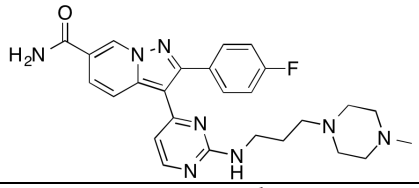
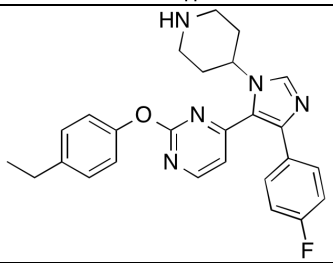
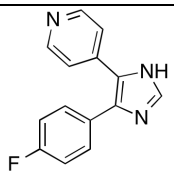
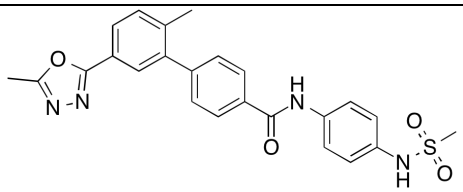
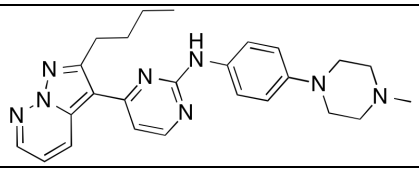
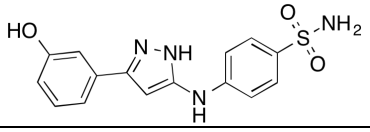
GSK1379727A	-0.0196	0	-0.0052	0	-0.0417	0	0.0079	0	-0.0113	-1	0.0021	0	-0.0481	0	0.0075	0
GI261520A	-0.0152	0	0.0113	0	-0.0044	0	-0.005	0	0.0055	0	0.0154	1	0.0281	0	-0.0169	-1
GW771127A	-0.01	0	0.004	0	-0.0192	0	-0.0061	0	0.0027	0	0.0145	1	0.012	0	-0.0132	-1
GW632580X	-0.0111	0	-0.007	0	-0.0109	0	0.0014	0	-0.004	0	0.013	1	-0.0164	0	-0.0114	-1
GW525701A	-0.0239	0	-0.004	0	0.0145	0	0.0036	0	0.0105	1	-0.0066	0	0.1124	0	0.0225	1
GW697465A	0.0102	0	-0.002	0	0.0165	0	-0.004	0	0.0136	1	-0.0062	0	0.0104	0	-0.011	-1
SB-317658	0.0065	0	-0.006	0	0.0117	0	0.0006	0	0.0092	1	-0.0009	0	0.025	0	0.0165	1
GW856804X	-0.011	0	0.0073	0	-0.0412	0	0.0039	0	-0.0069	-1	-0.0062	0	0.0151	0	0.0186	1
SB-737198	-0.0017	0	0.0021	0	-0.0458	0	0.0136	0	0.0099	1	-0.0114	0	0.0575	0	-0.0115	-1
GW711782X	0.0006	0	-0.0048	0	-0.009	0	-0.0017	0	0.0014	0	-0.0108	0	0.1141	0	0.0051	0
GSK1379762A	-0.0069	0	0.001	0	-0.0046	0	0.0133	0	0.0076	0	0.0058	0	-0.0076	0	0.0261	1
GW576609B	-0.005	0	-0.0062	0	-0.0051	0	-0.0053	0	0.0078	0	0.0057	0	0.0183	0	-0.009	-1
GW607117X	-0.0039	0	-0.0079	0	0.0034	0	0.0027	0	0.0023	0	-0.0053	0	-0.0158	0	0.0223	1
GW651576X	-0.0043	0	-0.0106	-1	-0.0055	0	0.0015	0	0.0014	0	0.002	0	0.005	0	-0.0157	-1
GW673715X	-0.0097	0	0.0057	0	-0.0048	0	0.0056	0	0.0007	0	0.0021	0	0.0147	0	-0.0125	-1
GSK466314A	0.0024	0	0.0067	0	-0.0165	0	0.0006	0	-0.0028	0	-0.0059	0	0.0306	0	-0.0166	-1
GW572399X	-0.0087	0	-0.0003	0	-0.0144	0	-0.0057	0	0.0022	0	-0.0023	0	0.0377	0	-0.0163	-1
GW829877X	-0.0043	0	-0.0047	0	-0.0033	0	-0.0006	0	-0.0027	0	0.0031	0	0.0089	0	-0.0155	-1
GSK257997A	0.0035	0	-0.0055	0	-0.0229	0	0.0029	0	0.0016	0	-0.0015	0	0.0314	0	-0.0108	-1
SB-211743	-0.0026	0	0.0017	0	-0.0357	0	0.0011	0	0.0005	0	0.0093	0	0.0291	0	-0.0088	0
SB-282975-A	0.0043	0	0.0105	0	-0.0276	0	0.0016	0	-0.0008	0	0.0079	0	0.1219	0	0.0029	0
SB-633825	-0.0036	0	-0.0009	0	-0.0324	0	-0.0064	0	-0.0007	0	0.0084	0	-0.0766	0	-0.0035	0
GSK180736A	-0.0239	0	0.0107	0	-0.004	0	0.0104	0	0.0035	0	-0.0068	0	0.1289	0	0.0041	0
GSK300014A	-0.0054	0	0.0263	2	-0.0123	0	0.0067	0	-0.0016	0	-0.0174	-1	0.0067	0	-0.0005	0
SB-390526	0.0016	0	-0.0286	-2	0.0107	0	0.0067	0	-0.0002	0	0.0064	0	0.0095	0	0.0024	0
GSK1379706A	-0.008	0	-0.0121	-1	-0.0186	0	-0.0032	0	-0.0002	0	-0.019	-1	0.0056	0	0.0002	0
GSK1379742A	-0.0138	0	-0.0113	-1	0.0072	0	-0.0008	0	-0.0063	-1	-0.0185	-1	-0.0004	0	0.0029	0
GSK1379717A	-0.0007	0	-0.0188	-1	-0.0068	0	0.0023	0	0.0074	0	-0.0146	-1	0.0441	0	0.0124	0
SB-341528	-0.0077	0	-0.0119	-1	-0.0222	0	-0.0051	0	0.0029	0	0.0129	1	0.0019	0	0.0002	0
SKF-97623	0.0045	0	0.0136	1	0.0189	0	0.0011	0	0.0105	1	0.0136	1	0.0034	0	-0.0014	0
GW743024X	-0.0033	0	0.0221	1	-0.0088	0	0.0007	0	0.0006	0	-0.0193	-1	-0.0077	0	-0.005	0
GW843682X	-0.0356	-1	-0.002	0	0.006	0	-0.0019	0	-0.0027	0	-0.0058	0	-0.0079	0	0.0104	0
GSK1379745A	-0.0264	0	-0.0126	-1	-0.0079	0	-0.0009	0	-0.0033	0	-0.0106	0	-0.0004	0	0.0028	0
GW693917X	-0.0113	0	-0.0108	-1	-0.0023	0	-0.0058	0	0.0044	0	0.0054	0	0.0089	0	-0.0052	0
GW829874X	-0.0122	0	-0.011	-1	-0.0094	0	0.0001	0	0.0044	0	0.0105	0	0.0105	0	-0.0064	0
GW631581B	-0.0156	0	-0.0114	-1	-0.0142	0	-0.0024	0	-0.0003	0	-0.0009	0	0.0274	0	-0.0033	0
GW830365A	-0.0179	0	-0.0122	-1	-0.0294	0	-0.0052	0	-0.0031	0	0.0018	0	0.0142	0	0.0112	0
GW852849X	-0.0438	-1	0.0011	0	0.0012	0	0.0079	0	-0.005	0	0.0043	0	0.0414	0	0.0139	0
GSK292658A	0.0008	0	-0.0185	-1	-0.0012	0	-0.0063	0	0.0036	0	-0.0116	0	0.0077	0	0.0086	0
GSK346294A	-0.0024	0	-0.0141	-1	-0.006	0	-0.0042	0	0.0039	0	0.0115	0	0.0636	0	0.0063	0
GW709199X	0.0033	0	-0.0197	-1	-0.0071	0	-0.0013	0	0.0001	0	0.0071	0	0.0012	0	0.0028	0
GW828206X	0.0015	0	-0.017	-1	-0.0009	0	1E-04	0	-0.0049	0	-0.0041	0	0.0036	0	-0.002	0
GW867588X	0.0023	0	0.0126	1	-0.0047	0	0.004	0	0.0016	0	0.0023	0	0.0168	0	-0.0006	0

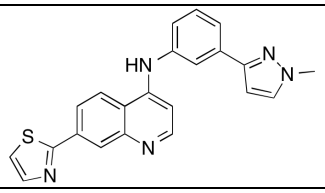
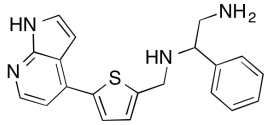
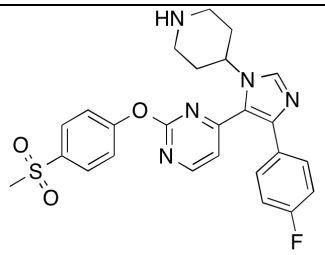
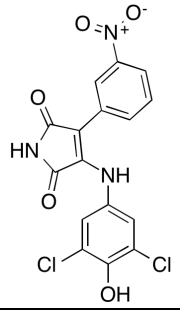
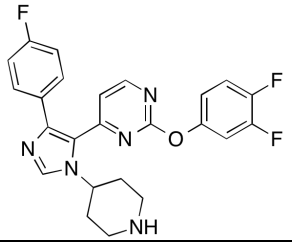
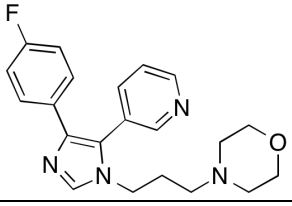
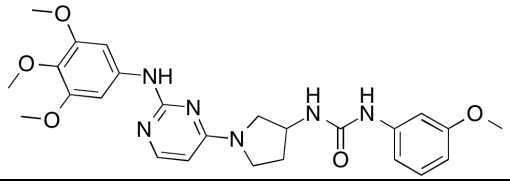
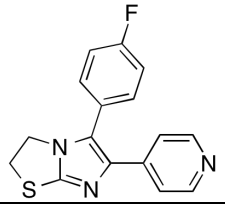
SB-361058	-0.0364	-1	0.0081	0	-0.0083	0	0.0113	0	0.0003	0	-0.0048	0	0.0475	0	0.0009	0
SB-711237	0.0002	0	0.0148	1	-0.0157	0	0.0046	0	-0.0044	0	-0.009	0	0.0075	0	0.0082	0
SB-759335-B	-0.0016	0	-0.0119	-1	-0.0002	0	-0.0021	0	-0.0014	0	0.0096	0	0.0151	0	0.0053	0
GSK1379741A	-0.0012	0	0.0055	0	-0.0131	0	-0.002	0	-0.0043	0	-0.0153	-1	-0.0065	0	-0.005	0
GSK1379724A	0.0009	0	-0.0018	0	0.0195	0	1E-04	0	0.0117	1	0.0177	1	0.0304	0	0.0022	0
GSK2213727A	-0.0065	0	-0.0087	0	0.0089	0	-0.0061	0	0.0035	0	0.0202	1	0.0604	0	0.0057	0
GSK2186269A	0.0034	0	-0.0026	0	0.0011	0	0.0101	0	0.0096	1	0.0133	1	0.0116	0	-0.0046	0
GW642125X	-0.0069	0	0.006	0	-0.0175	0	0.0102	0	-0.0055	0	0.0052	0	0.0504	0	-0.0012	0
GW695874X	-0.0021	0	0.0035	0	-0.0271	0	0.0056	0	-0.0052	0	-0.0056	0	0.0749	0	0	0
GW679410X	-0.0234	0	-0.0001	0	-0.0114	0	-0.0067	0	-0.0002	0	0.0141	1	0.0867	0	-0.0062	0
SB-735465	-0.0277	0	-0.0067	0	-0.0158	0	-0.0041	0	0.0107	1	0.0127	1	0.0671	0	0.0003	0
SB-738482	-0.023	0	-0.0023	0	-0.0251	0	-0.0041	0	-0.0054	0	0.0006	0	0.0886	0	-0.001	0
GI261656A	0.0023	0	-0.006	0	-0.0187	0	0.0026	0	0.0049	0	-0.0125	-1	0.0184	0	-0.0003	0
GSK1379800A	-0.003	0	-0.006	0	0.0243	0	0.0081	0	0.0123	1	-0.0079	0	0.0904	0	0.0119	0
GSK1398463A	0.0093	0	-0.0011	0	0.015	0	-0.004	0	-0.0055	0	0.0148	1	0.0169	0	-0.0006	0
GSK429286A	-0.009	0	-0.0002	0	0.0193	0	0.0042	0	0.0117	1	0.0083	0	0.0159	0	0.0031	0
GW869979X	0.007	0	0.0033	0	-0.0418	0	-0.0022	0	0.0106	1	0.0199	1	0.0168	0	-0.0041	0
SB-249175	-0.0006	0	-0.0084	0	0.0154	0	0.0024	0	0.0156	2	-0.0067	0	0.0601	0	-0.0073	0
GSK361065A	-0.0083	0	0.0093	0	-0.0024	0	0.0045	0	-0.0103	-1	-0.007	0	-0.0137	0	0.0069	0
GSK938890A	0.0061	0	0.0006	0	-0.0573	0	0.0087	0	0.0122	1	-0.001	0	0.0269	0	-0.0021	0
GW580496A	0.0064	0	0.0052	0	-0.007	0	0.0111	0	0.0048	0	-0.0227	-1	0.0044	0	0.0026	0
GW622055X	-0.0054	0	0.006	0	-0.0075	0	0.0062	0	0.0021	0	-0.0154	-1	0.056	0	0.0035	0
GW641155B	0.0017	0	0.0055	0	0.0044	0	-0.0006	0	0.0056	0	-0.0241	-2	0.0084	0	0.0081	0
GW795486X	0.0063	0	0.0009	0	0.0017	0	0.0091	0	0.0084	0	-0.0137	-1	0.0124	0	0.0058	0
GW809897X	-0.0018	0	0.0116	1	-0.0077	0	0.0006	0	0.0008	0	-0.0206	-1	0.0012	0	-0.0069	0
GW785404X	0.0029	0	0.0006	0	-0.0064	0	0.0089	0	-0.0043	0	0.0175	1	0.0148	0	0.0079	0
SB-693162	-0.0104	0	-0.0093	0	0.0089	0	0.0089	0	0.0005	0	0.0152	1	0.0263	0	-0.0037	0
GSK718429A	0.0047	0	0.0004	0	-0.0029	0	0.0013	0	0.0031	0	-0.0085	0	0.0202	0	0.0072	0
GW569530A	-0.0005	0	-0.0064	0	0.0181	0	0.0003	0	0.003	0	-0.0029	0	0.0134	0	0.0045	0
GW775608X	-0.0005	0	-0.0067	0	0.0206	0	-0.0054	0	0.0003	0	-0.0061	0	0.0163	0	0.0095	0
SB-210313	0.0032	0	0.0027	0	0.01	0	-0.0035	0	-0.0044	0	-0.0047	0	0.0449	0	0.0017	0
SB-220455	-0.0019	0	-0.0002	0	-0.0153	0	0.0023	0	-0.0038	0	-0.0014	0	0.0578	0	0.0141	0
GSK1379712A	-0.0044	0	-0.0002	0	-0.0142	0	0.014	0	-0.0046	0	-0.0075	0	0.0049	0	0.0049	0
GSK1379721A	-0.0118	0	-0.0057	0	-0.0282	0	-0.0046	0	-0.0016	0	-0.0052	0	0.0072	0	0.0132	0
GSK1379722A	-0.0062	0	-0.0005	0	-0.0305	0	-0.0003	0	-0.0019	0	-0.0052	0	0.027	0	0.0005	0
GW589961A	-0.0079	0	-0.0009	0	-0.0007	0	-0.0061	0	0.0075	0	0.006	0	0.0142	0	-0.0064	0
SB-742864	-0.0124	0	-0.0096	0	-0.0146	0	-0.0043	0	0.0004	0	0.0041	0	0.0512	0	0.0045	0
GW459057A	-0.0003	0	0.0031	0	-0.021	0	0.0009	0	0.0003	0	0.0098	0	0.0004	0	-0.0069	0
GW819077X	0.004	0	0.0032	0	-0.0203	0	0.0093	0	-0.0019	0	0.004	0	-0.004	0	-0.0034	0
SB-347804	0.0111	0	0.0011	0	-0.0248	0	0.0027	0	0.0027	0	0.0081	0	-0.0112	0	0.0043	0
SB-409513	0.002	0	0.0003	0	-0.0267	0	-0.0002	0	-0.0041	0	0.0026	0	0.0025	0	-0.0032	0
SB-734117	-0.0087	0	0.0009	0	-0.0546	0	0.0041	0	-0.0004	0	0.0043	0	0.0655	0	-0.0002	0
GW809885X	-0.0063	0	-0.0032	0	-0.0094	0	-0.0038	0	-0.001	0	0.0061	0	0.0234	0	0.0026	0

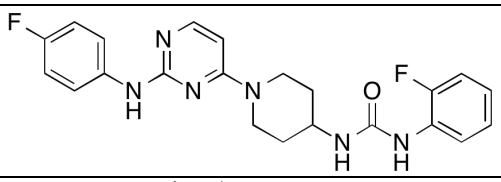
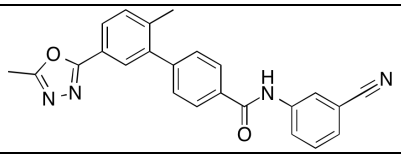
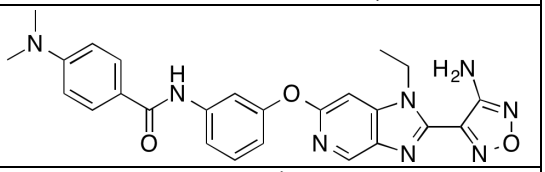
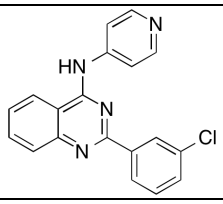
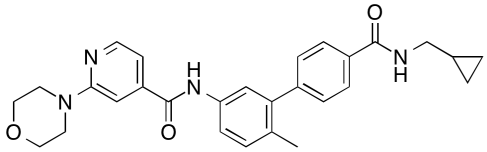
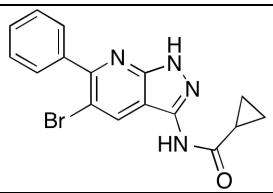
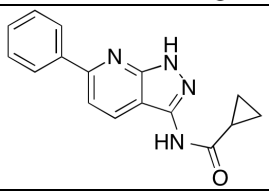
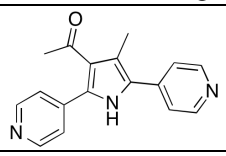
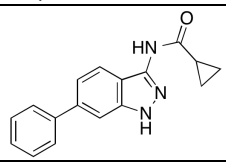
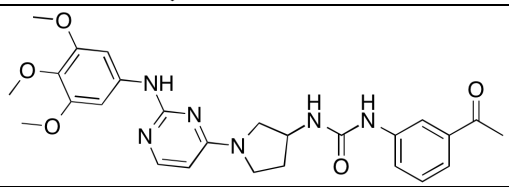
GW440146A	0.0059	0	-0.0037	0	-0.003	0	-0.0022	0	0.0038	0	0.0028	0	0.005	0	0.006	0
GW514786X	0.0077	0	-0.007	0	-0.0202	0	0.0032	0	0.0035	0	-0.0035	0	0.0117	0	0.0144	0
SB-376715	-0.0113	0	-0.0053	0	-0.0168	0	0.0038	0	0.0048	0	-0.0015	0	0.0018	0	0.0029	0
AH5015X	0.0068	0	-0.0104	-1	-0.0132	0	0.0033	0	0.0034	0	0.0051	0	0.0611	0	-0.0046	0
GSK2372690A	0.0005	0	-0.0073	0	0.0156	0	0.0009	0	0.0058	0	0.0009	0	-0.0266	0	0.0026	0
GW681251X	0.0031	0	0.0084	0	0.0093	0	0.0029	0	0.0087	1	-0.0027	0	0.0371	0	0.004	0
GW810578X	0.0024	0	-0.0076	0	0.015	0	-0.002	0	0.0084	0	-0.0021	0	0.0302	0	0.0043	0
SB-390766	-0.017	0	-0.0029	0	0.0007	0	-0.0029	0	0.0057	0	0.0038	0	0.0879	0	0.0054	0
SB-404290	-0.0001	0	-0.0049	0	0.011	0	-0.0037	0	0.0049	0	-1E-04	0	-0.0266	0	0	0
GSK466317A	-0.0172	0	0.0117	1	-0.0268	0	-0.0006	0	-0.0017	0	0.0027	0	0.0559	0	-0.0068	0
GSK483724A	0.0091	0	0.0073	0	-0.0255	0	-0.0041	0	-0.0003	0	-0.0017	0	0.0313	0	0.0084	0
GW572738X	0.0109	0	0.0085	0	-0.0265	0	-0.0052	0	-0.0026	0	0.0024	0	-0.0033	0	-0.0068	0
GW583340C	0.0118	1	0.0079	0	-0.0136	0	0.0101	0	-0.0039	0	-0.0031	0	-0.001	0	-0.0067	0
GW812171X	-0.0117	0	-0.0078	0	0.0185	0	0.0009	0	0.0019	0	-0.0009	0	0.0297	0	-0.0036	0
SB-431542-A	-0.0106	0	0.0093	0	-0.0399	0	0.0129	0	0.0041	0	0.0065	0	0.0412	0	0.0049	0
SB-733416	0.0021	0	-0.0008	0	0.0071	0	0.0041	0	0.0053	0	-0.0119	-1	0.001	0	0.0005	0
SB-736302	0.0066	0	0.0082	0	-0.0259	0	-0.0065	0	0.0014	0	-0.0003	0	0.001	0	-0.0027	0
GW701427A	-0.0107	0	-0.0023	0	-0.0127	0	0.0004	0	0.0048	0	-0.0058	0	-0.0251	0	0.0134	0
GW829055X	-0.0025	0	0.006	0	0.0063	0	0.0006	0	0.0029	0	-0.0068	0	0.0389	0	0.0047	0
GSK248233B	0.0055	0	-0.0091	0	0.0038	0	0.0011	0	-0.0005	0	0.0105	0	0.0054	0	0.0096	0
SB-738561	0.0006	0	-0.0035	0	-0.0152	0	0.0116	0	0.0041	0	0.0108	0	0.0391	0	0.0041	0
GW276655X	0.0026	0	-0.0032	0	0.0065	0	-0.0009	0	0.0002	0	-0.0053	0	0.0009	0	0.0012	0
GW278681X	-0.0041	0	-0.0008	0	-0.0219	0	-0.0094	-1	-0.0057	-1	0.0096	0	0.0178	0	0.0101	0
GW279320X	-0.0037	0	-0.0038	0	-0.0135	0	0.0038	0	-0.0032	0	0.0107	0	-0.0008	0	0.007	0
GW282974X	-0.0051	0	-0.0037	0	0.0047	0	-0.0053	0	0.0017	0	0.0034	0	0.0242	0	0.0113	0
GW300657X	-0.0038	0	-0.0022	0	0.0059	0	-0.0036	0	0.0043	0	-0.0004	0	0.0233	0	0.0154	0
GW432441X	-0.0168	0	0.0052	0	-0.0175	0	0.0075	0	0.0006	0	0.009	0	-0.1791	0	0.031	2
GW513184X	-0.0115	0	-0.0026	0	-0.0237	0	0.0054	0	-0.0096	-1	-0.0007	0	-0.0468	0	0.0077	0
GW549034X	-0.009	0	0.0042	0	0.0051	0	-0.001	0	-0.0044	0	-0.0018	0	0.0161	0	0.0045	0
GW618013X	-0.0157	0	-0.0017	0	-0.0569	0	0.0003	0	-0.0087	-1	0.0084	0	0.082	0	0.02	1
GW644007X	-0.0859	-2	-0.0011	0	-0.0583	0	0.0028	0	-0.0151	-2	-0.0181	-1	0.0822	0	-0.0015	0
GW679410X	-0.013	0	0.0061	0	-0.0119	0	-0.0036	0	-0.0013	0	0.0051	0	0.069	0	0.0054	0
GW708336X	-0.008	0	0.005	0	-0.0286	0	-0.002	0	-0.0039	0	-0.0113	0	0.0056	0	0.0103	0
GW784684X	-0.0113	0	0.0012	0	0.0101	0	-0.0059	0	-0.0026	0	-0.001	0	0.0133	0	0.0058	0
GW804482X	-0.0158	0	0.0036	0	0.0064	0	0.0087	0	-0.0086	-1	-0.0111	0	0.1298	0	0.0238	1
GW810372X	-0.001	0	0.0072	0	0.0177	0	0.0017	0	-0.0034	0	0.0177	1	0.0082	0	0.0135	0
GW827396X	-0.0068	0	-0.0046	0	-0.0105	0	0.008	0	-0.0032	0	-0.0032	0	0.0256	0	0.0324	2
SB-264865	-0.0291	0	0.0076	0	-0.0003	0	-0.0027	0	0.0032	0	0.0156	1	125.2444	2	-0.056	-2
SB-747651-A	-0.0017	0	0.0112	0	-0.039	0	0.0044	0	0.0009	0	0.0042	0	0.022	0	0.012	0

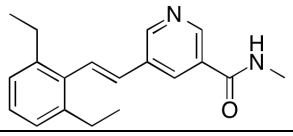
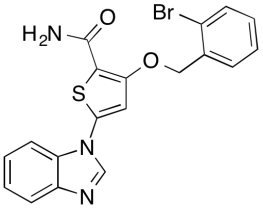
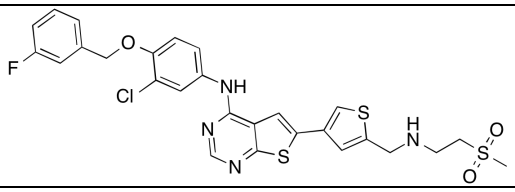
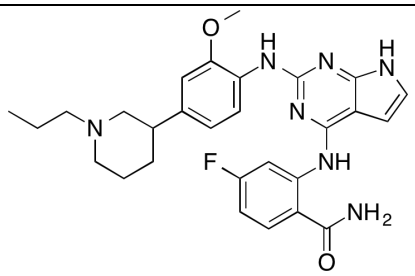
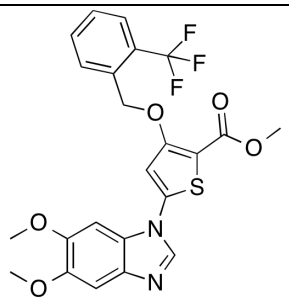
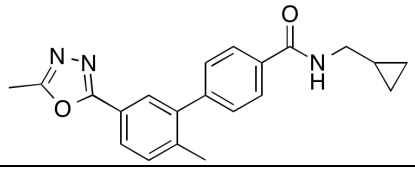
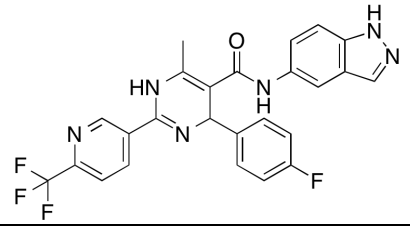
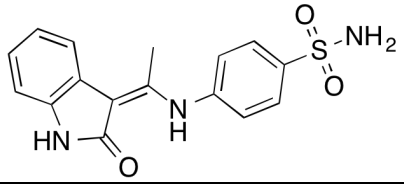
Table S3 Comparative assay data from the Brd4 Screen					
Compound Regno	[a] *PrOF* NMR	ΔT_m (°C)	[b] IC_{50} (μM)	[b] K_i (μM)	Structure
SB-284851-BT	+++	7.4 ± 0.2	2.2 ± 0.4	0.31 ± 0.04	
GSK2219329A	+++	6.3 ± 0.5			
GSK1379765A	+++	6.1 ± 0.3			
SB-590885-AAE	+++	5.1 ± 0.4	2.5±1.4	0.40 ± 0.23	
SB-264866	+++	4.8 ± 0.1	>100		
GSK260205A	+++	4.2 ± 0.8	39 ± 65	7 ± 12	

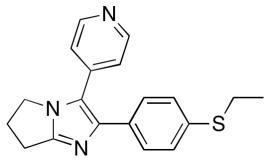
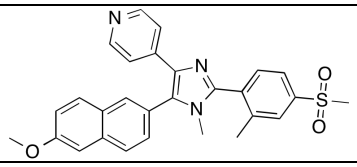
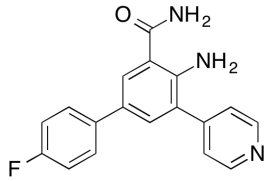
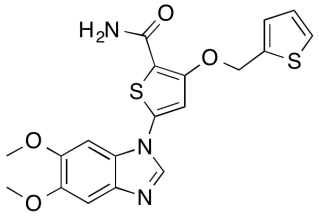
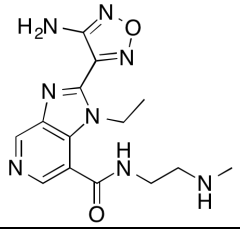
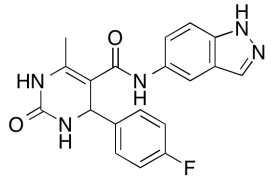
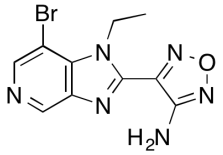
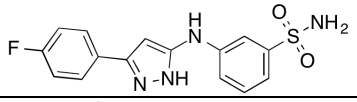
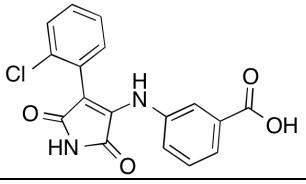
SB-250715	+++	4.1 ± 0.8	>100		
GW837331X	+++	3.8 ± 0.5	18% inhibited at 100		
SB-251527	+++	3.4 ± 0.6			
GSK2220400A	+++	3.1 ± 1.2			
GSK1379767A	+++	3.1 ± 3.9			
GW439255X	+++	3.0 ± 1.0			
SB-710363	++	2.7 ± 0.9			

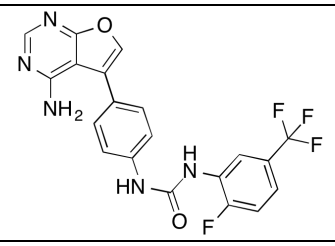
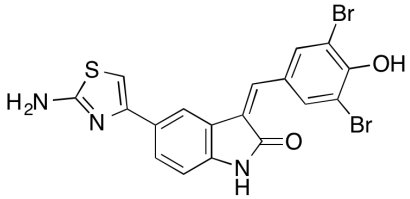
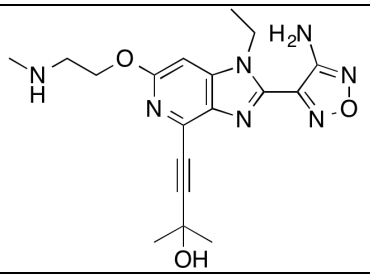
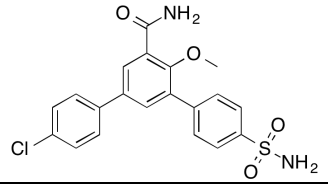
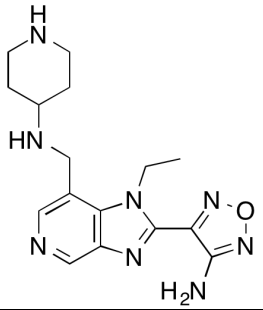
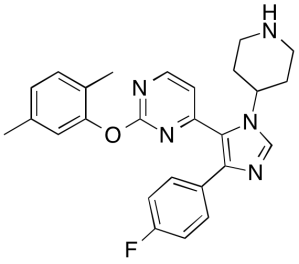
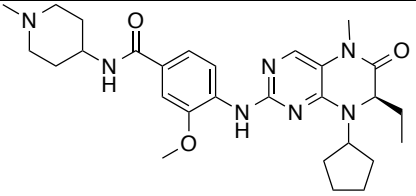
GW829055X	-	2.5 ± 0.7			
SB-400868-A	-	2.3 ± 0.8			
GW622475X	+++	2.2 ± 0.8			
SB-242719	+++	2.1 ± 0.5	70 ± 17	13 ± 3	
SB-217360	++	2.0 ± 0.8			
GW702865X	+++	2.0 ± 0.7			
GW684941X	+++	1.9 ± 0.5			
GW831090X	+	1.8 ± 0.5			

GW525701A	+	1.8 ± 0.6			
GSK1321565A	++	1.5 ± 0.6			
SB-254169	+++	1.5 ± 0.5			
SB-358518	+++	1.4 ± 0.1			
SB-253228	+++	1.3 ± 0.1			
SB-211743	+	1.3 ± 1.1			
GSK1379763A	+++	1.3 ± 0.3			
SKF-86055	+++	1.2 ± 0.3			

GSK1379800A	-	1.1 ± 0.5			
GW607117X	+	1.0 ± 0.4			
GSK248233B	-	0.9 ± 1.5			
GW873004X	++	0.8 ± 0.4			
GW775608X	-	0.7 ± 0.7			
SB-708998	++	0.6 ± 0.7			
SB-708999	++	0.6 ± 0.7			
GW493036X	++	0.6 ± 0.7			
SB-732941	++	0.6 ± 0.7			
GSK1379753A	+++	0.5 ± 0.5			

GW450241X	-	0.5 ± 0.5			
GSK1023156A	+++	0.4 ± 1.1			
GSK300014A	++	0.4 ± 0.5			
GSK1173862A	++	0.4 ± 0.5			
GSK1030058A	-	0.2 ± 1.0			
GW679662X	+++	0.2 ± 1.0			
GSK317354A	+++	0.0 ± 0.7			
GW335962X	+	-0.2 ± 0.8			

SKF-106164-A2	+++	-0.3 ± 1.2			
SB-633825	+	-0.4 ± 0.9	>100		
GSK620503A	+++	-0.7 ± 1.1			
GSK312948A	++	-0.8 ± 0.8			
GW876790X	++	-0.9 ± 0.9			
GSK180736A	+	-1.5 ± 0.8			
SB-738004	+++	-1.9 ± 1.1	>100		
GW824645A	++	-1.9 ± 0.7			
SB-390526	++	-1.9 ± 1.0	>100		

SB-707548-A	++	-2.1 ± 0.5	>100		
GW407323A	+++	-2.2 ± 1.0	>100		
GSK949675A	++	-2.4 ± 0.7	60% inhibition at 100		
GSK711701A	++	-2.7 ± 0.3	>100		
SB-747651-A	-	-4.6 ± 1.4			
SB-284852-BT			4.7 ± 1.4	0.58 ± 0.23	
BI2536			0.16 ± 0.05	Not determined	

[a] +++, a resonance from the protein in question has been completely broadened into baseline

++, a resonance from 5FW-Brd4 has been perturbed by 2 standard deviations in either chemical shift or linewidth +, a resonance from 5FW-Brd4 has been perturbed by 1 standard deviation in either chemical shift or linewidth

-, resonances are minimally to non perturbed

[b] values were obtained for via FA for Brd4 only