SUPPORTING INFORMATION

Design, synthesis and biological activity of N^4-phenylsubstituted-7*H*-pyrrolo[2,3-*d*]pyrimidin-4-amines as dual inhibitors of aurora kinase A and epidermal growth factor receptor kinase

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General procedures for determination of IC_{50} values for compounds 1-8

Kinase activity was measured by quantifying the amount of ADP produced from the kinase reaction. The luminescent signal from the assay was correlated with the amount of ADP present and is directly correlated with the amount of kinase activity. Compounds **1-18** and staurosporine were diluted in 10% DMSO and 2.5µl of the dilution was added to a 25µl reaction so that the final concentration of DMSO is 1% in all of reactions. The 25 µl reaction mixture contained 40 mM Tris, pH 7.4, 10 mM $MgCl_2$, 0.1 mg/ml BSA, 1 mM DTT, 10 µM ATP, Kinase substrate peptide, 10 µM ATP and the target kinase enzyme. EGFR reactions were conducted at 30 ^oC for 45 minutes using 0.2 mg/ml Poly (Glu, Tyr) as the EGFR substrate peptide and 5 ng of EGFR kinase. Aurora A reactions were done for 50 min at 30 ^oC using 0.2 mg/ml Kemptide and 220 ng of Aurora A kinase. After the kinase reaction at 30 ^oC, 25 µl of ADP-Glo reagent was added and incubated for 45 min at room temperature followed by another 40 min incubation with 50 µl of Kinase detection mixture. All luminescence signals were measured using a BioTek *Synergy 2* microplate reader. Kinase activity assays were performed in triplicate at each

concentration. The luminescence data were analyzed using the computer software, Graphpad Prism. The difference between luminescence intensities in the absence of Kinase (Lu_t) and in the presence of Kinase (Lu_c) was defined as 100 % activity ($Lu_t - Lu_c$). Using luminescence signal (Lu) in the presence of the compound, % activity was calculated as:

% activity = $\{(Lu_t - Lu)/(Lu_t - Lu_c)\}\times 100\%$, where Lu= the luminescence intensity in the presence of the compound. The values of % activity versus a series of compound concentrations were then plotted using non-linear regression analysis of Sigmoidal dose-response curve generated with the equation $Y=B+(T-B)/1+10^{((LogEC50-X)\times Hill\ Slope)}$, where Y=percent activity, B=minimum percent activity, T=maximum percent activity, X= logarithm of compound and Hill Slope=slope factor or Hill coefficient. The IC_{50} value was determined by the concentration causing a half-maximal percent activity.

3.1. Results of the Effect of the Compounds on Kinases

EGFR

Table S1: Data for the Effect of SK-34 (compound 1) on EGFR Activity

SK-34 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	7698	7680	8361	97	97	106
0	8176	7755	8129	103	98	103
1.0	7979	8710	8392	101	110	106
1.5	7329	7208	7428	92	91	94
2.0	5247	5646	6009	66	71	76
2.5	3191	3411	3245	39	42	40
3.0	1985	1862	1823	24	22	22
3.5	811	792	802	9	9	9
4.0	446	549	482	4	5	5
4.5	257	265	275	2	2	2
5.0	201	208	222	1	1	1
Background	129	121	131			

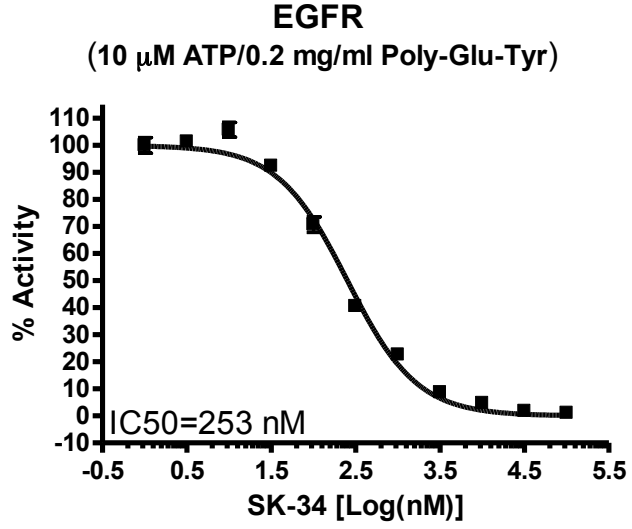


Table S2: Data for the Effect of SK-18 (compound 2) on EGFR Activity

SK-18 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8247	8359	8110	100	101	98
0	3604	3492	3444	43	41	41
1.0	2483	2486	2407	29	29	28
1.5	1042	888	1009	11	9	11
2.0	595	576	606	6	6	6
2.5	363	316	330	3	2	3
3.0	235	217	240	1	1	1
3.5	184	183	161	1	1	0
4.0	135	130	143	0	0	0
4.5	149	133	112	0	0	0
5.0	123	164	128	0	0	0
Background	119	134	126			

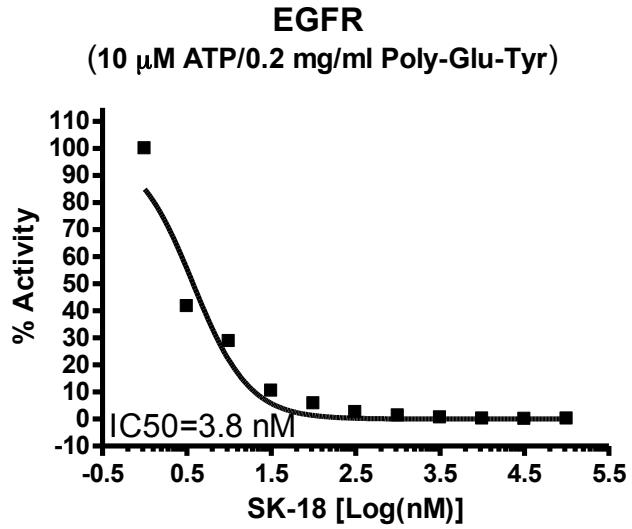


Table S3: Data for the Effect of SK-17 (compound 3) on EGFR Activity

SK-17 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8572	8464	7927	103	102	95
0	4808	4889	4706	57	58	56
1.0	3202	3158	3419	38	37	40
1.5	1210	1432	1434	13	16	16
2.0	695	683	781	7	7	8
2.5	328	416	405	2	4	3
3.0	231	245	260	1	1	2
3.5	162	185	165	0	1	0
4.0	136	153	143	0	0	0
4.5	133	131	131	0	0	0
5.0	132	141	128	0	0	0
Background	127	116	132			

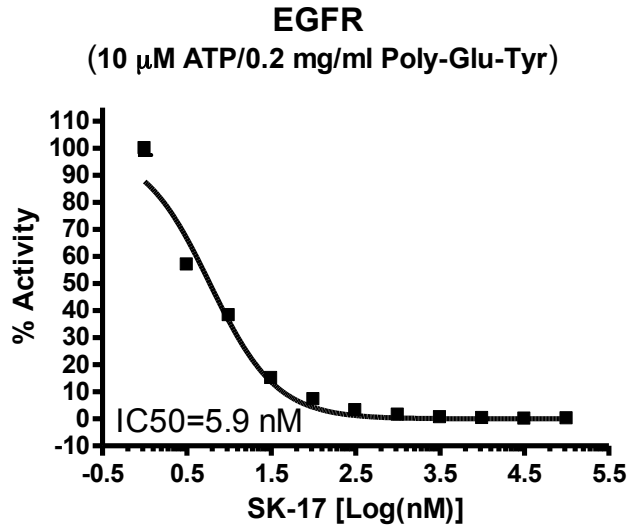


Table S4: Data for the Effect of TM-9 (compound 4) on EGFR Activity

TM-9 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	7106	7597	7685	95	102	103
0	7599	7194	7272	102	96	97
1.0	7608	7225	7193	102	97	96
1.5	4897	4575	4833	65	61	64
2.0	3785	3448	3952	50	45	52
2.5	1550	1517	1712	19	19	22
3.0	888	869	975	10	10	12
3.5	403	433	440	4	4	4
4.0	254	257	260	2	2	2
4.5	184	182	163	1	1	1
5.0	159	175	179	1	1	1
Background	107	135	117			

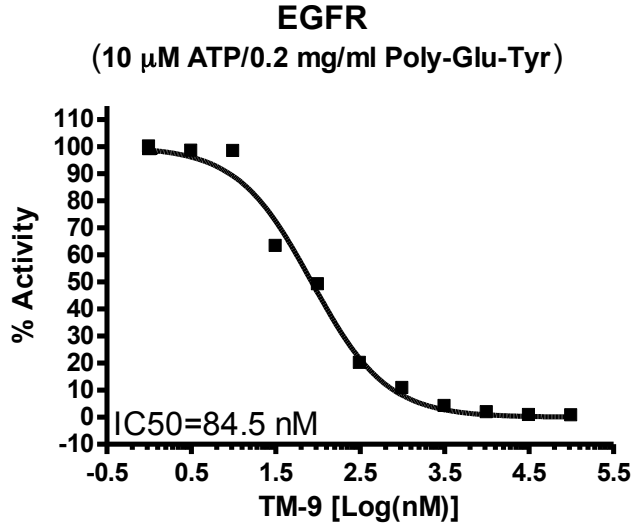


Table S5: Data for the Effect of SK-32 (compound 5) on Kinase Activity

SK-32 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	7168	7732	7684	95	103	102
0	3874	4474	4386	51	59	58
1.0	3328	3535	3663	43	46	48
1.5	1189	1284	1269	14	16	16
2.0	714	768	780	8	9	9
2.5	359	398	459	3	4	5
3.0	235	253	242	2	2	2
3.5	163	165	165	1	1	1
4.0	123	131	213	0	0	1
4.5	125	133	138	0	0	0
5.0	122	313	158	0	3	1
Background	114	119	111			

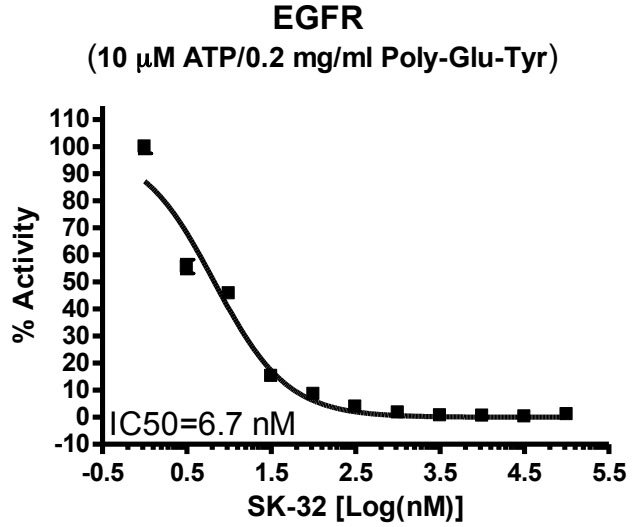


Table S6: Data for the Effect of BM-7 (compound 6) on EGFR Kinase Activity

BM-7 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	7916	8475	7946	98	105	98
0	7931	8294	8548	98	102	105
1.0	8243	8911	8738	102	110	108
1.5	8479	8559	8727	105	106	108
2.0	8059	8258	8420	99	102	104
2.5	7826	7572	7833	96	93	97
3.0	5845	6420	6359	72	79	78
3.5	3535	3967	3561	43	48	43
4.0	2000	2074	1912	23	24	22
4.5	783	857	774	8	9	8
5.0	439	448	403	4	4	4
Background	115	137	117			

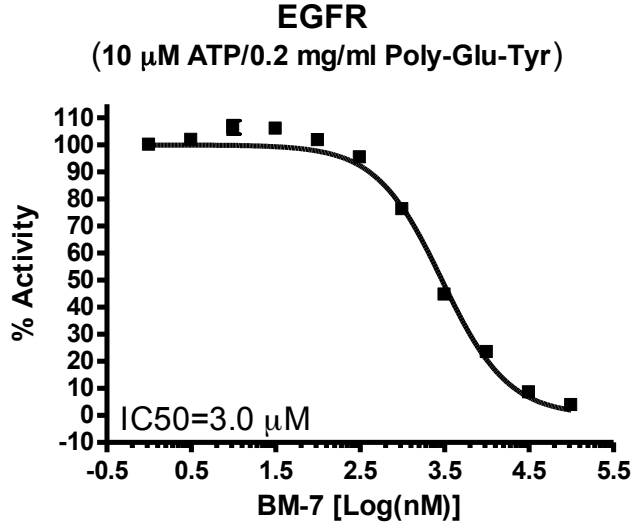


Table S7: Data for the Effect of BM-19 (compound 7) on EGFR Activity

BM-19 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	7606	7242	7558	102	97	101
0	3323	3805	4016	44	50	53
1.0	1415	1335	1613	18	17	20
1.5	1013	1097	1223	12	13	15
2.0	418	467	440	4	5	4
2.5	347	316	370	3	3	3
3.0	199	247	272	1	2	2
3.5	156	163	148	1	1	0
4.0	136	143	123	0	0	0
4.5	186	176	177	1	1	1
5.0	148	135	132	0	0	0
Background	125	110	117			

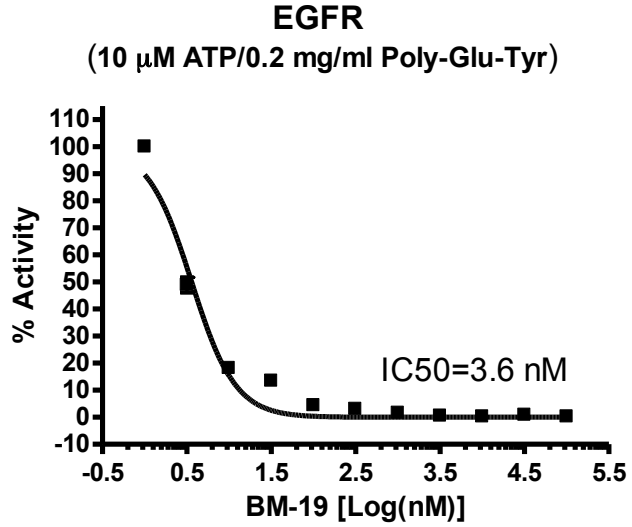


Table S8: Data for the Effect of AF-36 (compound 8) on EGFR Activity

AF-36 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	9729	10039	9851	98	102	100
0	9567	9812	9790	97	99	99
1.0	9381	10015	9043	95	102	91
1.5	9236	10085	8383	93	102	84
2.0	8064	8296	8177	80	83	82
2.5	5401	5165	5502	51	49	53
3.0	3054	2830	3160	26	23	27
3.5	1728	1521	1591	12	9	10
4.0	1075	1135	1002	4	5	4
4.5	867	946	738	2	3	1
5.0	778	736	811	1	1	2
Background	702	675	623			

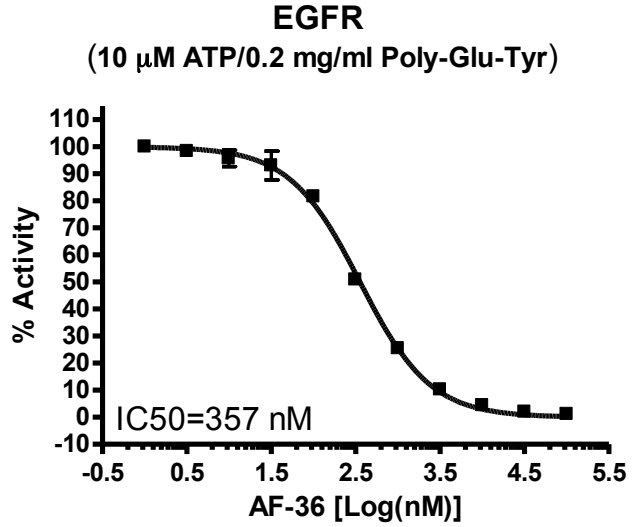


Table S9: Data for the Effect of BM-26 (compound 9) on Kinase Activity

BM-26 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8642	8755	9597	96	97	107
0	9265	8849	9375	103	98	105
1.0	10035	9759	9267	112	109	103
1.5	10113	9637	8565	113	108	95
2.0	8606	7989	7398	95	88	81
2.5	6831	5932	6251	74	63	67
3.0	3701	3604	4223	36	35	43
3.5	2166	2026	2618	18	16	23
4.0	1356	1259	1526	8	7	10
4.5	911	982	883	3	4	3
5.0	779	791	814	1	1	2
Background	609	681	715			

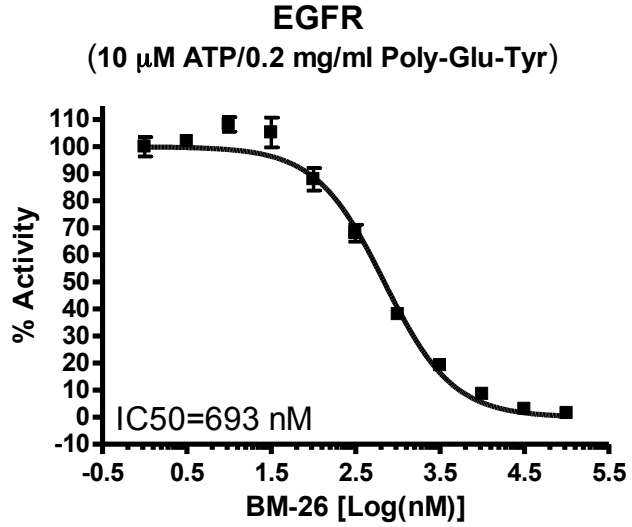


Table S10: Data for the Effect of BM-22 (compound 10) on Kinase Activity

BM-22 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8406	7924	8198	103	97	100
0	7381	7890	8454	90	96	103
1.0	7929	7395	7934	97	90	97
1.5	6377	6701	6538	78	82	80
2.0	4398	4664	4222	53	56	51
2.5	2560	2486	2394	30	29	28
3.0	1237	1082	1109	14	12	12
3.5	582	548	539	6	5	5
4.0	303	305	314	2	2	2
4.5	244	242	203	1	1	1
5.0	225	217	220	1	1	1
Background	123	115	147			

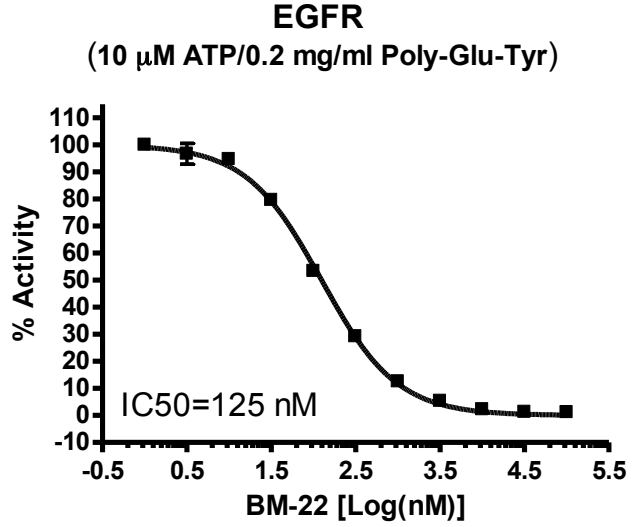


Table S11: Data for the Effect of BM-31 (compound 11) on Kinase Activity

BM-31 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	10193	9755	9586	104	99	97
0	6714	6349	6470	66	62	63
1.0	3992	3767	4275	36	34	39
1.5	2259	2151	2492	17	16	20
2.0	1419	1332	1727	8	7	11
2.5	1227	1057	1195	6	4	6
3.0	965	736	905	3	1	2
3.5	889	688	678	2	0	0
4.0	740	608	619	1	0	0
4.5	728	615	643	0	0	0
5.0	708	708	566	0	0	0
Background	737	705	605			

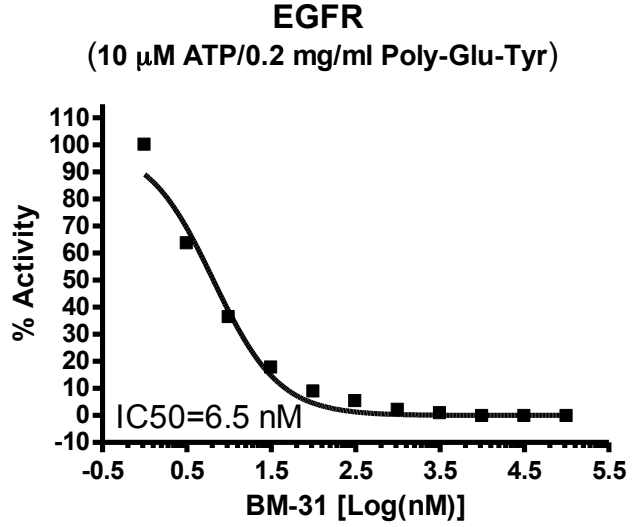


Table S12: Data for the Effect of BM-25 (compound 12) on Kinase Activity

BM-25 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	7404	7610	7571	98	101	101
0	5844	6675	5735	77	88	76
1.0	5246	5682	5046	69	75	66
1.5	2654	3010	2535	34	39	33
2.0	1529	1551	1306	19	19	16
2.5	846	766	685	10	9	8
3.0	520	496	462	5	5	5
3.5	280	784	271	2	9	2
4.0	174	185	188	1	1	1
4.5	147	155	153	0	0	0
5.0	117	138	134	0	0	0
Background	123	129	130			

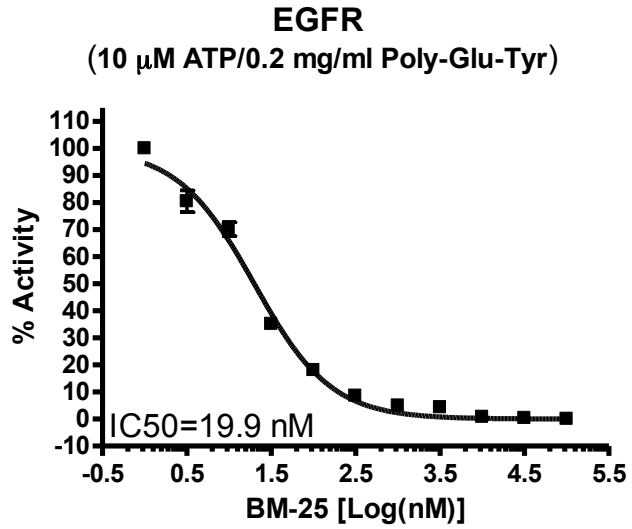


Table S13: Data for the Effect of BM-34 (compound 13) on Kinase Activity

BM-34 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	10673	11373	10570	98	105	97
0	10005	10067	9924	91	92	91
1.0	7423	8429	10354	66	76	95
1.5	6162	6962	6386	54	61	56
2.0	3683	3759	3931	29	30	32
2.5	2458	2668	2250	17	19	15
3.0	1558	1505	1377	8	8	6
3.5	991	1087	1035	3	4	3
4.0	749	857	839	0	1	1
4.5	675	866	766	0	1	0
5.0	714	714	801	0	0	1
Background	691	681	788			

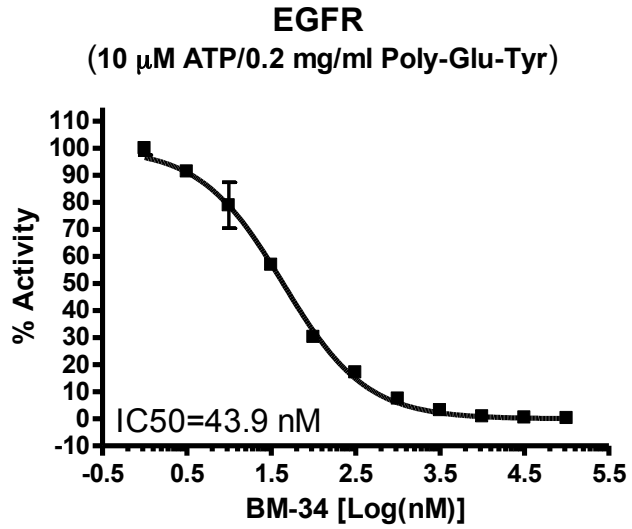


Table S14: Data for the Effect of BM-17 (compound 14) on Kinase Activity

BM-17 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8769	8304	7968	105	99	95
0	8375	7949	7887	100	95	94
1.0	8774	7492	8005	105	90	96
1.5	9013	6975	7766	108	83	93
2.0	7470	6322	7043	89	75	84
2.5	5272	4502	4827	62	53	57
3.0	3081	2364	2846	36	27	33
3.5	1463	1323	1426	16	14	16
4.0	830	670	686	8	6	7
4.5	451	373	389	4	3	3
5.0	550	473	489	5	4	4
Background	170	143	131			

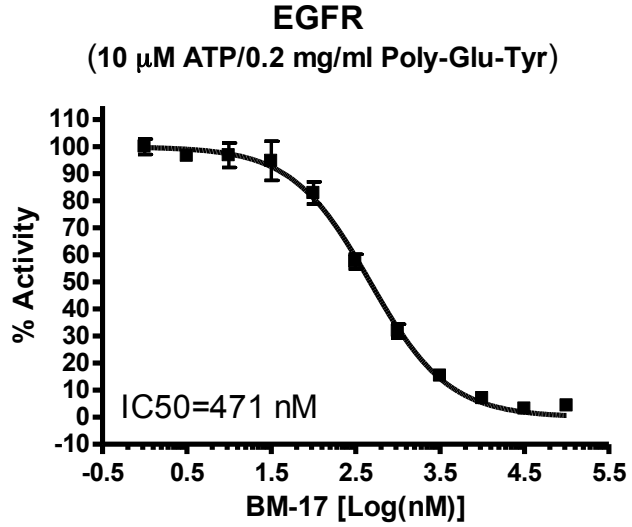


Table S15: Data for the Effect of BM-24 (compound 15) on Kinase Activity

BM-24 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8471	9578	9891	90	103	107
0	9075	9098	11146	97	98	121
1.0	10080	9442	11720	109	101	128
1.5	10467	10011	11258	113	108	122
2.0	10268	9446	9212	111	102	99
2.5	7351	7756	7961	77	82	84
3.0	5432	5760	5158	55	59	52
3.5	2430	2768	2653	20	24	23
4.0	1672	1714	1547	12	12	10
4.5	1014	1114	1007	4	5	4
5.0	965	880	926	4	3	3
Background	655	684	647			

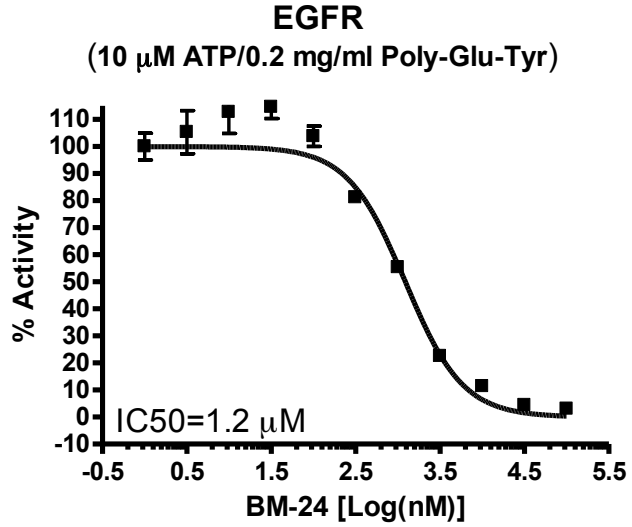


Table S16: Data for the Effect of RS-48 (compound 16) on Kinase Activity

RS-48 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	10446	10163	10100	102	99	99
0	10214	10492	10039	100	103	98
1.0	11377	10864	11095	111	106	109
1.5	11017	11768	10619	108	115	104
2.0	10837	10740	10951	106	105	107
2.5	10956	11243	11620	107	110	114
3.0	10698	10239	11292	105	100	111
3.5	8965	9550	9871	87	93	96
4.0	7535	7482	7669	73	73	74
4.5	8344	8648	9574	81	84	93
5.0	8127	8719	9104	79	85	89
Background	185	179	212			

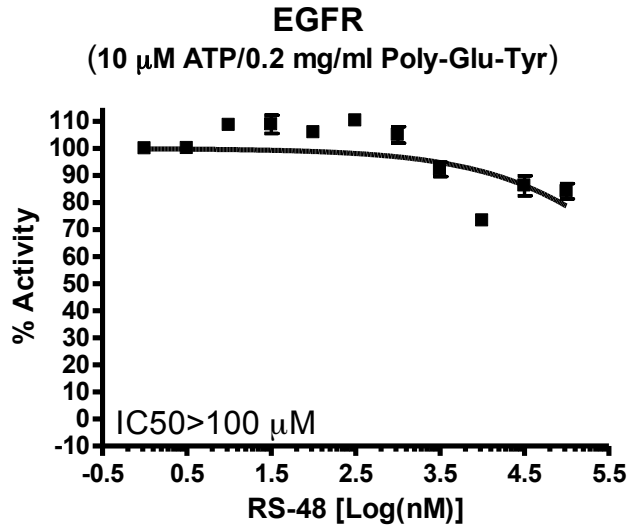


Table S17: Data for the Effect of BM-23 (compound 17) on Kinase Activity

BM-23 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	6679	7527	7688	91	103	105
0	6787	7360	7260	93	101	99
1.0	6567	6682	7107	90	91	97
1.5	5290	5651	6106	72	77	83
2.0	3648	3745	4072	49	51	55
2.5	1848	1747	2214	24	23	29
3.0	907	810	983	11	10	12
3.5	477	469	511	5	5	5
4.0	406	406	455	4	4	5
4.5	463	472	470	5	5	5
5.0	431	423	429	4	4	4
Background	119	123	108			

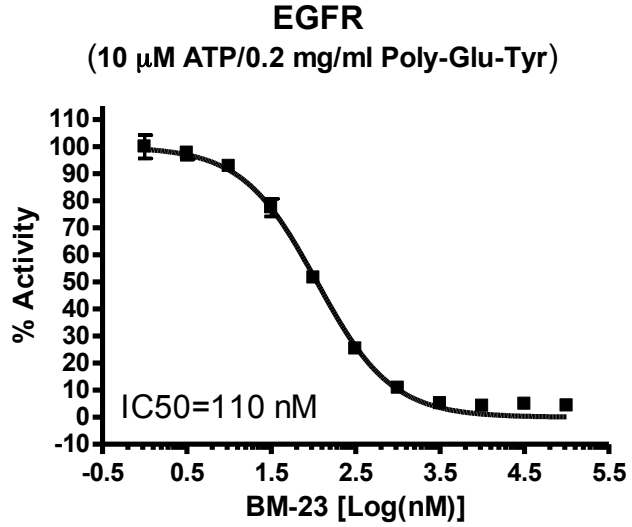


Table S18: Data for the Effect of SZ-34 (compound 18) on Kinase Activity

SZ-34 (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	9812	9614	10158	99	97	103
0	9452	9109	9358	96	92	95
1.0	8721	8170	8718	88	83	88
1.5	6593	6142	6443	66	62	65
2.0	4209	3862	4314	42	38	43
2.5	1767	1747	1751	16	16	16
3.0	969	945	1085	8	8	9
3.5	461	446	482	3	3	3
4.0	378	363	346	2	2	2
4.5	346	350	372	2	2	2
5.0	341	487	337	2	3	2
Background	189	190	183			

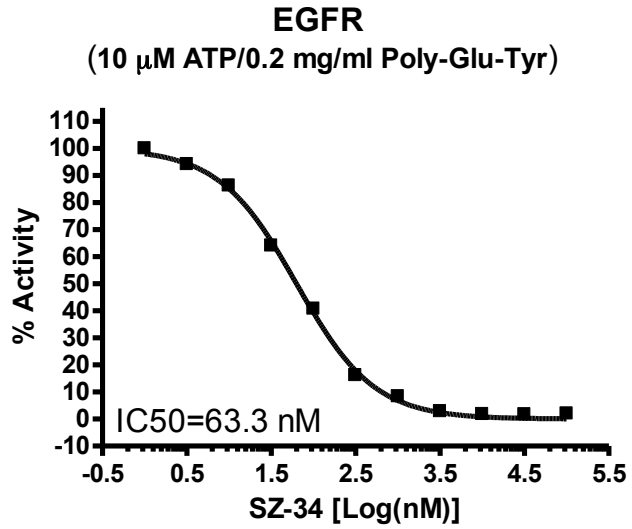


Table S19: Data for the Effect of Staurosporine on EGFR Activity

Staurosporine (Log [nM])	EGFR Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	8140	8688	8620	96	102	102
-1.0	7563	7968	8284	89	94	98
-0.5	8086	8558	8505	95	101	100
0	7867	8330	8179	93	98	96
1.0	6484	6960	7653	76	82	90
1.5	4694	5232	5158	54	61	60
2.0	2353	2450	2652	26	27	30
2.5	1134	1036	1137	12	10	12
3.0	573	642	620	5	6	5
3.5	329	345	366	2	2	2
4.0	249	247	243	1	1	1
Background	136	149	236			

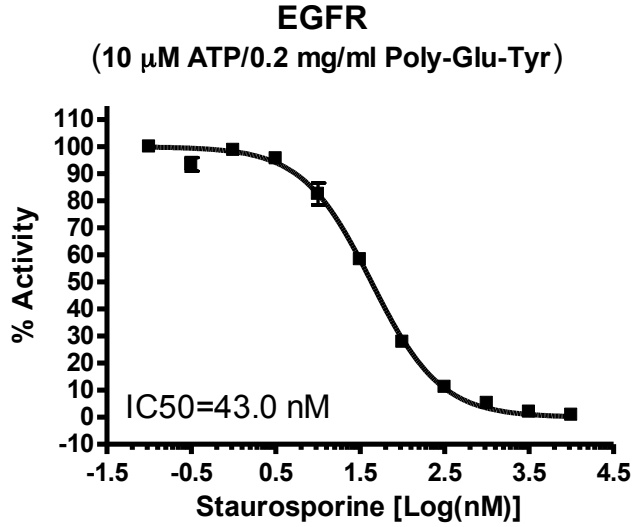


Table S20: Data for the Effect of SK-34 (compound 1) on AURKA Activity

SK-34 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	5578	5602	5577	100	100	100
0	5068	5094	5136	91	91	92
1.0	4849	5043	5114	87	90	91
1.5	5217	5477	5611	93	98	100
2.0	5357	5398	5607	96	97	100
2.5	5516	5724	5806	99	103	104
3.0	4800	5043	5211	86	90	93
3.5	3538	3942	3940	63	70	70
4.0	1654	1787	1871	28	31	32
4.5	717	773	796	11	12	13
5.0	347	395	394	5	5	5
Background	89	94	104			

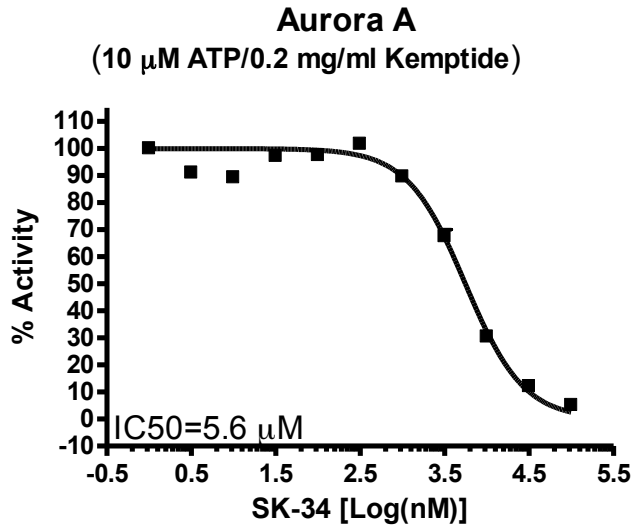


Table S21: Data for the Effect of SK-18 (compound 2) on AURKA Activity

SK-18 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	5264	5042	5127	102	98	100
0	5510	4820	4860	107	94	94
1.0	5603	4969	4952	109	97	96
1.5	5578	4922	5203	109	96	101
2.0	5270	5013	5387	102	97	105
2.5	4854	4562	4905	94	88	95
3.0	3650	3428	3600	70	66	69
3.5	1886	1812	1820	35	34	34
4.0	901	826	831	16	14	14
4.5	393	383	384	6	5	5
5.0	366	368	341	5	5	5
Background	131	94	96			

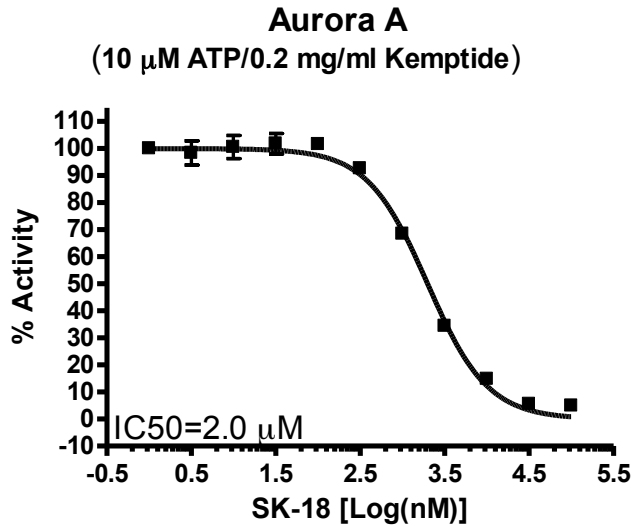


Table S22: Data for the Effect of SK-17 (compound 3) on AURKA Activity

SK-17 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	3875	3936	3969	99	100	101
0	3725	3643	3908	95	93	100
1.0	3884	3792	3972	99	96	101
1.5	3892	3705	4112	99	94	105
2.0	4127	4093	4204	105	104	107
2.5	4077	4114	4057	104	105	103
3.0	3075	2967	3034	78	75	77
3.5	2130	2260	2097	53	57	52
4.0	761	714	708	17	16	16
4.5	351	327	353	7	6	7
5.0	322	280	292	6	5	5
Background	93	93	83			

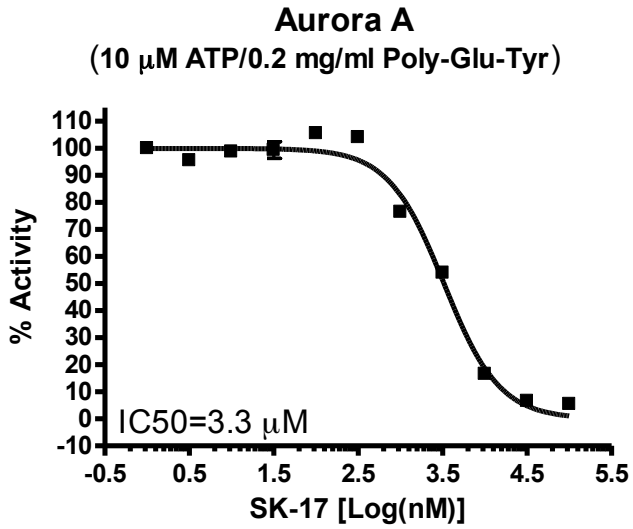


Table S23: Data for the Effect of TM-9 (compound 4) on AURKA Activity

TM-9 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4310	4797	4341	96	107	97
0	4387	4548	4329	98	101	97
1.0	4454	4380	4502	99	98	100
1.5	4668	4832	4550	104	108	102
2.0	4697	4783	4659	105	107	104
2.5	4622	4432	4506	103	99	101
3.0	3949	4169	3875	88	93	86
3.5	2972	3099	3064	66	69	68
4.0	1163	1292	1202	25	28	25
4.5	580	563	545	11	11	11
5.0	466	501	462	9	10	9
Background	93	76	76			

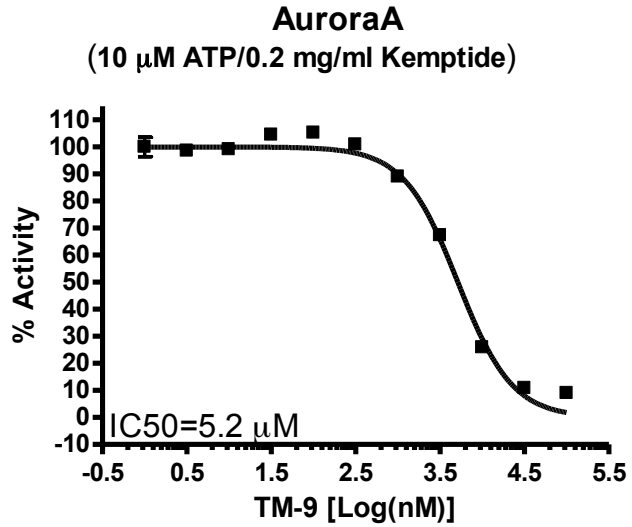


Table S24: Data for the Effect of SK-32 (compound 5) on AURKA Activity

SK-32 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4416	4531	4800	96	99	105
0	4357	4466	4728	95	97	103
1.0	4756	4350	4445	104	95	97
1.5	4514	4649	4672	98	101	102
2.0	4780	4903	4795	104	107	105
2.5	4736	4921	4847	103	108	106
3.0	4166	4752	4185	91	104	91
3.5	2575	2402	2681	55	51	58
4.0	808	1023	942	16	21	19
4.5	580	623	598	11	12	11
5.0	584	612	665	11	12	13
Background	92	97	81			

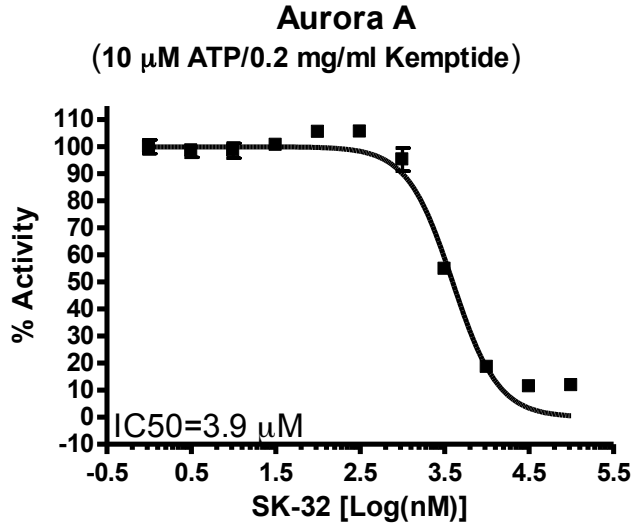


Table S25: Data for the Effect of BM-7 (compound 6) on AURKA Activity

BM-7 (Log [nM])	AuroraA Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4334	4284	4248	101	100	99
0	4436	4028	3776	104	94	88
1.0	4065	3841	3893	95	89	91
1.5	4759	4272	4706	111	100	110
2.0	4308	4074	4129	100	95	96
2.5	4623	4268	4520	108	100	106
3.0	3791	3909	3639	88	91	84
3.5	3723	3454	3267	86	80	76
4.0	1386	1497	1254	30	33	27
4.5	708	701	640	14	14	13
5.0	433	348	282	8	6	4
Background	176	88	76			

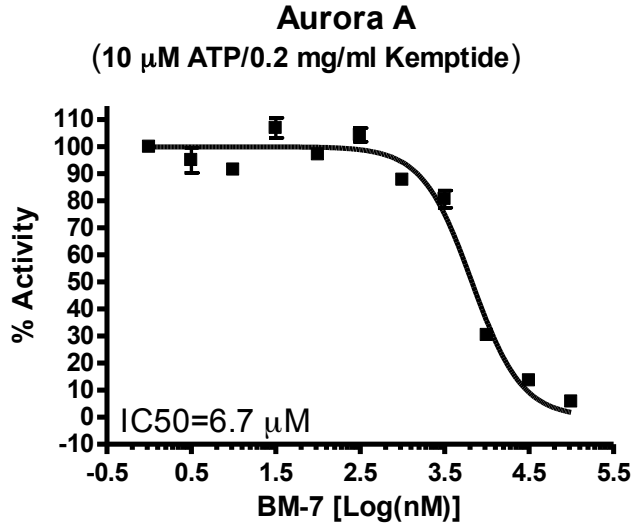


Table S26: Data for the Effect of BM-19 (compound 7) on AURKA Activity

BM-19 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	5013	4935	5330	98	97	105
0	4855	5181	4855	95	102	95
1.0	5100	5260	5047	100	103	99
1.5	5090	5239	5227	100	103	103
2.0	5094	5374	5354	100	106	105
2.5	4839	4931	4845	95	97	95
3.0	4823	5237	4747	95	103	93
3.5	2097	2110	1950	40	40	37
4.0	891	901	837	16	16	15
4.5	1656	1607	1615	31	30	30
5.0	934	854	899	17	15	16
Background	124	98	100			

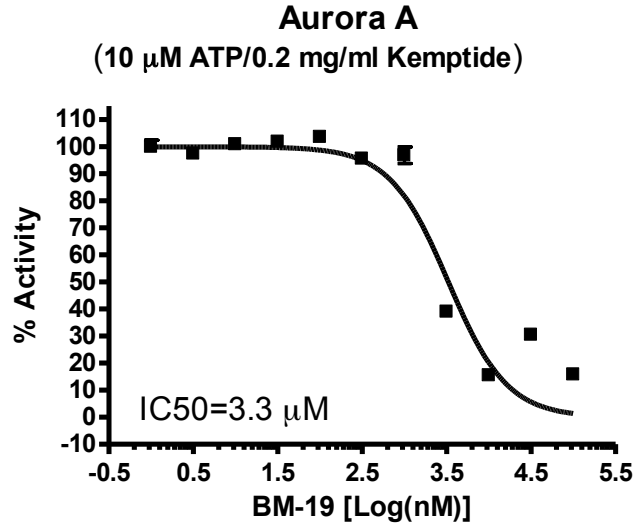


Table S27: Data for the Effect of AF-36 (compound 8) on AURKA Activity

AF-36 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	3685	4270	3915	93	108	99
0	4065	4229	3922	103	107	99
1.0	4346	3983	4371	110	101	111
1.5	4290	4254	4144	109	108	105
2.0	4297	4292	4296	109	109	109
2.5	3823	3977	4464	96	101	113
3.0	3343	3214	3640	84	80	92
3.5	2232	2308	2415	55	57	59
4.0	1294	1236	1256	30	28	29
4.5	556	576	578	11	11	11
5.0	464	429	443	8	7	8
Background	150	143	163			

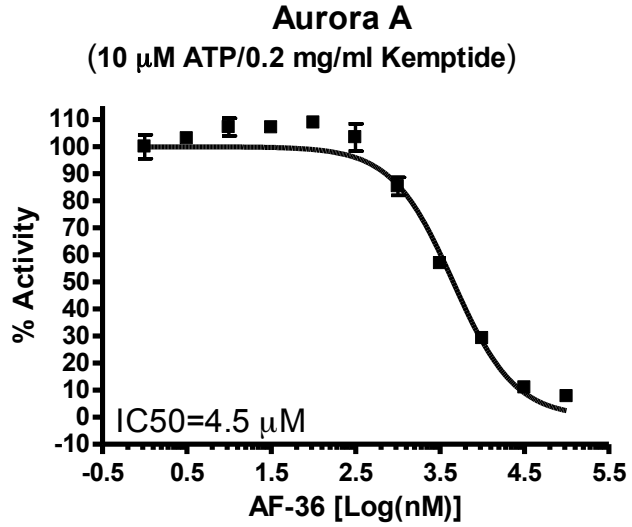


Table S28: Data for the Effect of BM-26 (compound 9) on Kinase Activity

BM-26 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	3868	4131	3910	97	104	98
0	3999	4099	4157	101	103	105
1.0	4501	4095	4228	114	103	107
1.5	4381	4093	4325	111	103	109
2.0	4050	4237	4501	102	107	114
2.5	3935	4051	4369	99	102	110
3.0	3469	3595	3616	87	90	91
3.5	2541	2681	2490	63	66	61
4.0	1353	1268	1299	32	29	30
4.5	747	712	655	16	15	13
5.0	494	478	486	9	9	9
Background	139	141	135			

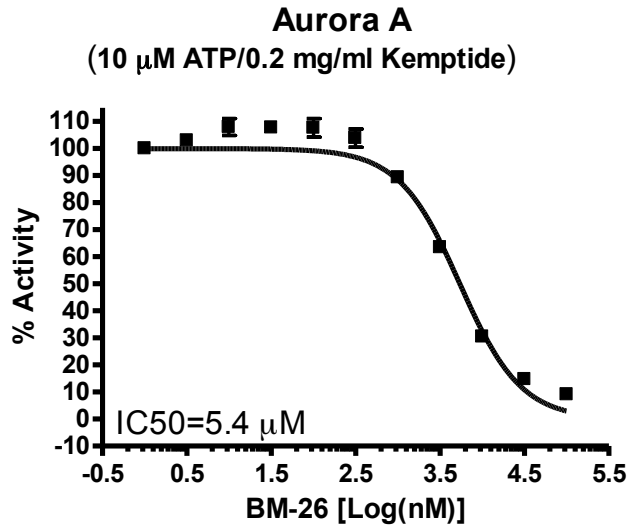


Table S29: Data for the Effect of BM-22 (compound 10) on Kinase Activity

BM-22 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4934	4986	4984	99	100	100
0	4857	4318	4783	98	87	96
1.0	4805	4689	4691	97	94	94
1.5	4944	4709	4733	100	95	95
2.0	5056	4805	5035	102	97	101
2.5	4952	4638	4862	100	93	98
3.0	4114	4141	4097	82	83	82
3.5	3037	2771	2702	60	55	53
4.0	1093	1027	1090	20	19	20
4.5	521	524	548	9	9	9
5.0	577	587	547	10	10	9
Background	98	97	102			

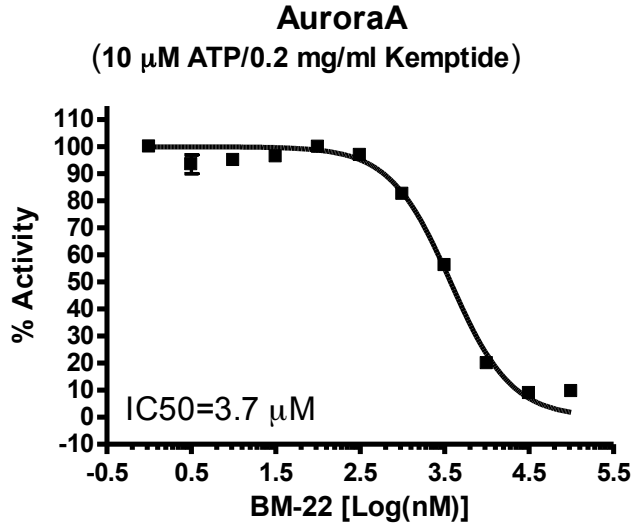


Table S30: Data for the Effect of BM-31 (compound 11) on Kinase Activity

BM-31 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4407	4193	3800	107	102	92
0	4081	4120	3719	99	100	90
1.0	4475	3951	4167	109	95	101
1.5	4228	4442	3961	102	108	96
2.0	3908	4279	4413	94	104	107
2.5	3951	4046	4079	95	98	99
3.0	3323	3521	3489	80	85	84
3.5	1838	2057	2108	42	48	49
4.0	925	1013	901	19	22	19
4.5	467	508	456	8	9	8
5.0	353	298	289	5	4	3
Background	150	163	157			

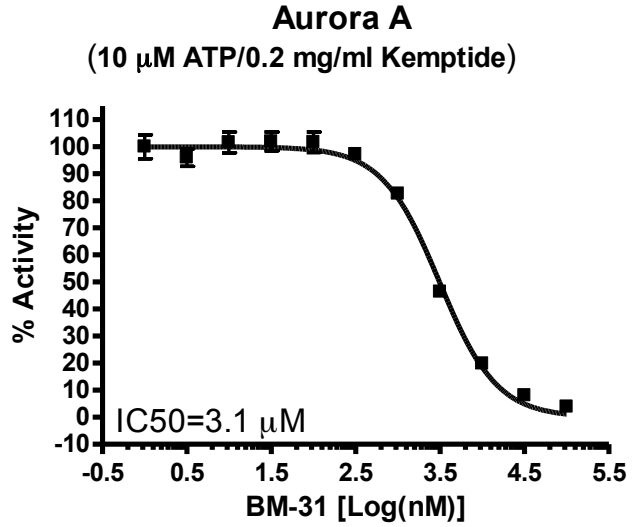


Table S31: Data for the Effect of BM-25 (compound 12) on Kinase Activity

BM-25 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4617	4910	4949	96	102	103
0	4881	5079	4586	101	105	95
1.0	4843	4906	4688	100	102	97
1.5	4697	4844	4665	97	100	97
2.0	4638	4895	5042	96	101	105
2.5	4318	4590	4604	89	95	95
3.0	4307	4382	4425	89	91	92
3.5	2388	2451	2623	48	50	53
4.0	926	902	904	17	17	17
4.5	453	492	477	7	8	8
5.0	272	277	263	4	4	3
Background	115	99	85			

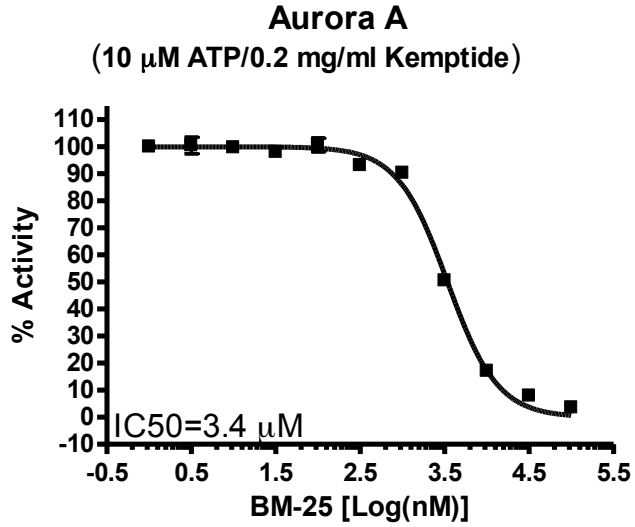


Table S32: Data for the Effect of BM-34 (compound 13) on Kinase Activity

BM-34 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4440	4084	4139	105	97	98
0	3989	4279	4060	94	101	96
1.0	4333	4252	4457	103	101	106
1.5	4506	4747	4983	107	113	119
2.0	4631	4550	4758	110	108	113
2.5	4535	4530	4726	108	108	112
3.0	3994	4240	3965	94	100	94
3.5	3132	2699	3103	73	63	72
4.0	1467	1201	1297	32	26	28
4.5	697	568	606	13	10	11
5.0	732	618	691	14	11	13
Background	157	164	153			

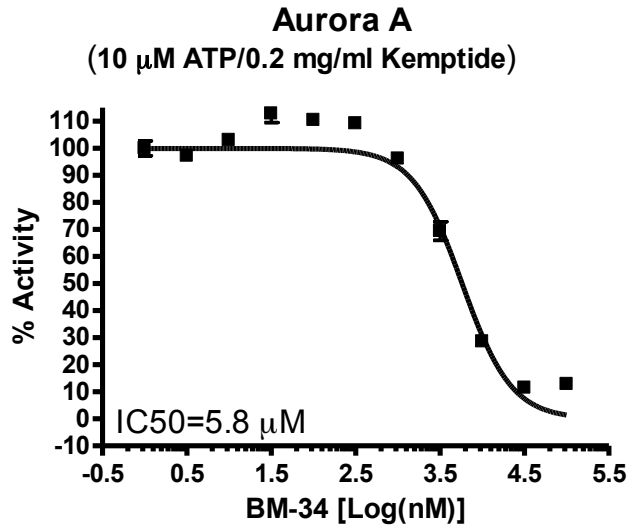


Table S33: Data for the Effect of BM-17 (compound 14) on Kinase Activity

BM-17 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4898	4803	4768	102	100	99
0	4682	4436	4551	97	92	94
1.0	4935	4693	4706	102	97	98
1.5	5329	4628	4728	111	96	98
2.0	4963	4705	4928	103	98	102
2.5	4869	5083	4873	101	106	101
3.0	4192	4158	4478	87	86	93
3.5	3529	3301	3538	73	68	73
4.0	1433	1264	1381	28	25	27
4.5	755	729	782	14	13	14
5.0	727	636	759	13	11	14
Background	98	87	107			

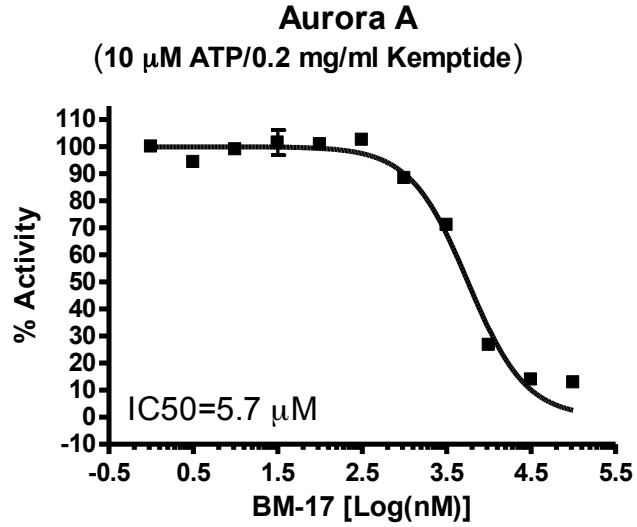


Table S34: Data for the Effect of BM-24 (compound 15) on Kinase Activity

BM-24 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4370	4017	4234	104	95	101
0	3984	4087	4270	95	97	102
1.0	4279	4321	4304	102	103	102
1.5	4400	4424	4509	105	105	107
2.0	4134	4490	4575	98	107	109
2.5	4316	4311	4496	103	103	107
3.0	3883	4284	4117	92	102	98
3.5	2811	3127	2989	66	73	70
4.0	1941	2086	2077	44	48	48
4.5	876	868	916	18	18	19
5.0	577	577	594	11	11	11
Background	138	145	151			

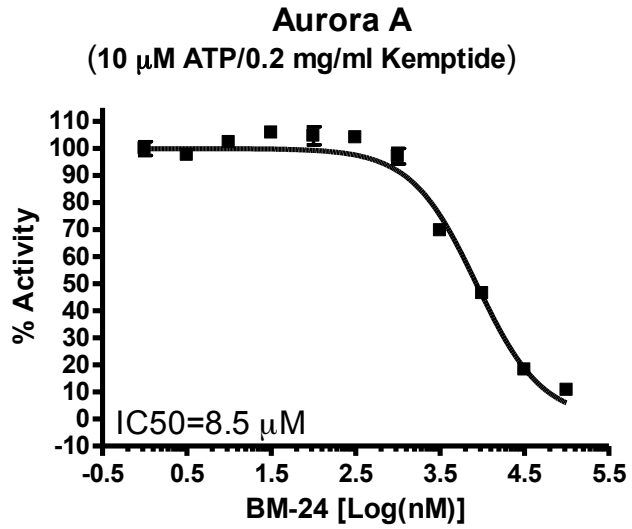


Table S35: Data for the Effect of RS-48 (compound 16) on Kinase Activity

RS-48 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	5639	5518	5756	100	98	102
0	5322	5167	5357	94	91	95
1.0	5072	5097	5543	90	90	98
1.5	4873	5105	5307	86	90	94
2.0	4807	4865	5322	85	86	94
2.5	4763	4987	5286	84	88	94
3.0	4360	4787	4726	77	85	84
3.5	3307	3405	3314	58	60	58
4.0	2601	2406	2630	45	42	46
4.5	3187	3466	3670	56	61	64
5.0	3167	3298	3643	55	58	64
Background	110	100	103			

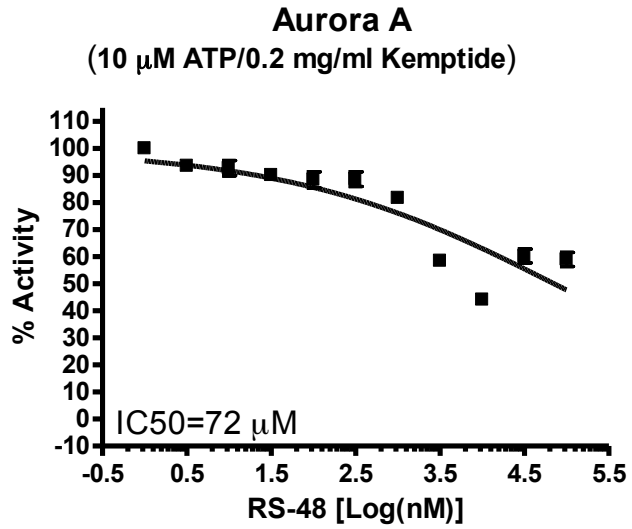


Table S36: Data for the Effect of BM-23 (compound 17) on Kinase Activity

BM-23 (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4863	4877	5271	97	97	105
0	4998	4727	4671	100	94	93
1.0	4852	4880	4833	97	97	97
1.5	5131	4948	5289	103	99	106
2.0	4851	5011	4906	97	100	98
2.5	5093	4820	4740	102	96	95
3.0	3856	4095	3994	77	81	79
3.5	3297	3208	3170	65	63	63
4.0	2374	2142	2242	46	42	44
4.5	2130	2031	2019	41	39	39
5.0	1738	1784	1649	34	34	32
Background	93	95	89			

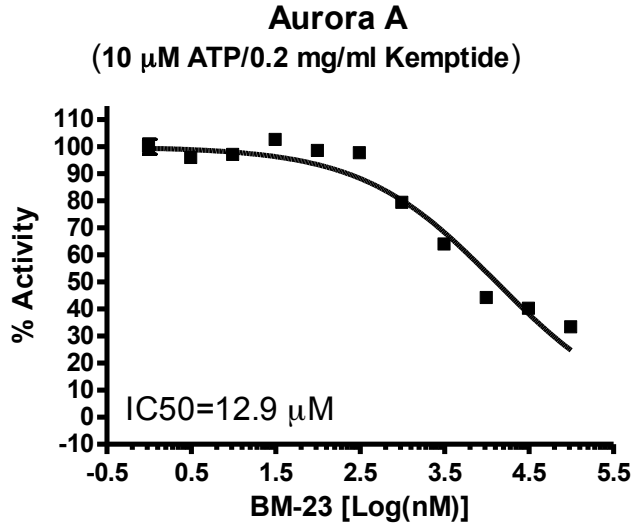


Table S37: Data for the Effect of SZ-34 (compound 18) on Kinase Activity

SZ-34 (Log [nM])	Aurora A Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	6175	5774	5749	105	98	97
0	6502	5506	6122	110	93	104
1.0	6071	5505	5958	103	93	101
1.5	6174	5661	6189	105	96	105
2.0	6071	5522	5887	103	93	100
2.5	5338	5074	5472	90	86	93
3.0	4583	4351	5029	77	73	85
3.5	3037	2695	2850	51	45	47
4.0	1970	1823	1902	32	30	31
4.5	1784	1589	1644	29	26	26
5.0	1824	1589	1623	30	26	26
Background	104	109	127			

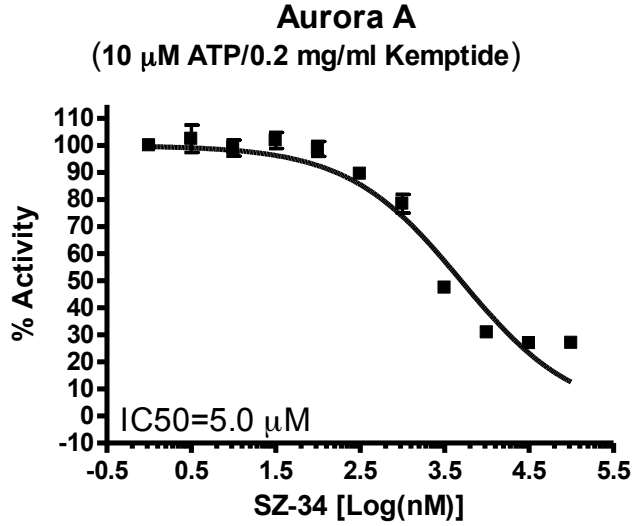
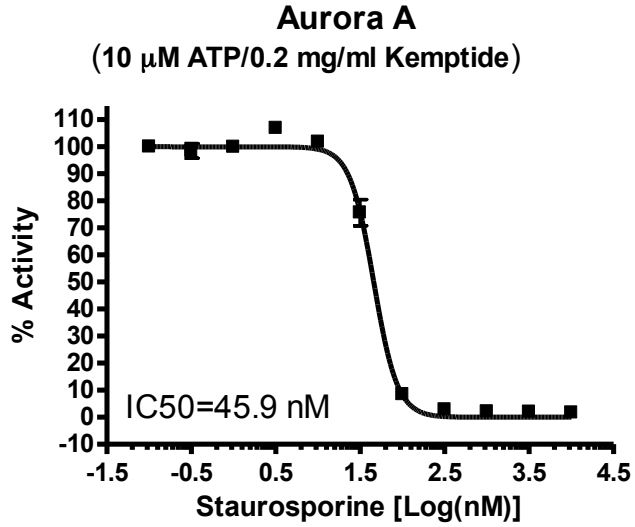


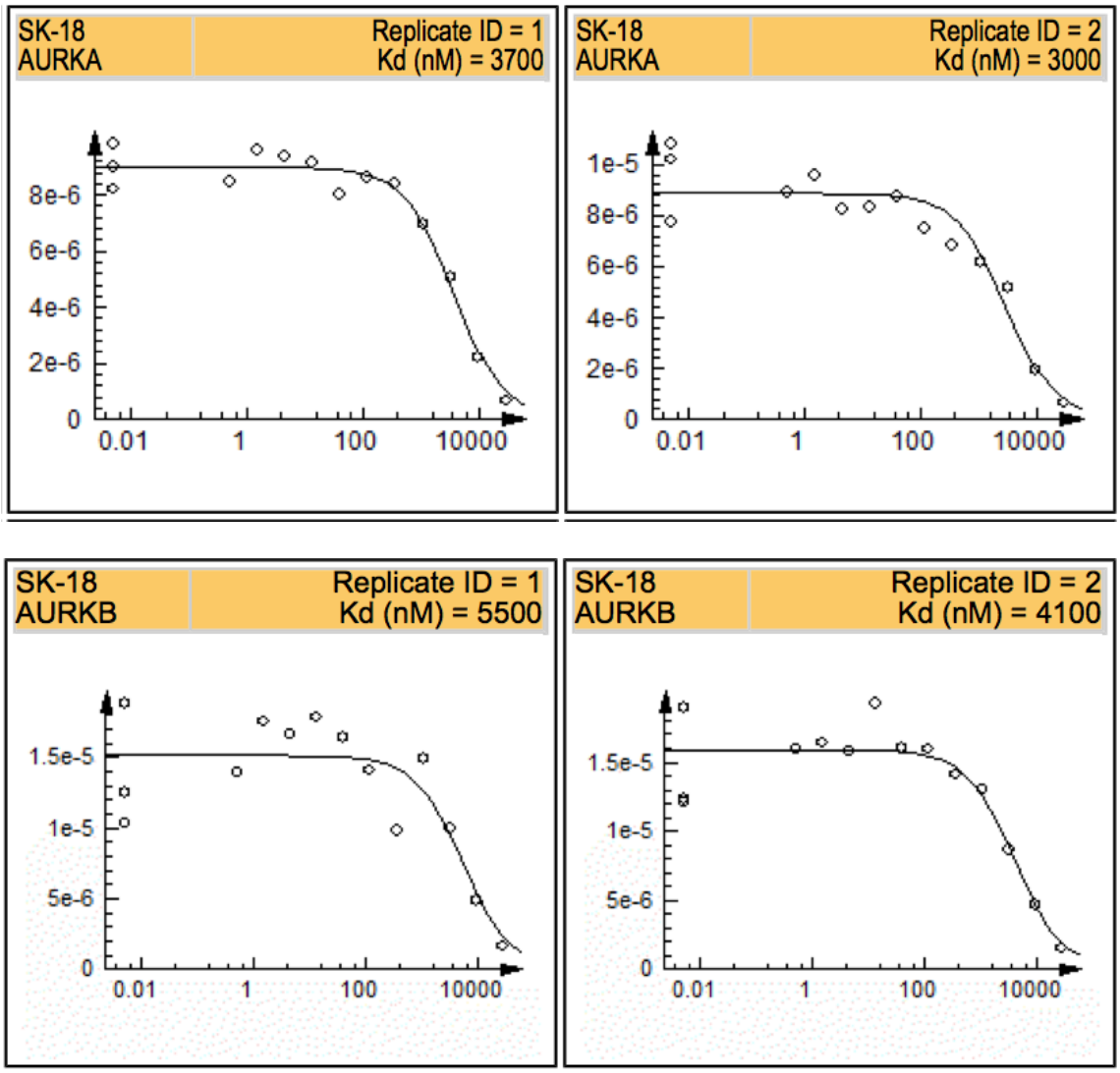
Table S38: Data for the Effect of Staurosporine on AURKA Activity

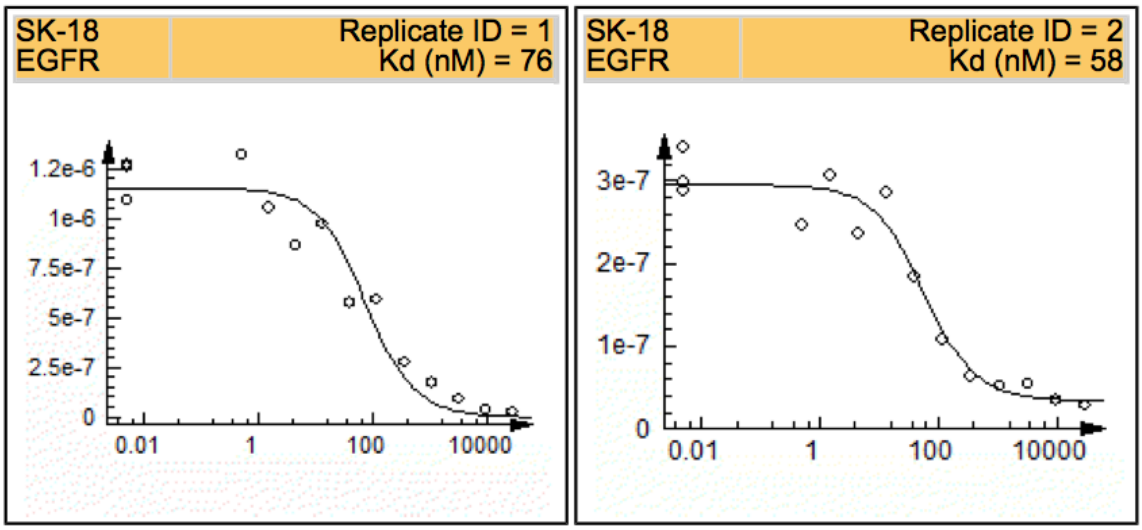
Staurosporine (Log [nM])	AuroraA Activity Luminescence			% Activity		
	Set1	Set2	Set3	Set1	Set2	Set3
No Compound	4725	4805	5039	97	99	104
-1.0	4868	4529	4954	100	93	102
-0.5	4781	4837	4938	98	100	102
0	5302	4980	5271	109	103	109
1.0	4961	4893	4971	102	101	102
1.5	3565	3380	4147	73	69	85
2.0	484	544	472	8	9	8
2.5	232	239	224	3	3	3
3.0	178	183	227	2	2	3
3.5	194	185	204	2	2	2
4.0	179	176	178	2	2	2
Background	102	90	96			



Binding Affinities for EGFR, AURKA and AURKB

The assay was performed externally at DiscoverX Corporation using a competition binding assay that quantitatively measures the ability of a compound to compete with an immobilized, active-site directed ligand for target kinases AURKA, AURKB and EGFR.[23] The assay is performed by combining three components: DNA-tagged kinase; immobilized ligand; and a test compound. The ability of the test compound to compete with the immobilized ligand was measured via quantitative PCR of the DNA tag. An 11-point 3-fold serial dilution of each test compound was prepared in 100% DMSO at 100x final test concentration and subsequently diluted to 1x in the assay (final DMSO concentration = 1%). Compound Kds were determined using a compound top concentration = 30,000 nM. If the initial Kd determined was < 0.5 nM (the lowest concentration tested), the measurement was repeated with a serial dilution starting at a lower top concentration. Binding constants (Kds) were calculated with a standard dose-response curve using the Hill equation.




SK-18
EGFR
Replicate ID = 1
Kd (nM) = 76
1.2e-6
1e-6
7.5e-7
5e-7
2.5e-7
0
0.01
1
100
10000
SK-18
EGFR
Replicate ID = 2
Kd (nM) = 58
3e-7
2e-7
1e-7
0
0.01
1
100
10000