

Novel 11-substituted ellipticines as potent anticancer agents with divergent activity against cancer cells

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Figures S1-S3 ¹H NMRs of relevant compounds

Figure S4 Three-fold dilution topoisomerase II inhibition assay of compounds **13** and **16**

Figure S5-S10 One dose NCI 60 cancer cell growth data (10 μ M)

Figure S11-S13 Five dose NCI 60 cancer cell growth data with GI50, TGI and LC50 data for compound **11**

Figure S14-S16 Five dose NCI 60 cancer cell growth data with GI50, TGI and LC50 data for compound **13**

Figure S17: COMPARE Analysis data for compound **13** in direct comparison with SCH1473759 (NSC761691), an Aurora kinase inhibitor.

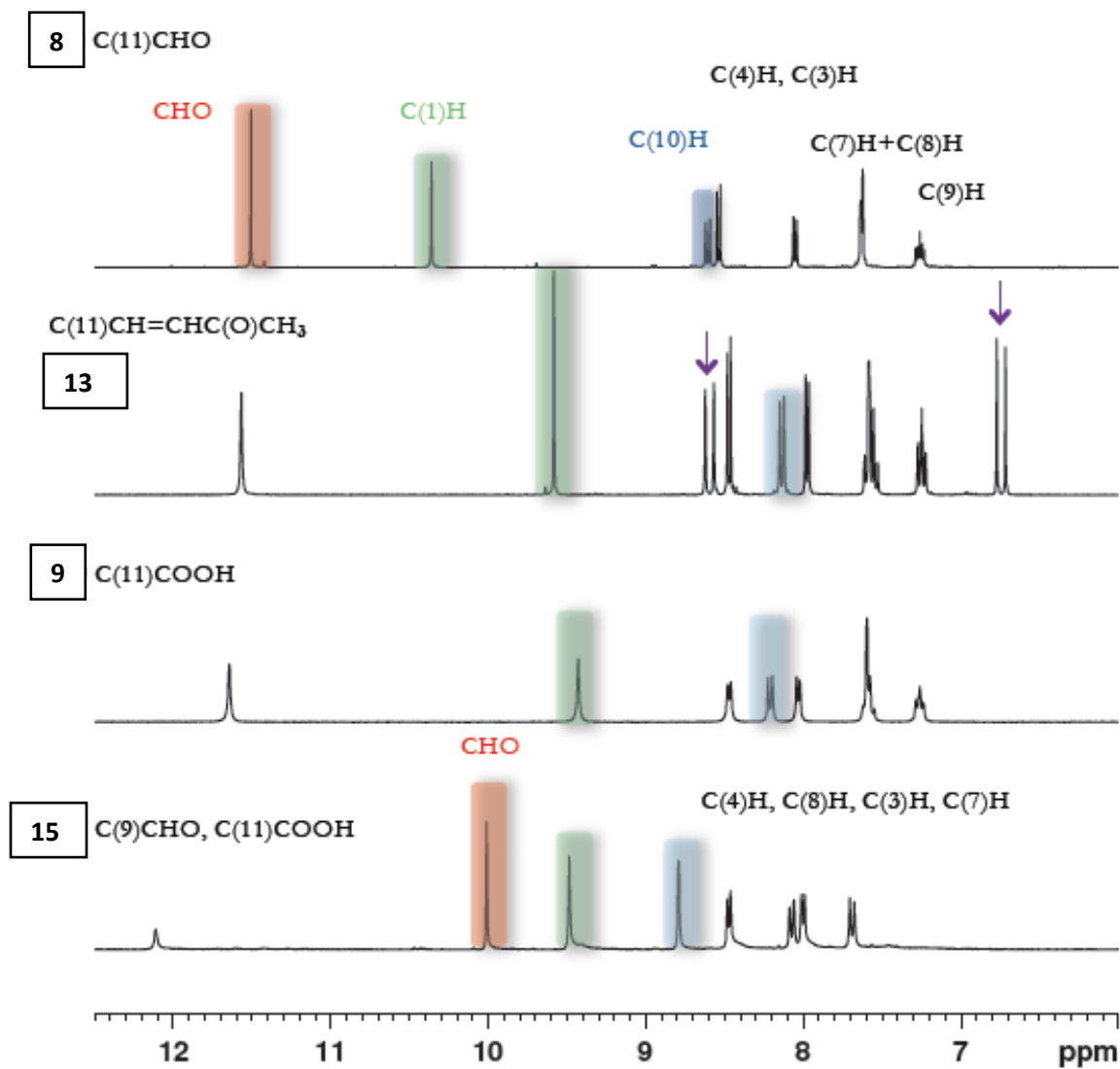


Figure S1: Stacked ¹H NMR plots of the aromatic regions of 11-substituted Ellipticines 8, 9, 13, and 15 measured in DMSO-*d*₆ at 300MHz

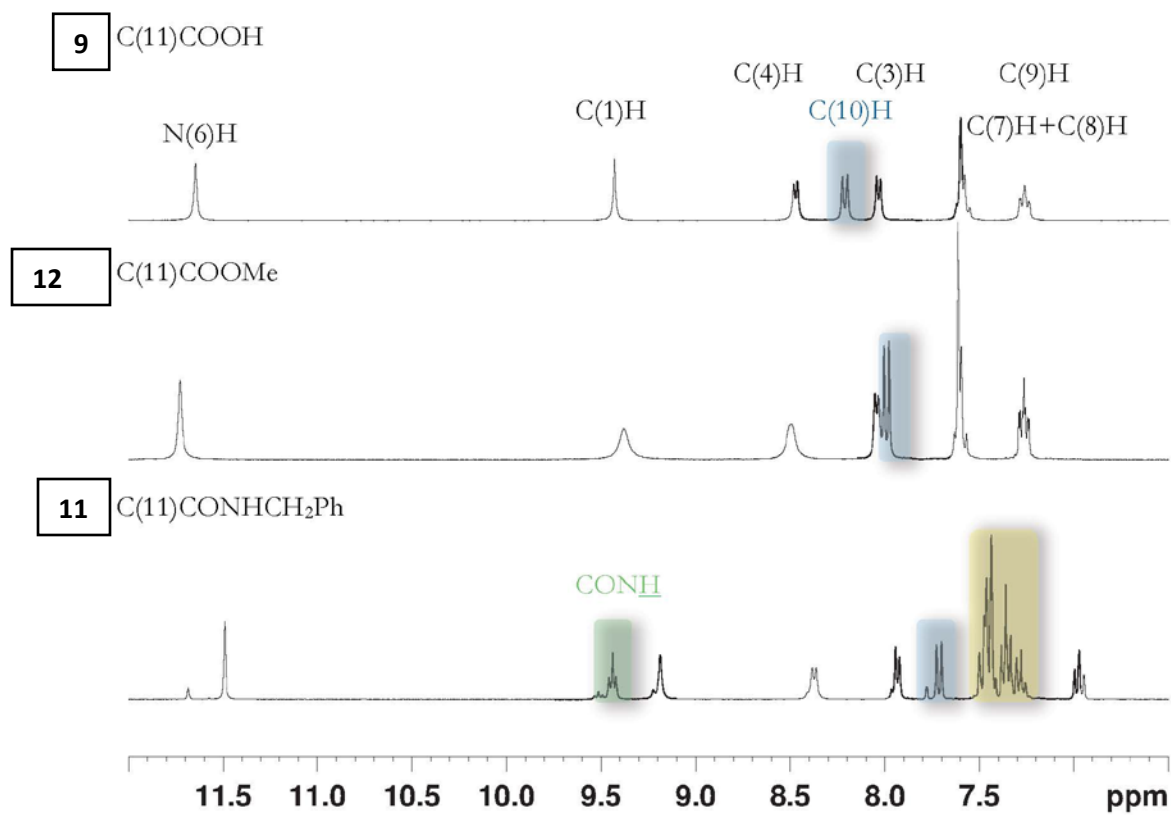


Figure S2: Stacked ¹H NMR plots of the aromatic regions of 11-substituted Ellipticines 9, 11 and 12 measured in DMSO-*d*₆ at 300MHz

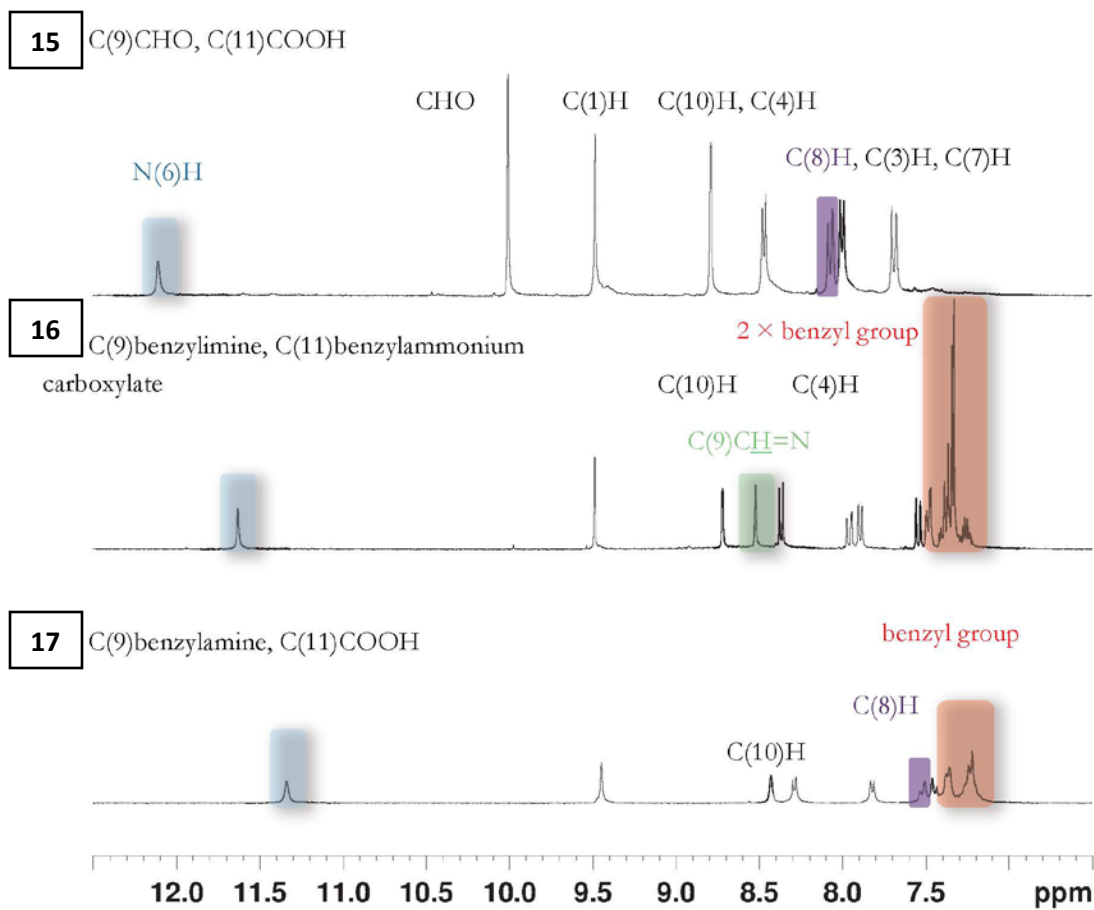


Figure S3: Stacked ^1H NMR plots of the aromatic regions of 11-substituted Ellipticines 15, 16 and 17 measured in $\text{DMSO-}d_6$ at 300MHz

Figure S4: Three fold dilution assay for compound 13 (lanes 1-3; 100-1uM) and 16 (lanes 4-6; 100-1uM); A & B are positive and negative control respectively.

μM : 100 10 1 100 10 1
A B 1 2 3 4 5 6

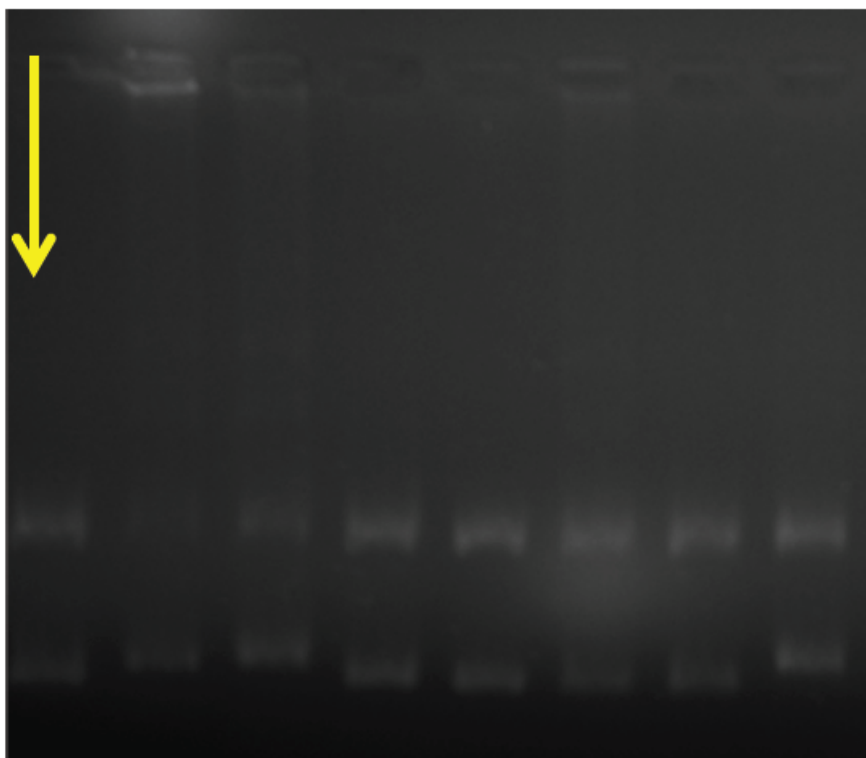


Figure S5: One dose assay (10μM) NCI 60 cell lines growth data for compound 9

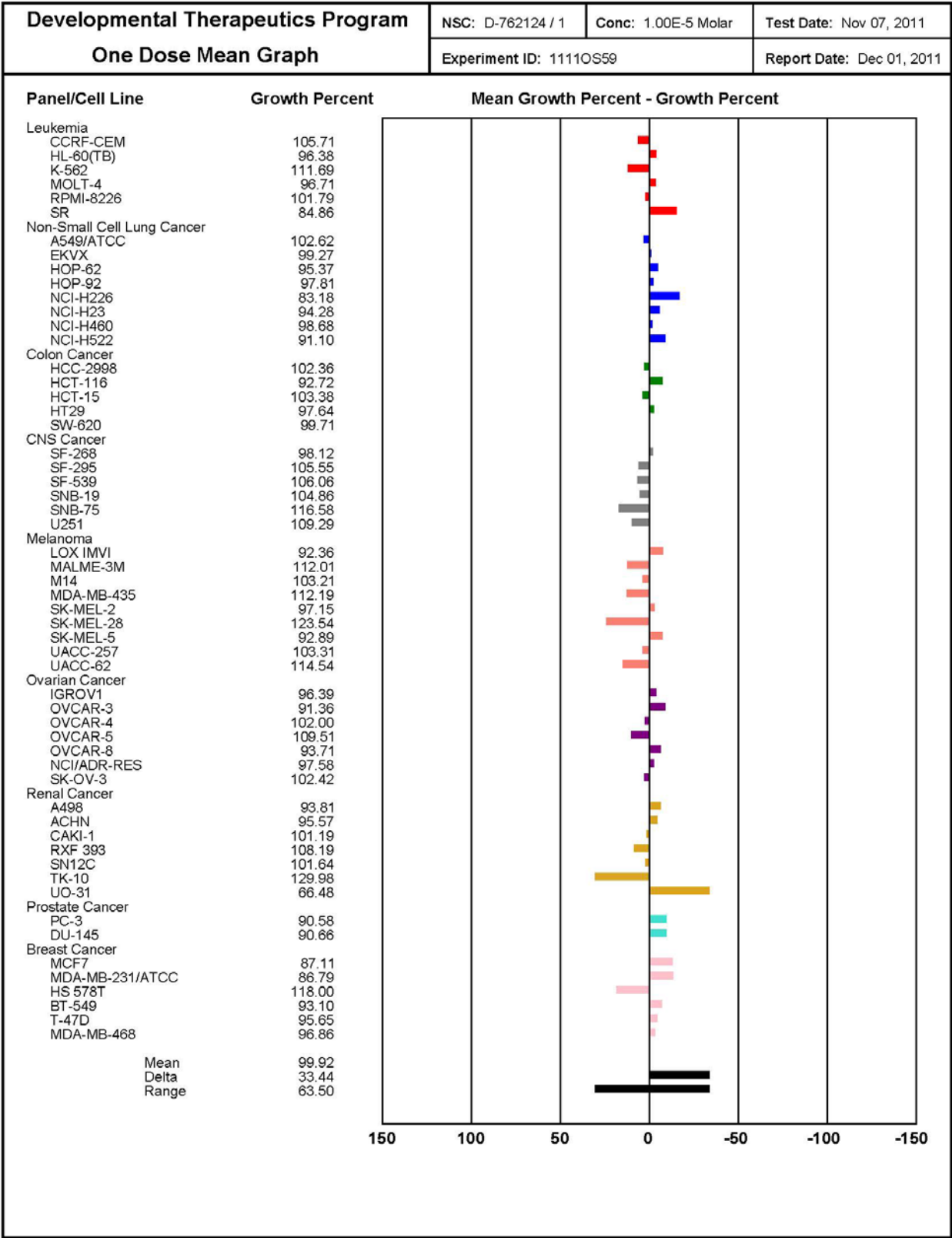


Figure S6: One dose assay (10μM) NCI 60 cell lines growth data for compound 11

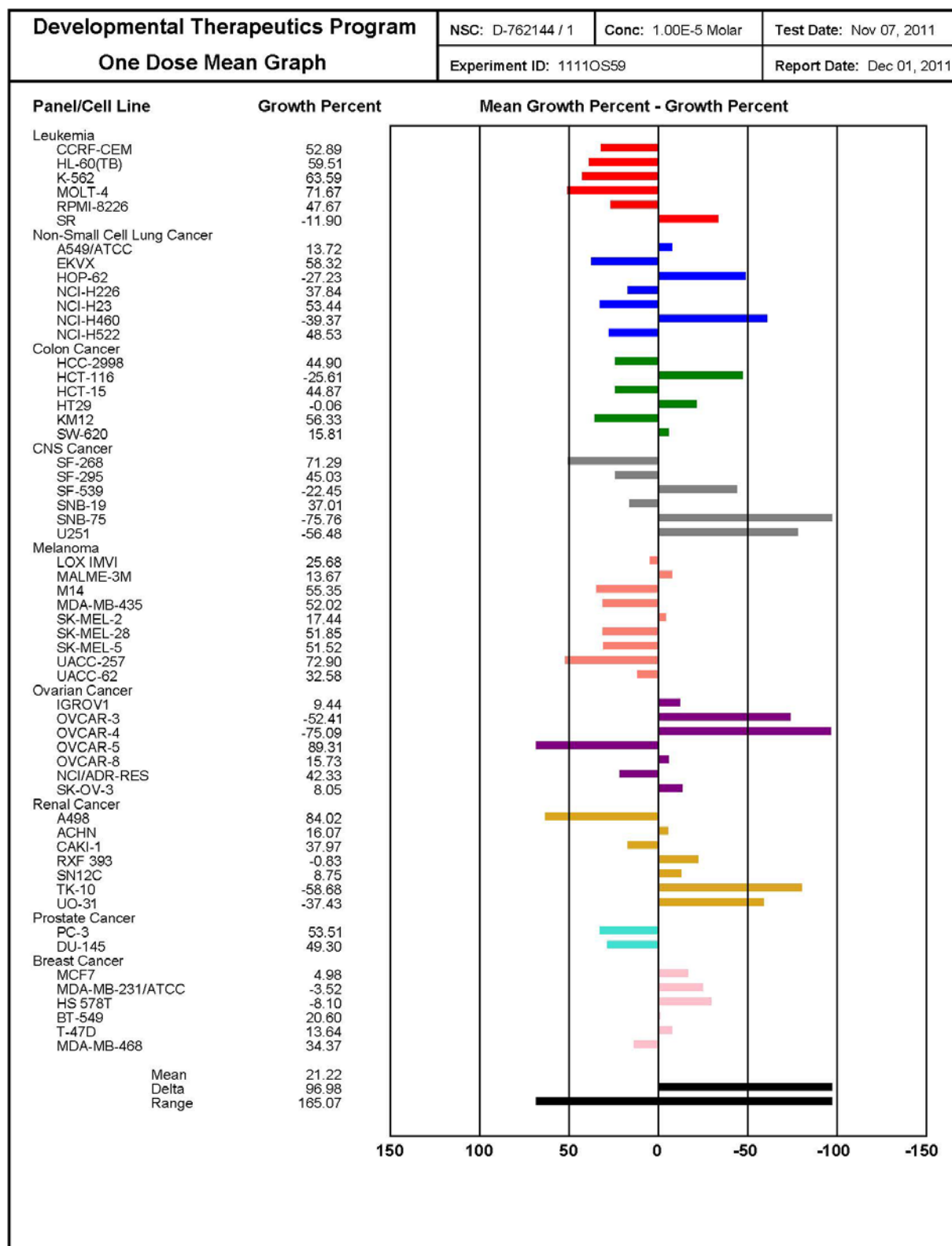


Figure S7: One dose assay (10µM) NCI 60 cell lines growth data for compound 13

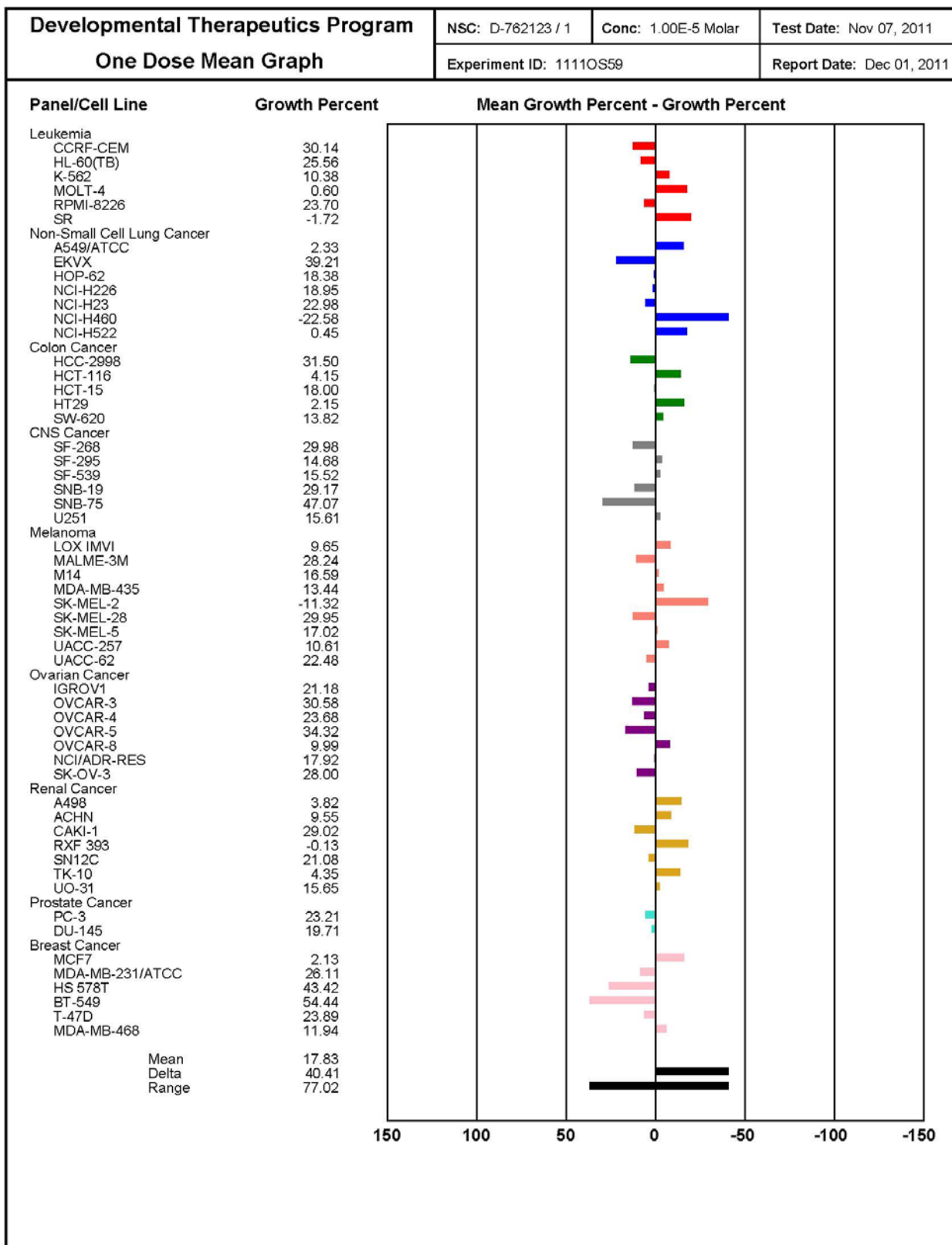


Figure S8: One dose assay (10µM) NCI 60 cell lines growth data for compound 15

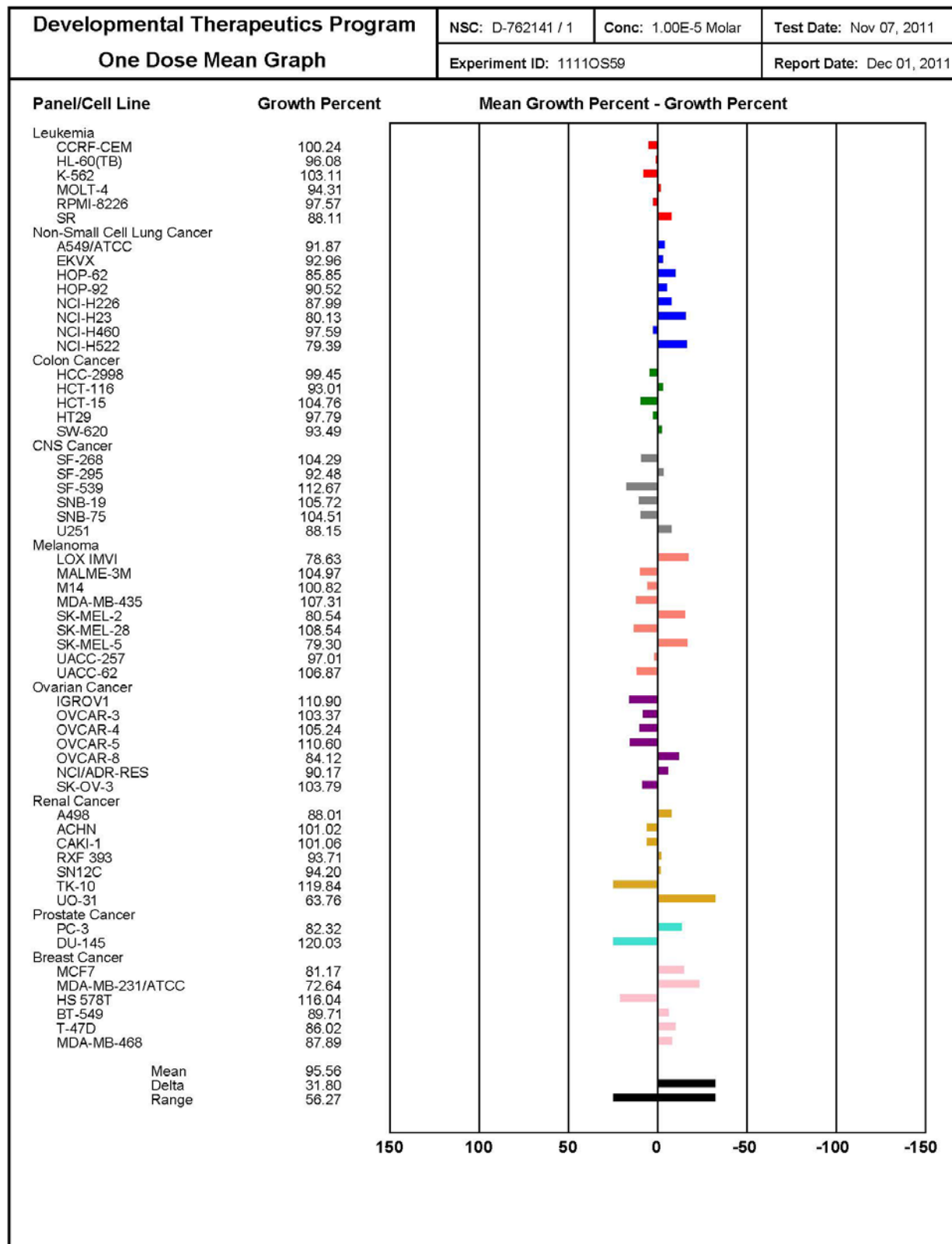


Figure S9: One dose assay (10 μ M) NCI 60 cell lines growth data for compound 16

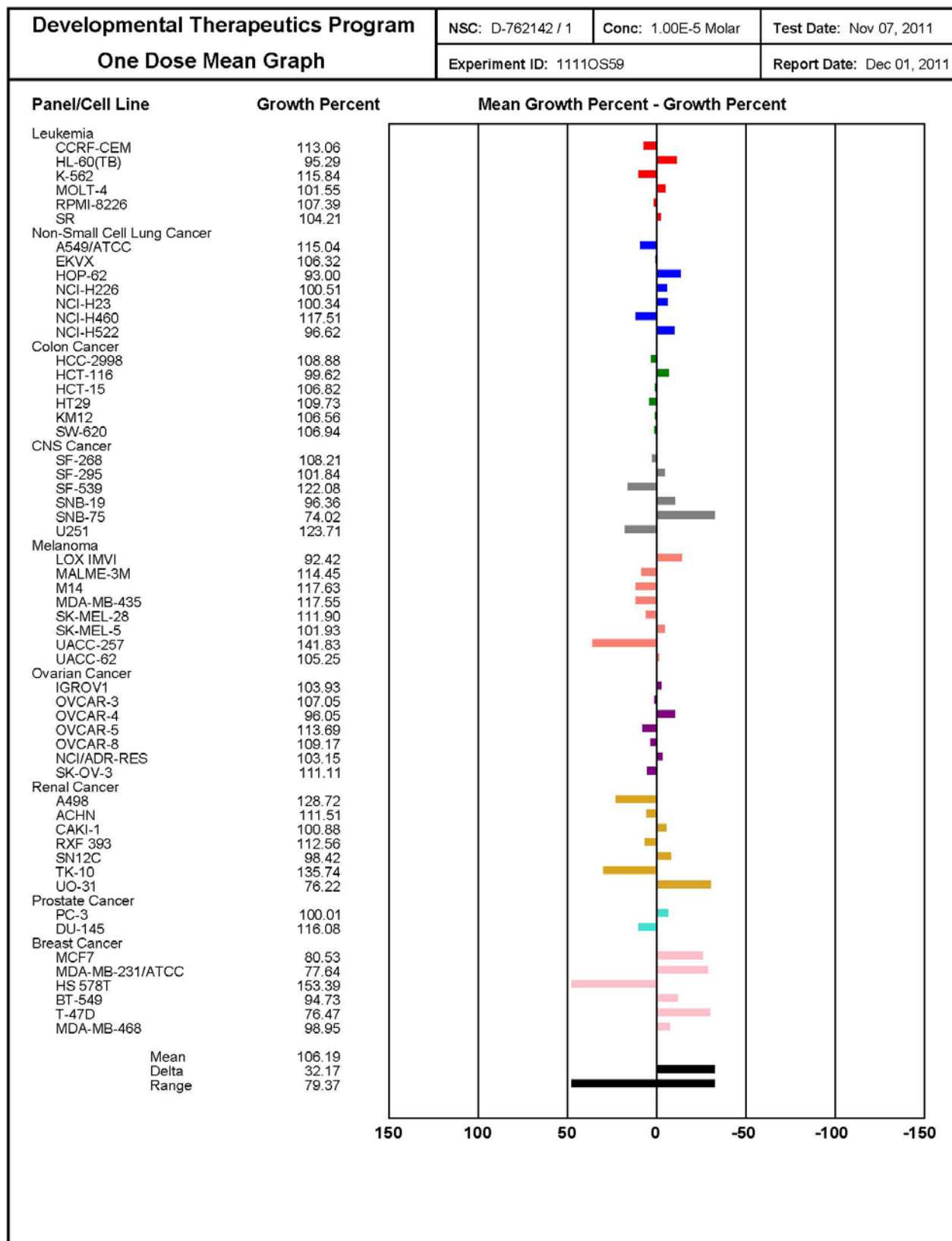


Figure S10: One dose assay (10µM) NCI 60 cell lines growth data for compound 17

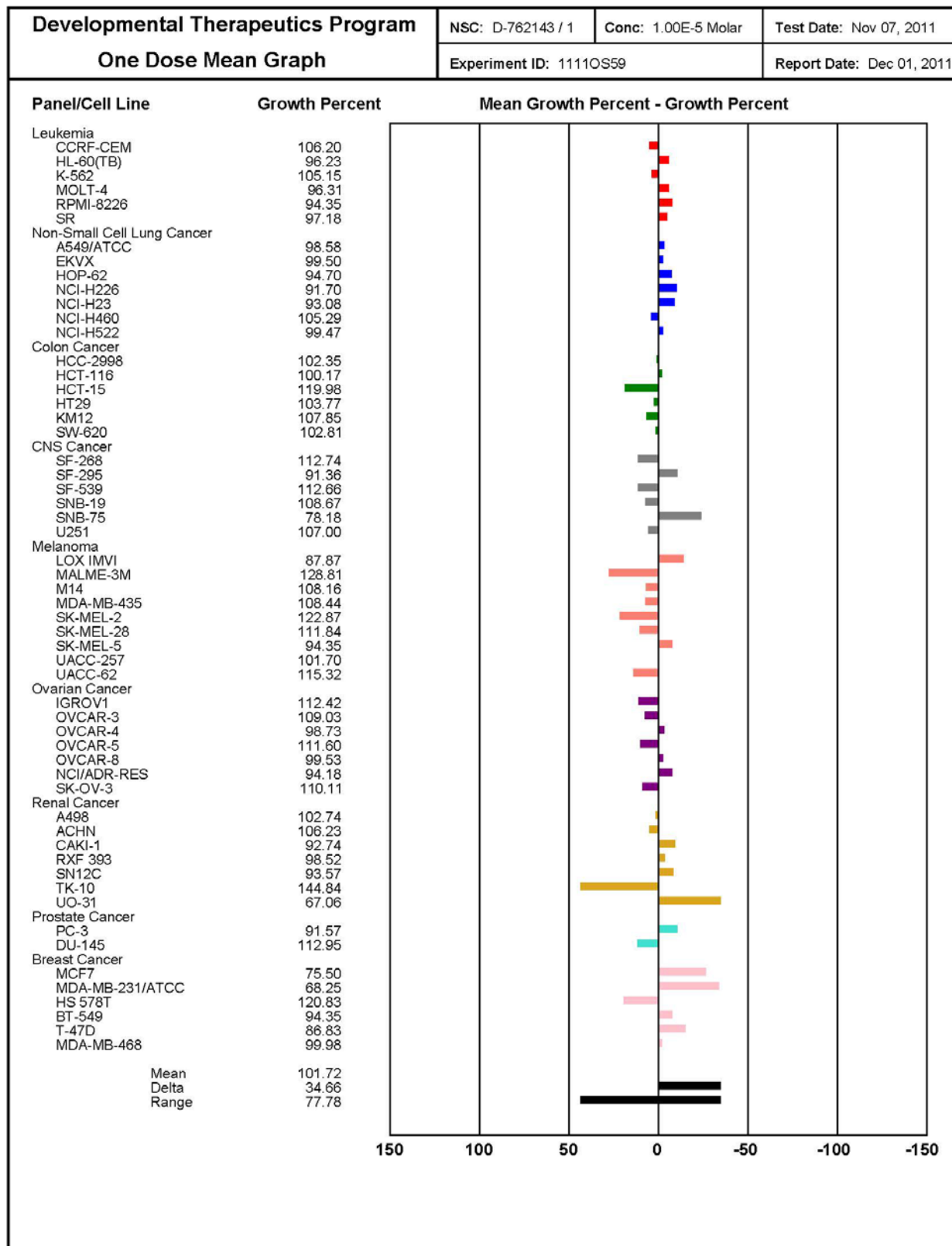


Figure S11: Five Dose Assay data graph from NCI 60 cell lines growth for compound 11

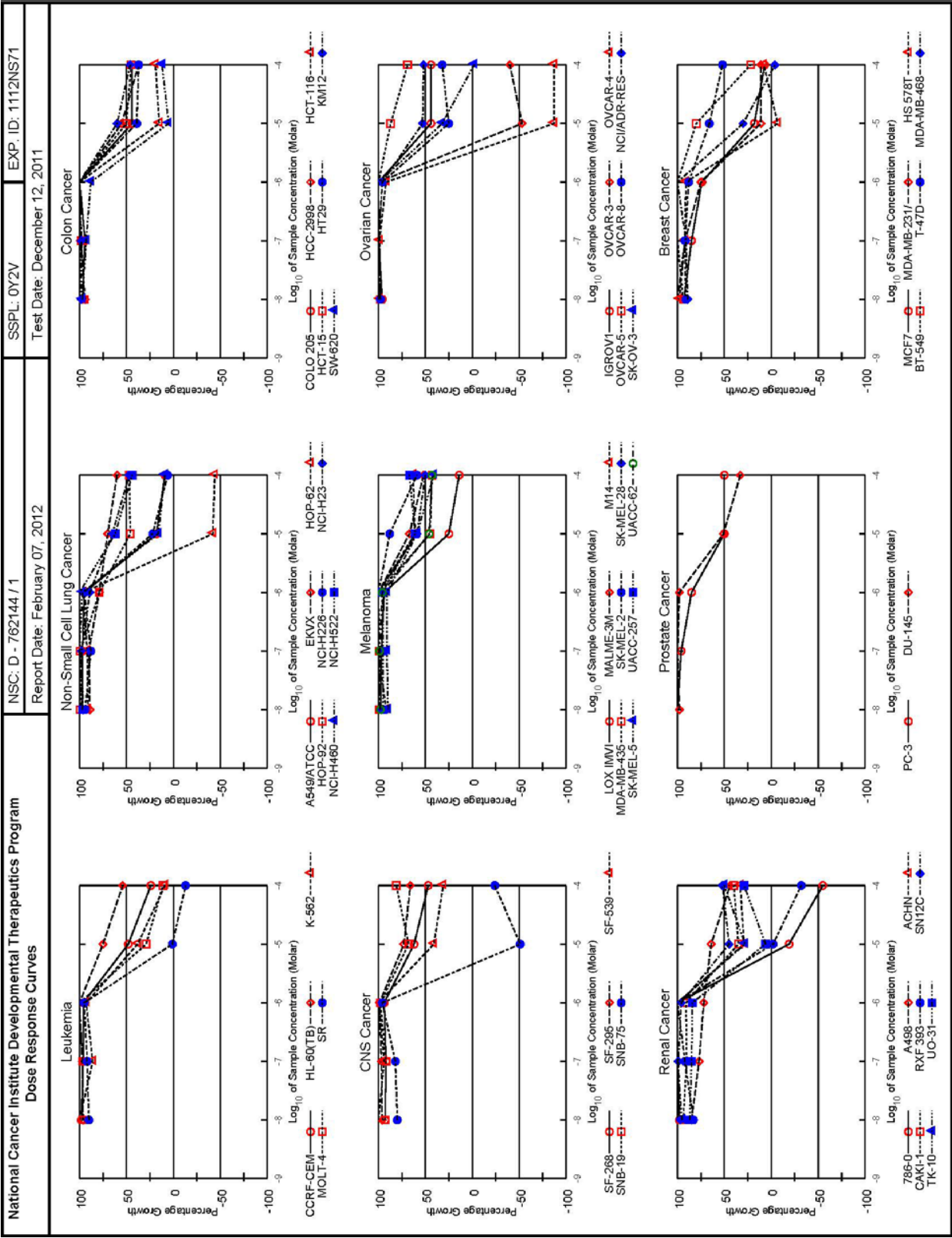


Figure S12: Complete Five Dose Assay data from NCI 60 cell lines for compound 11

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results																	
NSC : D - 762144 / 1			Experiment ID : 1112NS71						Test Type : 08				Units : Molar				
Report Date : February 07, 2012			Test Date : December 12, 2011						QNS :				MC :				
COMI : CM-5-278-4-2 (111980)			Stain Reagent : SRB Dual-Pass Related						SSPL : 0Y2V								
Panel/Cell Line	Time Zero	Ctrl	Log10 Concentration						Percent Growth						GI50	TGI	LC50
			Mean Optical Densities														
			-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0					
Leukemia																	
CCRF-CEM	0.438	2.023	1.985	1.958	1.961	1.199	0.811	98	96	96	48	24	9.08E-6	> 1.00E-4	> 1.00E-4		
HL-60(TB)	0.860	2.718	2.644	2.667	2.942	2.257	1.864	96	97	112	75	54	> 1.00E-4	> 1.00E-4	> 1.00E-4		
K-562	0.167	1.357	1.415	1.192	1.277	0.621	0.280	105	86	93	38	9	6.10E-6	> 1.00E-4	> 1.00E-4		
MOLT-4	0.461	1.988	1.945	1.936	2.078	0.910	0.635	97	97	106	29	11	5.38E-6	> 1.00E-4	> 1.00E-4		
SR	0.316	1.902	1.744	1.770	1.825	0.337	0.276	90	92	95	1	-13	3.03E-6	1.24E-5	> 1.00E-4		
Non-Small Cell Lung Cancer																	
A549/ATCC	0.314	1.552	1.513	1.517	1.494	0.533	0.420	97	97	95	18	9	3.83E-6	> 1.00E-4	> 1.00E-4		
EKVX	0.576	1.271	1.196	1.199	1.123	1.066	0.991	89	90	79	70	60	> 1.00E-4	> 1.00E-4	> 1.00E-4		
HOP-62	0.303	0.745	0.705	0.708	0.727	0.175	0.169	91	92	96	-42	-44	2.15E-6	4.94E-6	> 1.00E-4		
HOP-92	0.988	1.431	1.426	1.428	1.338	1.191	1.195	99	99	79	46	47	7.49E-6	> 1.00E-4	> 1.00E-4		
NCI-H226	0.638	1.286	1.248	1.207	1.257	0.784	0.678	94	88	95	22	6	4.19E-6	> 1.00E-4	> 1.00E-4		
NCI-H23	0.861	2.362	2.310	2.327	2.203	1.843	1.564	96	98	89	65	47	6.75E-5	> 1.00E-4	> 1.00E-4		
NCI-H460	0.285	2.455	2.519	2.548	2.382	0.622	0.470	103	104	97	16	9	3.76E-6	> 1.00E-4	> 1.00E-4		
NCI-H522	0.678	1.462	1.439	1.460	1.505	1.162	1.024	97	100	105	62	44	4.64E-5	> 1.00E-4	> 1.00E-4		
Colon Cancer																	
COLO 205	0.279	0.969	0.949	0.931	0.997	0.580	0.585	97	94	104	44	44	7.84E-6	> 1.00E-4	> 1.00E-4		
HCC-2998	0.591	1.723	1.654	1.715	1.756	1.216	1.010	94	99	103	55	37	1.93E-5	> 1.00E-4	> 1.00E-4		
HCT-116	0.219	1.617	1.624	1.651	1.646	0.422	0.486	100	102	102	15	19	3.93E-6	> 1.00E-4	> 1.00E-4		
HCT-15	0.292	1.980	1.896	1.947	2.048	1.133	1.055	95	98	104	50	45	9.91E-6	> 1.00E-4	> 1.00E-4		
HT29	0.198	1.156	1.200	1.222	1.235	0.570	0.551	105	107	108	39	37	6.90E-6	> 1.00E-4	> 1.00E-4		
KM12	0.493	2.113	2.077	2.081	2.115	1.458	1.239	98	98	100	60	46	5.12E-5	> 1.00E-4	> 1.00E-4		
SW-620	0.244	1.693	1.654	1.590	1.518	0.313	0.420	97	93	88	5	12	2.86E-6	> 1.00E-4	> 1.00E-4		
CNS Cancer																	
SF-268	0.496	1.653	1.577	1.564	1.585	1.218	1.046	93	92	94	62	47	6.78E-5	> 1.00E-4	> 1.00E-4		
SF-295	0.819	2.588	2.521	2.535	2.566	2.116	1.979	96	97	99	73	66	> 1.00E-4	> 1.00E-4	> 1.00E-4		
SF-539	0.695	1.786	1.786	1.715	1.814	1.144	1.039	100	94	103	41	31	7.17E-6	> 1.00E-4	> 1.00E-4		
SNB-19	0.650	1.915	1.826	1.817	1.888	1.509	1.673	93	92	98	68	81	> 1.00E-4	> 1.00E-4	> 1.00E-4		
SNB-75	0.735	1.242	1.141	1.150	1.221	0.358	0.560	80	82	96	-51	-24	2.05E-6	4.48E-6	.		
Melanoma																	
LOX IMVI	0.255	1.633	1.612	1.590	1.551	0.606	0.445	98	97	94	25	14	4.38E-6	> 1.00E-4	> 1.00E-4		
MALME-3M	0.588	1.774	1.772	1.842	1.786	1.383	1.201	100	106	101	67	52	> 1.00E-4	> 1.00E-4	> 1.00E-4		
M14	0.415	1.396	1.319	1.447	1.450	1.016	1.038	92	105	105	61	63	> 1.00E-4	> 1.00E-4	> 1.00E-4		
MDA-MB-435	0.473	1.999	1.979	1.982	2.027	1.153	1.132	99	99	102	45	43	8.02E-6	> 1.00E-4	> 1.00E-4		
SK-MEL-2	0.861	1.768	1.789	1.824	1.850	1.663	1.395	102	106	109	88	59	> 1.00E-4	> 1.00E-4	> 1.00E-4		
SK-MEL-28	0.507	1.332	1.309	1.377	1.334	0.994	0.922	97	106	100	59	50	> 1.00E-4	> 1.00E-4	> 1.00E-4		
SK-MEL-5	0.523	2.400	2.220	2.241	2.238	1.627	1.286	90	91	91	59	41	3.05E-5	> 1.00E-4	> 1.00E-4		
UACC-257	0.550	1.294	1.257	1.258	1.267	1.002	1.049	95	95	96	61	67	> 1.00E-4	> 1.00E-4	> 1.00E-4		
UACC-62	0.579	2.143	2.119	2.120	2.080	1.306	1.250	98	99	96	46	43	8.49E-6	> 1.00E-4	> 1.00E-4		
Ovarian Cancer																	
IGROV1	0.590	1.333	1.305	1.335	1.368	0.920	0.914	96	100	105	44	44	8.07E-6	> 1.00E-4	> 1.00E-4		
OVCAR-3	0.517	1.343	1.351	1.386	1.422	0.245	0.310	101	105	110	-53	-40	2.33E-6	4.74E-6	.		
OVCAR-4	0.534	1.091	1.086	1.083	1.045	0.068	0.070	99	99	92	-87	-87	1.71E-6	3.25E-6	6.19E-6		
OVCAR-5	0.597	1.539	1.517	1.584	1.610	1.417	1.246	98	105	108	87	69	> 1.00E-4	> 1.00E-4	> 1.00E-4		
OVCAR-8	0.417	1.796	1.764	1.809	1.739	0.757	0.856	98	101	96	25	32	4.41E-6	> 1.00E-4	> 1.00E-4		
NCI/ADR-RES	0.532	1.782	1.807	1.792	1.738	1.195	1.184	102	101	96	53	52	> 1.00E-4	> 1.00E-4	> 1.00E-4		
SK-OV-3	0.487	1.113	1.116	1.123	1.130	0.690	0.476	100	102	103	32	-2	5.62E-6	8.55E-5	> 1.00E-4		
Renal Cancer																	
786-O	0.834	2.295	2.263	2.322	2.378	0.673	0.375	98	102	106	-19	-55	2.79E-6	7.00E-6	7.20E-5		
A498	1.307	1.779	1.709	1.670	1.647	1.611	1.515	85	77	72	64	44	5.05E-5	> 1.00E-4	> 1.00E-4		
ACHN	0.312	1.332	1.385	1.380	1.442	0.606	0.646	105	105	111	29	33	5.51E-6	> 1.00E-4	> 1.00E-4		
CAKI-1	0.638	1.954	1.880	1.820	1.835	1.099	1.166	94	90	91	35	40	5.39E-6	> 1.00E-4	> 1.00E-4		
RXF 393	0.656	1.103	1.027	1.069	1.123	0.646	0.445	83	92	105	-2	-32	3.27E-6	9.66E-6	> 1.00E-4		
SN12C	0.466	1.951	1.906	1.936	1.889	1.127	1.240	97	99	96	45	52	.	> 1.00E-4	> 1.00E-4		
TK-10	0.738	1.336	1.308	1.340	1.524	0.906	1.039	95	101	131	28	50	.	> 1.00E-4	> 1.00E-4		
UO-31	0.555	1.769	1.606	1.590	1.577	0.625	0.911	87	85	84	6	29	2.73E-6	> 1.00E-4	> 1.00E-4		
Prostate Cancer																	
PC-3	0.513	1.957	1.962	1.896	1.746	1.230	1.231	100	96	85	50	50	9.76E-6	> 1.00E-4	> 1.00E-4		
DU-145	0.381	1.272	1.255	1.301	1.257	0.834	0.675	98	103	98	51	33	1.12E-5	> 1.00E-4	> 1.00E-4		
Breast Cancer																	
MCF7	0.268	1.547	1.452	1.355	1.219	0.499	0.361	93	85	74	18	7	2.71E-6	> 1.00E-4	> 1.00E-4		
MDA-MB-231/ATCC	0.490	1.150	1.171	1.097	0.983	0.560	0.561	103	92	75	11	11	2.43E-6	> 1.00E-4	> 1.00E-4		
HS 578T	1.204	1.930	1.914	1.869	1.863	1.119	1.261	98	92	91	-7	8	2.61E-6	.	> 1.00E-4		
BT-549	0.840	1.463	1.427	1.528	1.611	1.337	0.980	94	110	124	80	22	3.31E-5	> 1.00E-4	> 1.00E-4		
T-47D	0.624	1.623	1.536	1.540	1.503	1.288	1.148	91	92	88	66	52	> 1.00E-4	> 1.00E-4	> 1.00E-4		
MDA-MB-468	0.549	0.844	0.811	0.816	0.888	0.638	0.526	89	91	115	30	-4	5.82E-6	7.54E-5	> 1.00E-4		

Figure S13: Complete Five Dose Assay data from NCI 60 cell lines for compound 11

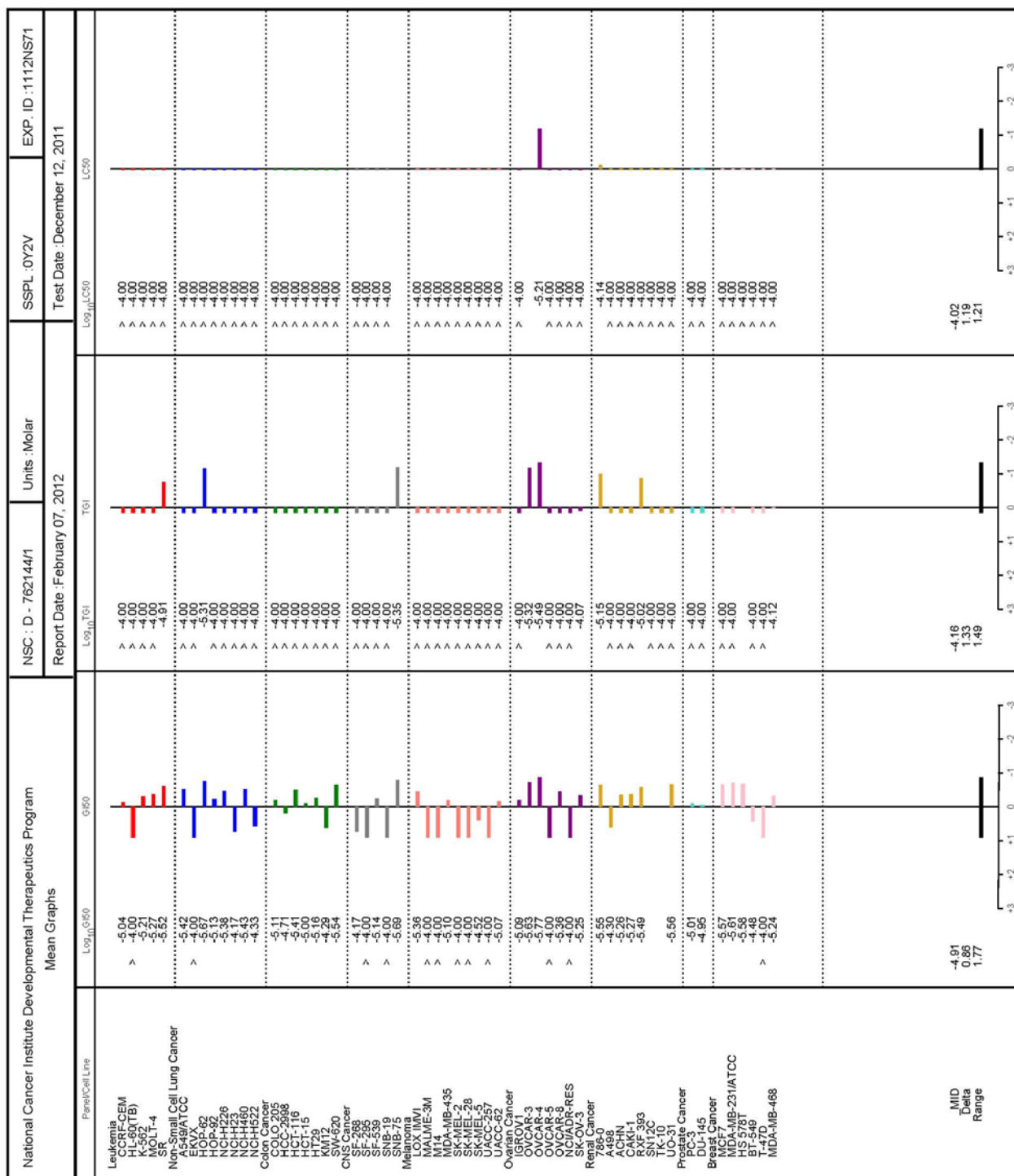


Figure S14: Five Dose Assay data graph from NCI 60 cell lines for compound 13

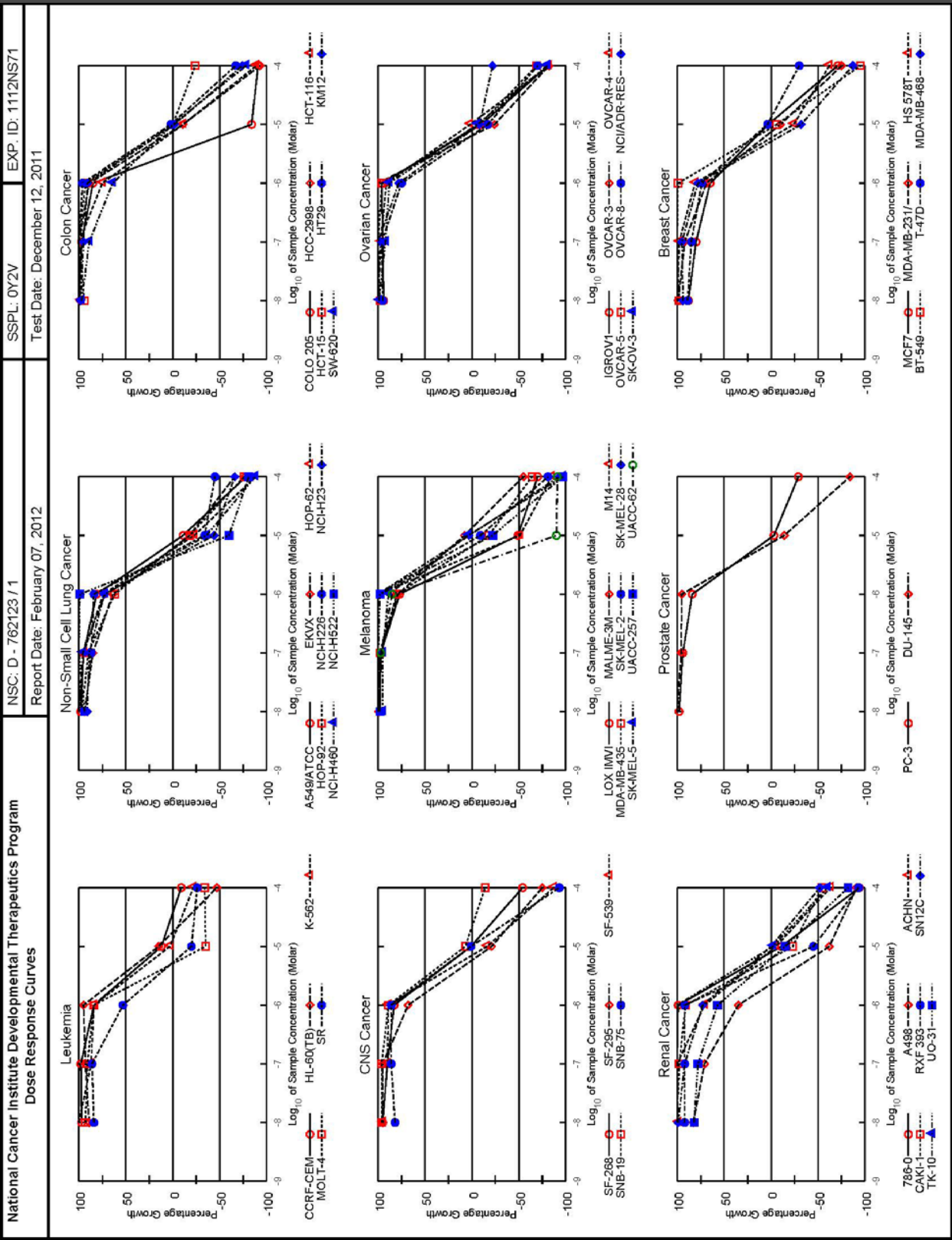


Figure S15: Complete Five Dose Assay data from NCI 60 cell lines for compound 13

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results															
NSC : D - 762123 / 1			Experiment ID : 1112NS71						Test Type : 08			Units : Molar			
Report Date : February 07, 2012			Test Date : December 12, 2011						QNS :			MC :			
COMI : CM3-112-5 (111402)			Stain Reagent : SRB Dual-Pass Related						SSPL : 0Y2V						
Log10 Concentration															
Panel/Cell Line	Time Zero	Ctrl	Mean Optical Densities					Percent Growth					GI50	TGI	LC50
			-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0			
Leukemia															
CCRF-CEM	0.438	2.083	2.030	2.052	1.821	0.643	0.398	97	98	84	12	-9	2.99E-6	3.74E-5	> 1.00E-4
HL-60(TB)	0.860	2.628	2.434	2.502	2.537	1.121	0.460	89	93	95	15	-47	3.63E-6	1.74E-5	> 1.00E-4
K-562	0.167	1.390	1.401	1.230	1.193	0.200	0.131	101	87	84	3	-22	2.61E-6	1.28E-5	> 1.00E-4
MOLT-4	0.461	1.879	1.785	1.752	1.652	0.300	0.306	93	91	84	-35	-34	1.93E-6	5.08E-6	> 1.00E-4
SR	0.316	1.791	1.549	1.585	1.105	0.254	0.235	84	86	53	-20	-26	1.12E-6	5.37E-6	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.314	1.418	1.392	1.366	1.207	0.281	0.071	98	95	81	-11	-78	2.17E-6	7.65E-6	3.87E-5
EKVX	0.576	1.239	1.201	1.142	1.000	0.471	0.197	94	85	64	-18	-66	1.48E-6	5.99E-6	4.64E-5
HOP-62	0.303	0.691	0.709	0.670	0.591	0.233	0.037	105	95	74	-23	-88	1.77E-6	5.77E-6	2.60E-5
HOP-92	0.988	1.386	1.374	1.347	1.237	0.815	0.239	97	90	62	-18	-76	1.43E-6	6.04E-6	3.80E-5
NCI-H226	0.638	1.272	1.226	1.191	1.168	0.422	0.353	93	87	84	-34	-45	1.93E-6	5.15E-6	> 1.00E-4
NCI-H23	0.861	2.235	2.117	2.081	1.860	0.482	0.291	91	89	73	-44	-66	1.57E-6	4.20E-6	1.86E-5
NCI-H460	0.285	2.290	2.302	2.215	1.736	0.182	0.035	101	96	72	-36	-88	1.61E-6	4.64E-6	1.85E-5
NCI-H522	0.678	1.392	1.347	1.390	1.383	0.274	0.126	94	100	99	-60	-81	2.03E-6	4.20E-6	8.70E-6
Colon Cancer															
COLO 205	0.279	0.955	0.963	0.935	0.851	0.045	0.024	101	97	85	-84	-91	1.60E-6	3.17E-6	6.28E-6
HCC-2998	0.591	1.600	1.593	1.673	1.492	0.527	0.040	99	107	89	-11	-93	2.47E-6	7.78E-6	2.98E-5
HCT-116	0.219	1.514	1.484	1.607	1.196	0.195	0.025	98	107	75	-11	-89	1.97E-6	7.47E-6	3.18E-5
HCT-15	0.292	1.807	1.723	1.803	1.700	0.291	0.222	94	100	93	.	-24	2.88E-6	9.92E-6	> 1.00E-4
HT29	0.198	1.114	1.112	1.135	1.081	0.216	0.065	100	102	96	2	-67	3.09E-6	1.07E-5	5.61E-5
KM12	0.493	2.032	2.003	1.962	1.891	0.484	0.130	98	95	91	-2	-74	2.76E-6	9.53E-6	4.67E-5
SW-620	0.244	1.548	1.511	1.407	1.076	0.247	0.054	97	89	64	.	-78	1.65E-6	1.01E-5	4.40E-5
CNS Cancer															
SF-268	0.496	1.531	1.483	1.423	1.358	0.506	0.228	95	90	83	1	-54	2.53E-6	1.04E-5	8.41E-5
SF-295	0.819	2.664	2.568	2.563	2.069	0.644	0.207	95	95	68	-21	-75	1.58E-6	5.75E-6	3.43E-5
SF-539	0.695	1.677	1.628	1.578	1.572	0.585	0.090	95	90	89	-16	-87	2.36E-6	7.07E-6	3.02E-5
SNB-19	0.650	1.873	1.829	1.825	1.743	0.737	0.557	96	96	89	7	-14	3.01E-6	2.15E-5	> 1.00E-4
SNB-75	0.735	1.285	1.188	1.209	1.206	0.742	0.049	82	86	86	1	-93	2.65E-6	1.03E-5	3.48E-5
Melanoma															
LOX IMVI	0.255	1.506	1.480	1.471	1.218	0.129	0.077	98	97	77	-49	-70	1.63E-6	4.06E-6	1.07E-5
MALME-3M	0.588	1.793	1.778	1.772	1.542	0.681	0.264	99	98	79	8	-55	2.56E-6	1.33E-5	8.29E-5
M14	0.415	1.237	1.254	1.329	1.286	0.202	0.063	102	111	106	-51	-85	2.27E-6	4.71E-6	9.79E-6
MDA-MB-435	0.473	1.925	1.902	1.903	1.634	0.387	0.172	98	98	80	-18	-64	2.02E-6	6.51E-6	5.00E-5
SK-MEL-2	0.861	1.601	1.603	1.669	1.671	0.780	0.166	100	109	109	-9	-81	3.16E-6	8.33E-6	3.71E-5
SK-MEL-28	0.507	1.416	1.437	1.487	1.457	0.534	0.033	102	108	105	3	-93	3.44E-6	1.07E-5	3.54E-5
SK-MEL-5	0.523	2.479	2.373	2.387	2.265	0.610	0.018	95	95	89	4	-97	2.90E-6	1.11E-5	3.46E-5
UACC-257	0.550	1.136	1.123	1.153	1.123	0.427	0.017	98	103	98	-22	-97	2.50E-6	6.51E-6	2.35E-5
UACC-62	0.579	1.948	1.981	1.913	1.738	0.059	0.051	102	97	85	-90	-91	1.58E-6	3.06E-6	5.91E-6
Ovarian Cancer															
IGROV1	0.590	1.284	1.245	1.251	1.255	0.532	0.112	94	95	96	-10	-81	2.71E-6	8.06E-6	3.66E-5
OVCAR-3	0.517	1.310	1.330	1.314	1.310	0.395	0.091	102	101	100	-24	-82	2.53E-6	6.43E-6	2.80E-5
OVCAR-4	0.534	1.141	1.140	1.123	1.088	0.544	0.097	100	97	91	2	-82	2.88E-6	1.04E-5	4.15E-5
OVCAR-5	0.597	1.453	1.436	1.539	1.422	0.551	0.186	98	110	96	-8	-69	2.78E-6	8.42E-6	4.91E-5
OVCAR-8	0.417	1.651	1.591	1.600	1.340	0.345	0.124	95	96	75	-17	-70	1.86E-6	6.48E-6	4.14E-5
NCI/ADR-RES	0.532	1.678	1.697	1.716	1.426	0.488	0.413	102	103	78	-8	-22	2.11E-6	8.00E-6	> 1.00E-4
SK-OV-3	0.487	1.113	1.109	1.062	1.037	0.459	0.100	99	92	88	-6	-80	2.54E-6	8.68E-6	3.98E-5
Renal Cancer															
786-0	0.834	2.220	2.217	2.229	2.203	0.746	0.053	100	101	99	-11	-94	2.79E-6	8.01E-6	2.98E-5
A498	1.307	1.744	1.669	1.620	1.460	0.494	0.114	83	71	35	-62	-91	3.86E-7	2.29E-6	7.48E-6
ACHN	0.312	1.277	1.264	1.286	0.999	0.297	0.117	99	101	71	-5	-63	1.90E-6	8.64E-6	6.07E-5
CAKI-1	0.638	1.856	1.882	1.832	1.743	0.492	0.292	102	98	91	-23	-54	2.28E-6	6.28E-6	7.32E-5
RXF 393	0.656	1.086	1.053	1.050	1.051	0.363	0.044	92	92	92	-45	-93	2.03E-6	4.70E-6	1.28E-5
SN12C	0.466	1.816	1.809	1.708	1.447	0.472	0.223	99	92	73	.	-52	2.06E-6	1.02E-5	9.10E-5
TK-10	0.738	1.246	1.259	1.334	1.447	0.721	0.298	102	117	139	-2	-60	4.27E-6	9.62E-6	6.79E-5
UO-31	0.555	1.719	1.508	1.464	1.217	0.474	0.103	82	78	57	-15	-82	1.25E-6	6.24E-6	3.38E-5
Prostate Cancer															
PC-3	0.513	1.913	1.891	1.826	1.684	0.496	0.363	98	94	84	-3	-29	2.43E-6	9.14E-6	> 1.00E-4
DU-145	0.381	1.201	1.222	1.166	1.157	0.328	0.060	103	96	95	-14	-84	2.58E-6	7.44E-6	3.26E-5
Breast Cancer															
MCF7	0.268	1.555	1.401	1.296	1.103	0.305	0.079	88	80	65	3	-71	1.74E-6	1.09E-5	5.23E-5
MDA-MB-231/ATCC	0.490	0.995	0.989	0.953	0.839	0.440	0.124	99	92	69	-10	-75	1.74E-6	7.44E-6	4.13E-5
HS 578T	1.204	1.793	1.791	1.780	1.679	0.917	0.457	100	98	81	-24	-62	1.96E-6	5.91E-6	4.84E-5
BT-549	0.840	1.393	1.384	1.470	1.386	0.793	0.044	98	114	99	-6	-95	2.93E-6	8.84E-6	3.15E-5
T-47D	0.624	1.643	1.536	1.486	1.381	0.665	0.440	89	85	74	4	-30	2.21E-6	1.31E-5	> 1.00E-4
MDA-MB-468	0.549	0.835	0.817	0.822	0.772	0.374	0.074	94	95	78	-32	-87	1.79E-6	5.12E-6	2.14E-5

Figure S16: Complete Five Dose Assay data from NCI 60 cell lines for compound 13

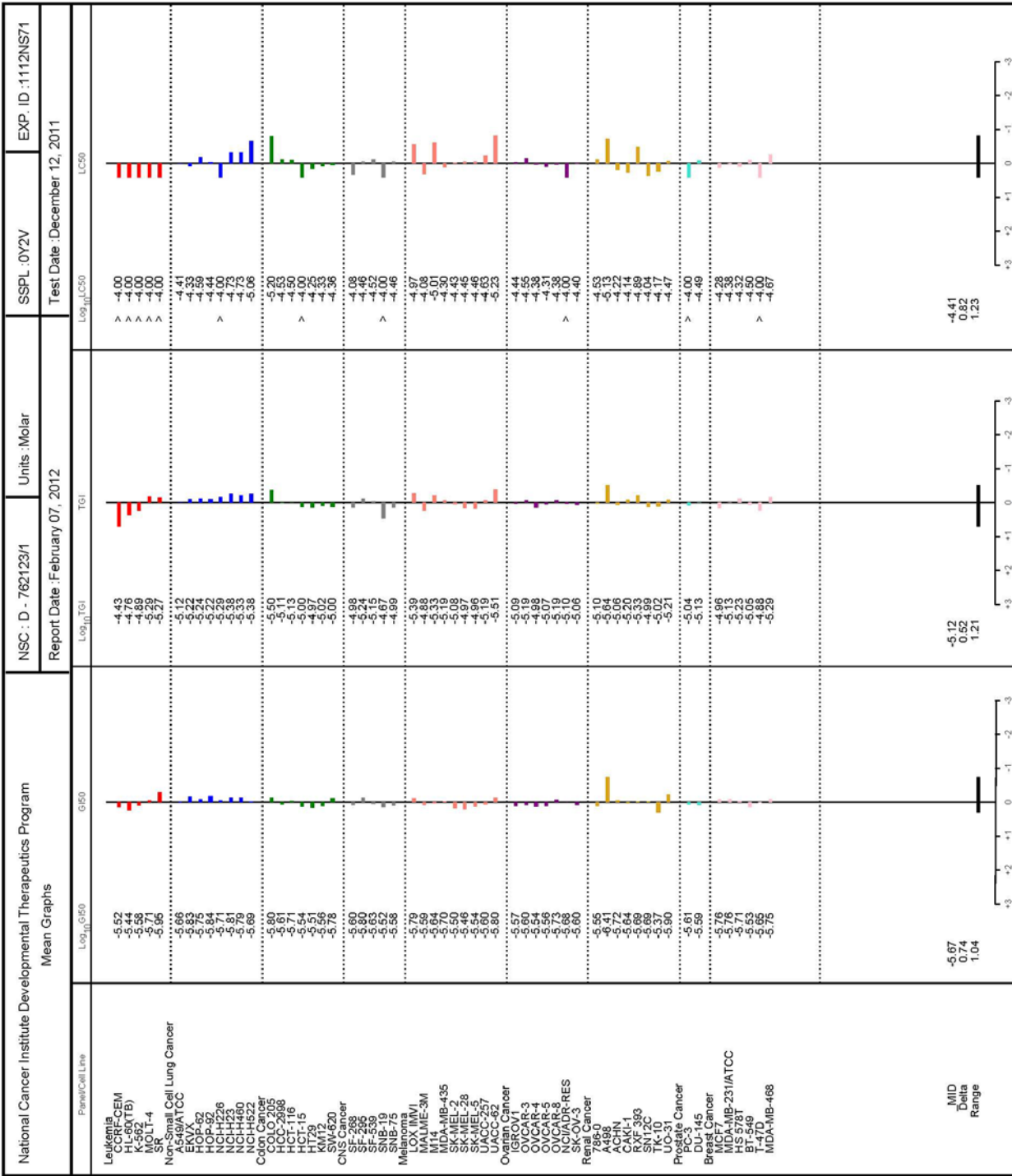


Figure S17: COMPARE Analysis data for compound 13 (Black Bars) in direct comparison with SCH1473759 (NSC761691, Red Lines), an Aurora kinase inhibitor.

