

## **(Supplementary Information)**

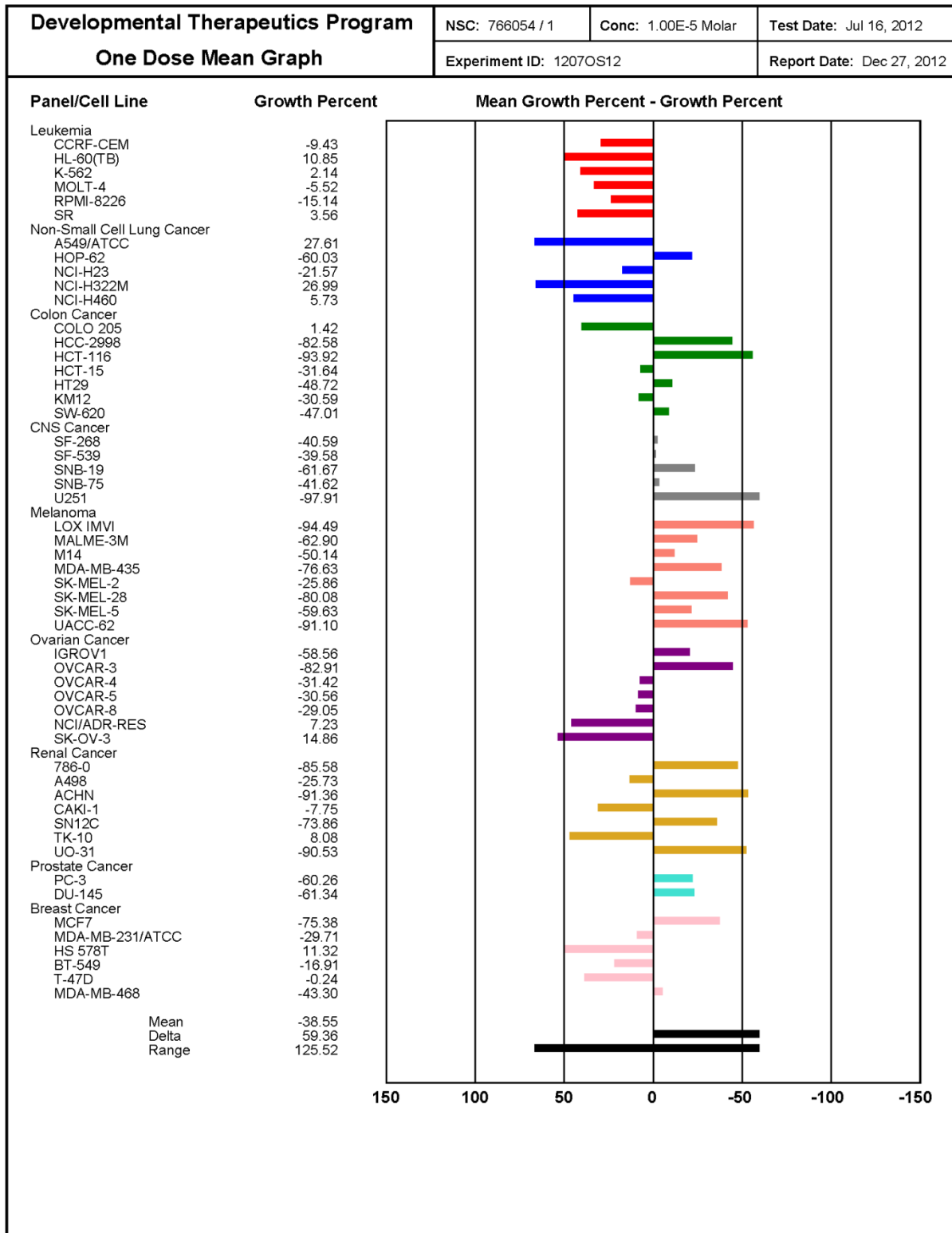
# **Novel 3,5-bis(arylidene)-4-piperidone based monocarbonyl analogues of curcumin: Anticancer activity evaluation and mode of action study**

**Anuj Thakur,<sup>a</sup> Sunny Manohar,<sup>a</sup> Christian E. Vélez Gerena,<sup>b</sup> Beatriz Zayas,<sup>b</sup>  
Vineet Kumar,<sup>c</sup> Sanjay V. Malhotra<sup>\*c</sup> and Diwan S. Rawat<sup>\*a</sup>**

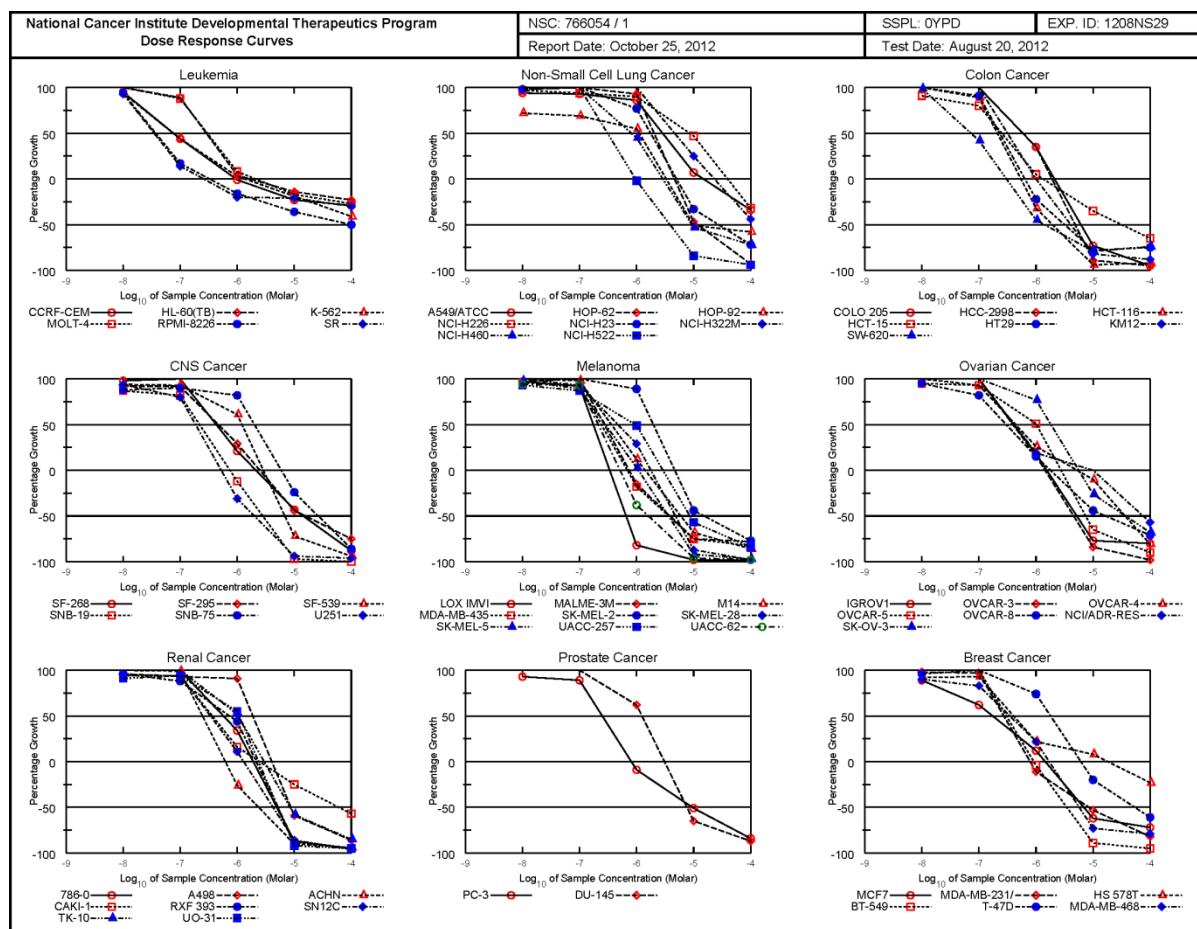
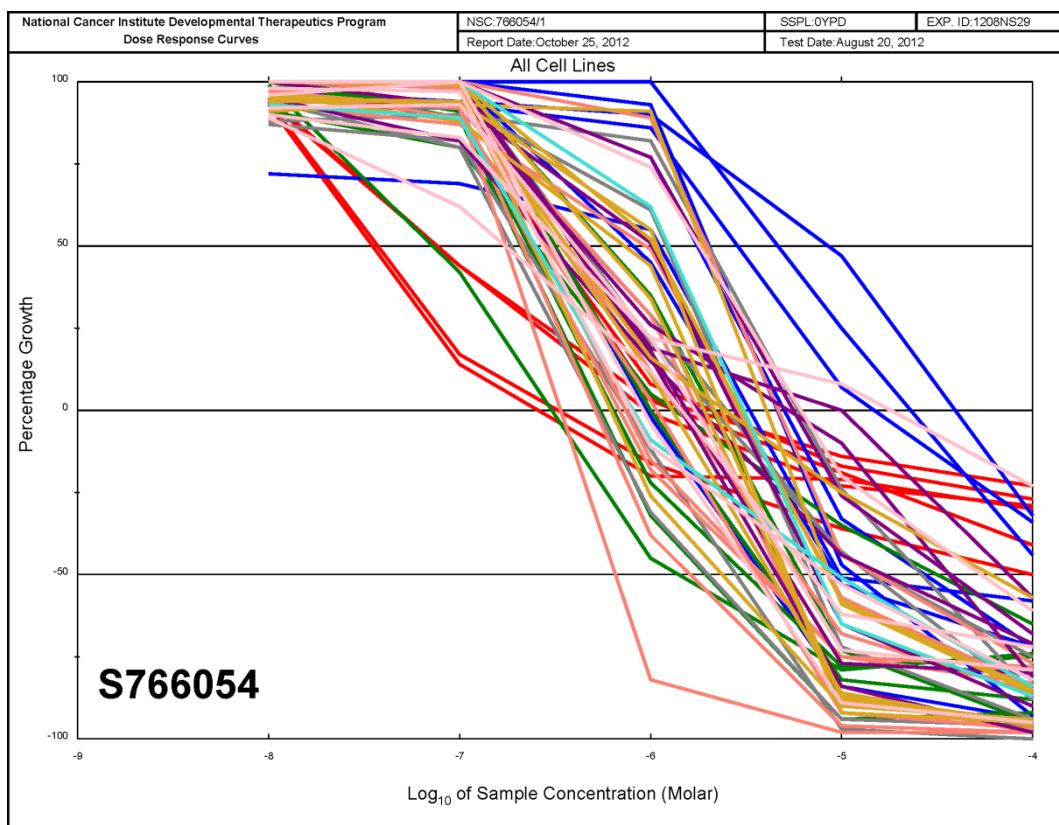
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## One dose data of Compound 10

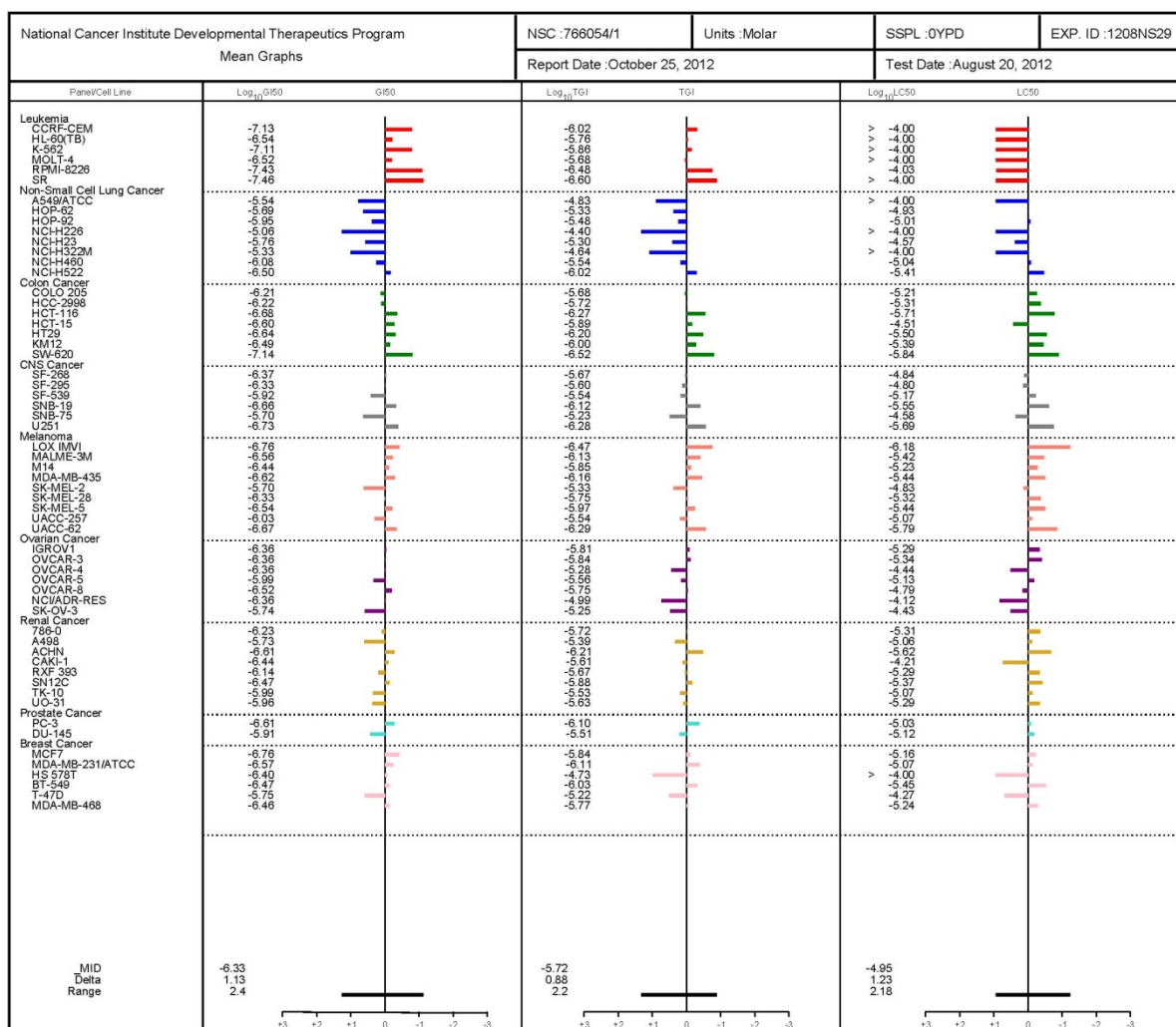


## Five dose data of Compound 10

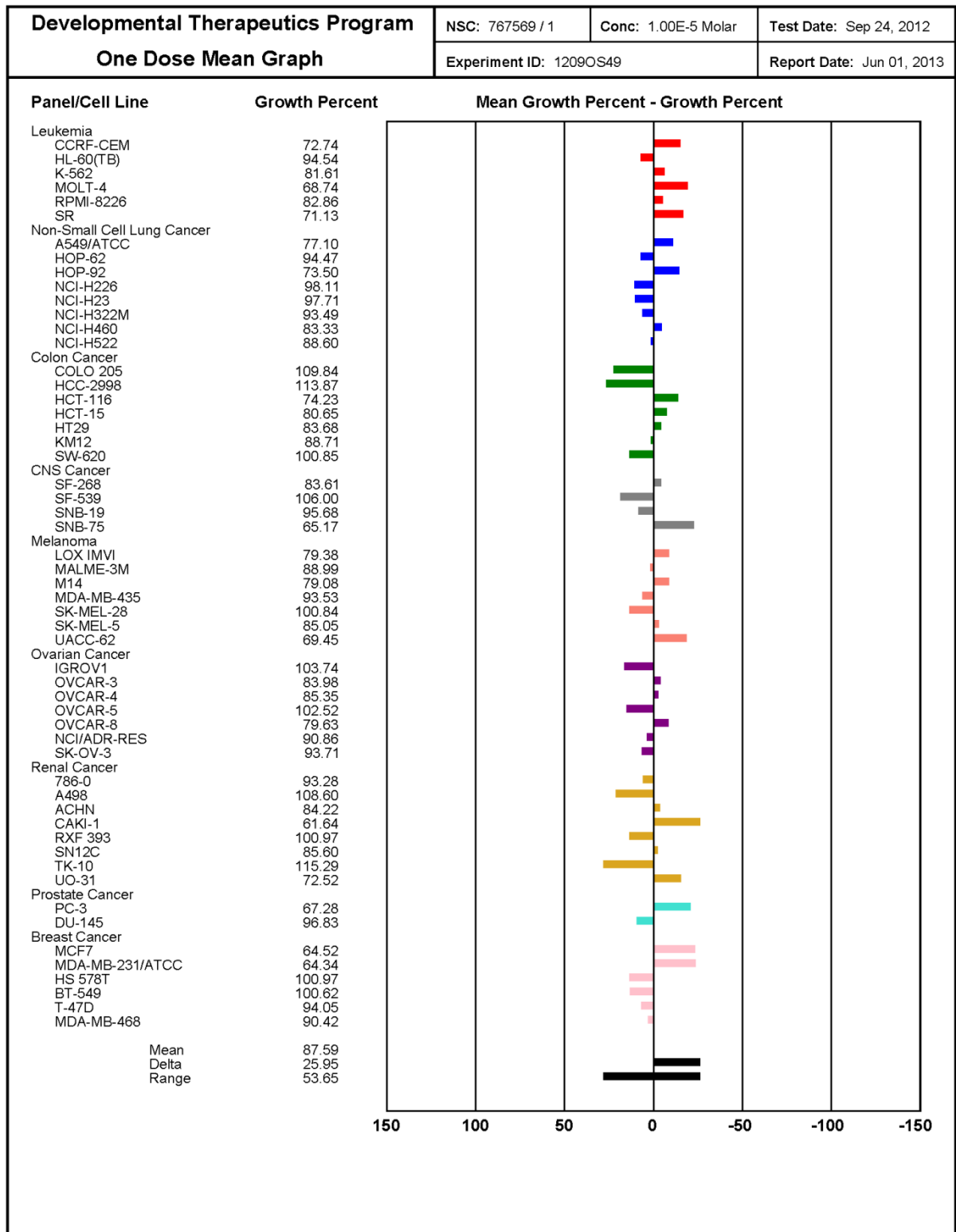


# National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

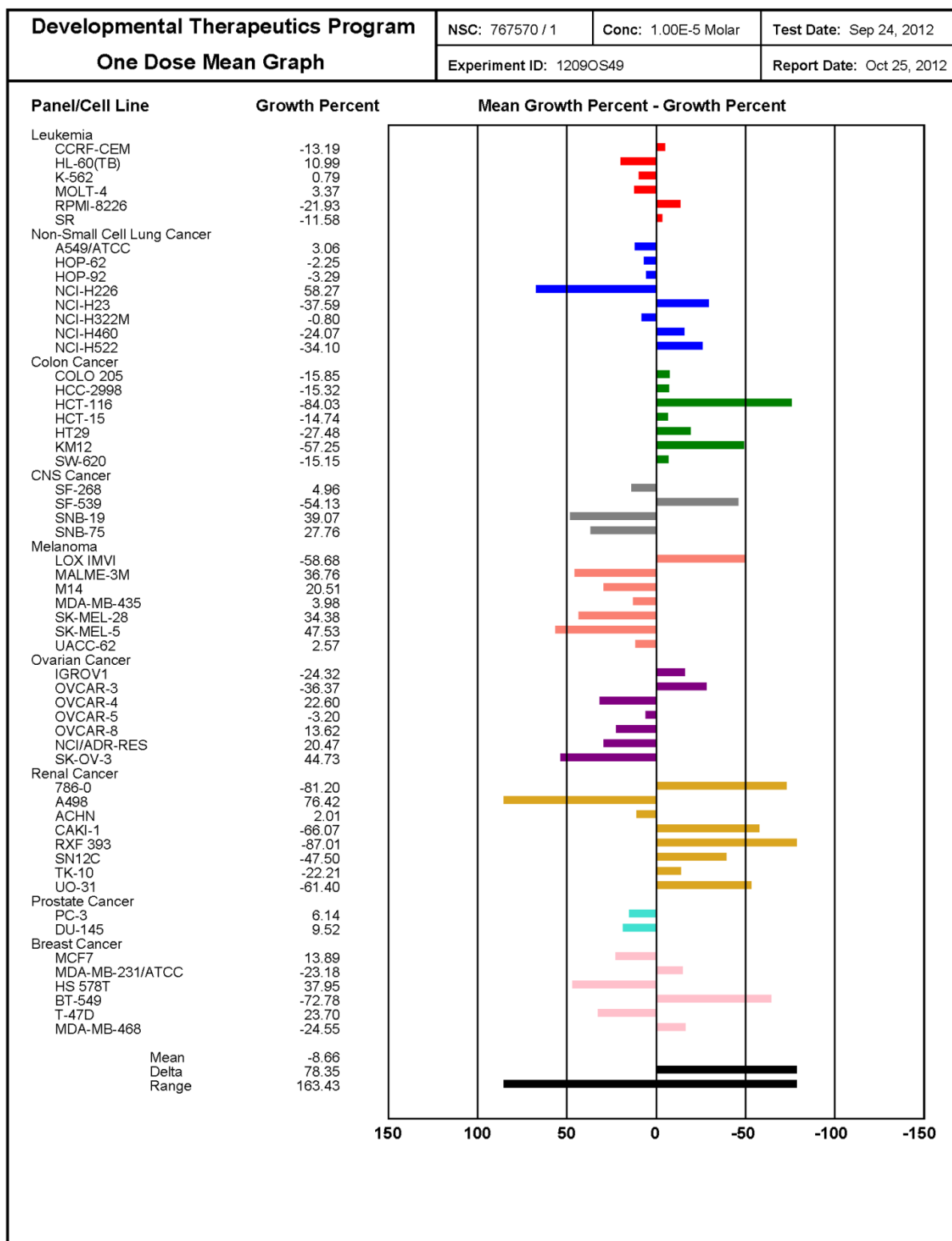
NSC : 766054 / 1			Experiment ID : 1208NS29										Test Type : 08		Units : Molar	
Report Date : October 25, 2012			Test Date : August 20, 2012										QNS :		MC :	
COMI : ATH 57 (119143)			Stain Reagent : SRB Dual-Pass Related										SSPL : 0YPD			
Log10 Concentration																
Panel/Cell Line	Time Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50	
Leukemia																
CCRF-CEM	0.413	2.207	2.114	1.194	0.409	0.320	0.295	95	44	-1	-23	-29	7.48E-8	9.51E-7	> 1.00E-4	
HL-60(TB)	0.726	2.271	2.524	2.102	0.794	0.627	0.562	116	89	4	-14	-23	2.89E-7	1.74E-6	> 1.00E-4	
K-562	0.223	1.728	1.636	0.892	0.268	0.181	0.132	94	44	3	-19	-41	7.72E-8	1.37E-6	> 1.00E-4	
MOLT-4	0.825	2.840	2.837	2.600	0.986	0.687	0.601	100	88	8	-17	-27	2.99E-7	2.11E-6	> 1.00E-4	
RPMI-8226	0.766	2.582	2.464	1.080	0.644	0.488	0.380	94	17	-16	-36	-50	3.72E-8	3.31E-7	9.38E-5	
SR	0.315	1.508	1.426	0.477	0.252	0.250	0.220	93	14	-20	-21	-30	3.48E-8	2.52E-7	> 1.00E-4	
Non-Small Cell Lung Cancer																
A549/ATCC	0.517	2.285	2.184	2.170	2.046	0.635	0.343	94	93	86	7	-34	2.86E-6	1.46E-5	> 1.00E-4	
HOP-62	0.438	1.069	1.055	1.131	1.026	0.234	0.032	98	110	93	-47	-93	2.04E-6	4.64E-6	1.19E-5	
HOP-92	1.492	1.799	1.712	1.704	1.661	0.731	0.621	72	69	55	-51	-58	1.11E-6	3.30E-6	9.78E-6	
NCI-H226	0.689	1.312	1.292	1.276	1.252	0.983	0.470	97	94	90	47	-32	8.62E-6	3.96E-5	> 1.00E-4	
NCI-H23	1.221	3.157	3.127	3.155	2.709	0.816	0.337	98	100	77	-33	-72	1.75E-6	4.99E-6	2.68E-5	
NCI-H322M	0.826	1.763	1.780	1.789	1.776	1.059	0.459	102	103	101	25	-44	4.70E-6	2.28E-5	> 1.00E-4	
NCI-H460	0.303	2.702	2.776	2.796	1.387	0.141	0.085	103	104	45	-53	-72	8.28E-7	2.87E-6	9.22E-6	
NCI-H522	1.093	2.526	2.533	2.548	1.074	0.174	0.063	100	102	-2	-84	-94	3.16E-7	9.62E-7	3.85E-6	
Colon Cancer																
COLO 205	0.406	1.738	1.835	1.820	0.869	0.111	0.022	107	106	35	-73	-95	6.12E-7	2.11E-6	6.14E-6	
HCC-2998	1.066	2.964	2.997	3.053	1.721	0.120	0.048	102	105	35	-89	-95	6.02E-7	1.91E-6	4.85E-6	
HCT-116	0.234	2.531	2.700	2.273	0.159	0.013	0.018	107	89	-32	-94	-92	2.09E-7	5.43E-7	1.94E-6	
HCT-15	0.272	2.386	2.204	1.964	0.369	0.176	0.095	91	80	5	-35	-65	2.50E-7	1.30E-6	3.07E-5	
HT29	0.239	1.435	1.494	1.323	0.187	0.054	0.060	105	91	-22	-78	-75	2.29E-7	6.38E-7	3.19E-6	
KM12	0.471	2.370	2.488	2.424	0.473	0.083	0.058	106	103	.	-82	-88	3.27E-7	1.00E-6	4.04E-6	
SW-620	0.321	2.331	2.309	1.164	0.178	0.069	0.084	99	42	-45	-79	-74	7.21E-8	3.05E-7	1.45E-6	
CNS Cancer																
SF-268	0.646	1.992	1.963	1.990	0.933	0.369	0.077	98	100	21	-43	-88	4.31E-7	2.15E-6	1.44E-5	
SF-295	0.932	2.800	2.658	2.652	1.476	0.523	0.234	92	92	29	-44	-75	4.66E-7	2.50E-6	1.57E-5	
SF-539	0.922	2.384	2.302	2.287	1.816	0.256	0.057	94	93	61	-72	-94	1.21E-6	2.87E-6	6.81E-6	
SNB-19	0.341	1.418	1.280	1.226	0.302	0.011	0.002	87	82	-12	-97	-100	2.20E-7	7.52E-7	2.82E-6	
SNB-75	0.740	1.612	1.505	1.522	1.452	0.560	0.106	88	90	82	-24	-86	1.99E-6	5.90E-6	2.62E-5	
U251	0.540	2.190	2.095	1.867	0.375	0.032	0.022	94	80	-31	-94	-96	1.88E-7	5.30E-7	2.02E-6	
Melanoma																
LOX IMVI	0.507	2.744	2.667	2.573	0.092	0.010	0.012	97	92	-82	-98	-98	1.75E-7	3.39E-7	6.56E-7	
MALME-3M	0.498	0.755	0.748	0.757	0.424	0.123	0.111	97	101	-15	-75	-78	2.74E-7	7.42E-7	3.81E-6	
M14	0.381	1.831	1.876	1.801	0.549	0.121	0.052	103	98	12	-68	-86	3.59E-7	1.40E-6	5.91E-6	
MDA-MB-435	0.645	2.605	2.529	2.452	0.528	0.161	0.112	96	92	-18	-75	-83	2.41E-7	6.85E-7	3.63E-6	
SK-MEL-2	1.130	2.292	2.354	2.426	2.170	0.629	0.256	105	112	89	-44	-77	1.97E-6	4.66E-6	1.48E-5	
SK-MEL-28	0.529	1.516	1.521	1.448	0.817	0.070	0.012	100	93	29	-87	-98	4.73E-7	1.79E-6	4.82E-6	
SK-MEL-5	0.512	2.232	2.203	2.050	0.566	0.039	0.014	98	89	3	-92	-97	2.86E-7	1.08E-6	3.60E-6	
UACC-257	0.859	1.861	1.792	1.728	1.350	0.370	0.140	93	87	49	-57	-84	9.39E-7	2.90E-6	8.60E-6	
UACC-62	0.738	2.891	2.771	2.730	0.460	0.028	0.018	94	93	-38	-96	-98	2.12E-7	5.14E-7	1.62E-6	
Ovarian Cancer																
IGROV1	0.626	1.786	1.857	1.857	0.839	0.141	0.128	106	106	18	-77	-80	4.36E-7	1.55E-6	5.17E-6	
OVCAR-3	0.673	1.781	1.889	1.911	0.849	0.107	0.016	110	112	16	-84	-98	4.41E-7	1.44E-6	4.56E-6	
OVCAR-4	0.743	1.523	1.520	1.468	0.948	0.667	0.140	100	93	26	-10	-81	4.41E-7	5.23E-6	3.63E-5	
OVCAR-5	0.703	1.651	1.602	1.585	1.187	0.245	0.073	95	93	51	-65	-90	1.02E-6	2.75E-6	7.40E-6	
OVCAR-8	0.418	1.883	1.814	1.626	0.634	0.232	0.123	95	82	15	-44	-71	3.01E-7	1.77E-6	1.63E-5	
NCI/ADR-RES	0.709	2.413	2.478	2.521	1.026	0.715	0.308	104	106	19	-	-57	4.39E-7	1.01E-5	7.67E-5	
SK-OV-3	0.609	1.479	1.506	1.529	1.282	0.452	0.194	103	106	77	-26	-68	1.84E-6	5.62E-6	3.72E-5	
Renal Cancer																
786-O	0.666	2.484	2.558	2.555	1.281	0.088	0.033	104	104	34	-87	-95	5.87E-7	1.91E-6	4.95E-6	
A498	1.472	2.379	2.347	2.320	2.296	0.610	0.209	96	93	91	-59	-86	1.88E-6	4.05E-6	8.76E-6	
ACHN	0.359	1.766	1.782	1.745	0.267	0.036	0.021	101	99	-26	-90	-94	2.46E-7	6.22E-7	2.39E-6	
CAKI-1	0.844	2.716	2.597	2.605	1.140	0.633	0.367	94	94	16	-25	-57	3.65E-7	2.43E-6	6.19E-5	
RXF 393	0.639	1.083	1.063	1.030	0.833	0.075	0.033	96	88	44	-88	-95	7.23E-7	2.14E-6	5.13E-6	
SN12C	1.067	3.214	3.101	3.087	1.314	0.147	0.040	95	94	11	-86	-96	3.42E-7	1.31E-6	4.26E-6	
TK-10	0.758	1.534	1.557	1.583	1.158	0.319	0.111	103	106	52	-58	-85	1.03E-6	2.96E-6	8.46E-6	
UO-31	0.836	2.268	2.144	2.183	1.628	0.064	0.040	91	94	55	-92	-95	1.09E-6	2.37E-6	5.17E-6	
Prostate Cancer																
PC-3	0.658	1.733	1.656	1.610	0.597	0.320	0.103	93	89	-9	-51	-84	2.48E-7	8.03E-7	9.28E-6	
DU-145	0.565	1.789	1.867	1.929	1.324	0.198	0.076	106	111	62	-65	-87	1.24E-6	3.08E-6	7.62E-6	
Breast Cancer																
MCF7	0.433	2.433	2.208	1.679	0.671	0.165	0.123	89	62	12	-62	-72	1.75E-7	1.45E-6	6.88E-6	
MDA-MB-231/ATCC	0.640	1.460	1.447	1.432	0.567	0.301	0.115	98	97	-11	-53	-82	2.70E-7	7.84E-7	8.48E-6	
HS 578T	0.925	2.014	1.926	1.936	1.160	0.107	0.714	92	93	22	8	-23	3.99E-7	1.86E-5	> 1.00E-4	
BT-549	0.802	1.731	1.748	1.831	0.774	0.092	0.039	102	111	-4	-89	-95	3.40E-7	9.31E-7	3.52E-6	
T-47D	0.716	1.693	1.657	1.707	1.438	0.571	0.281	96	101	74	-20	-61	1.79E-6	6.09E-6	5.43E-5	
MDA-MB-468	0.705	1.561	1.476	1.418	0.893	0.193	0.147	90	83	22	-73	-79	3.49E-7	1.71E-6	5.77E-6	



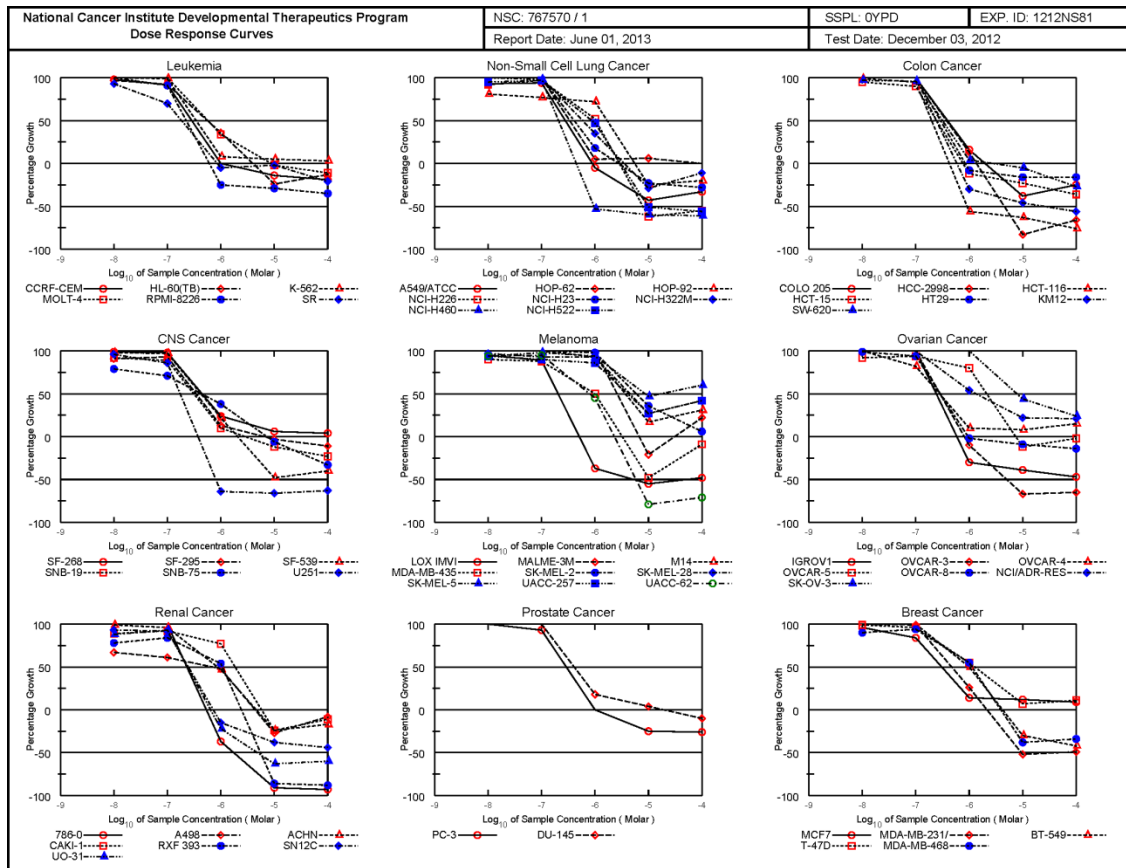
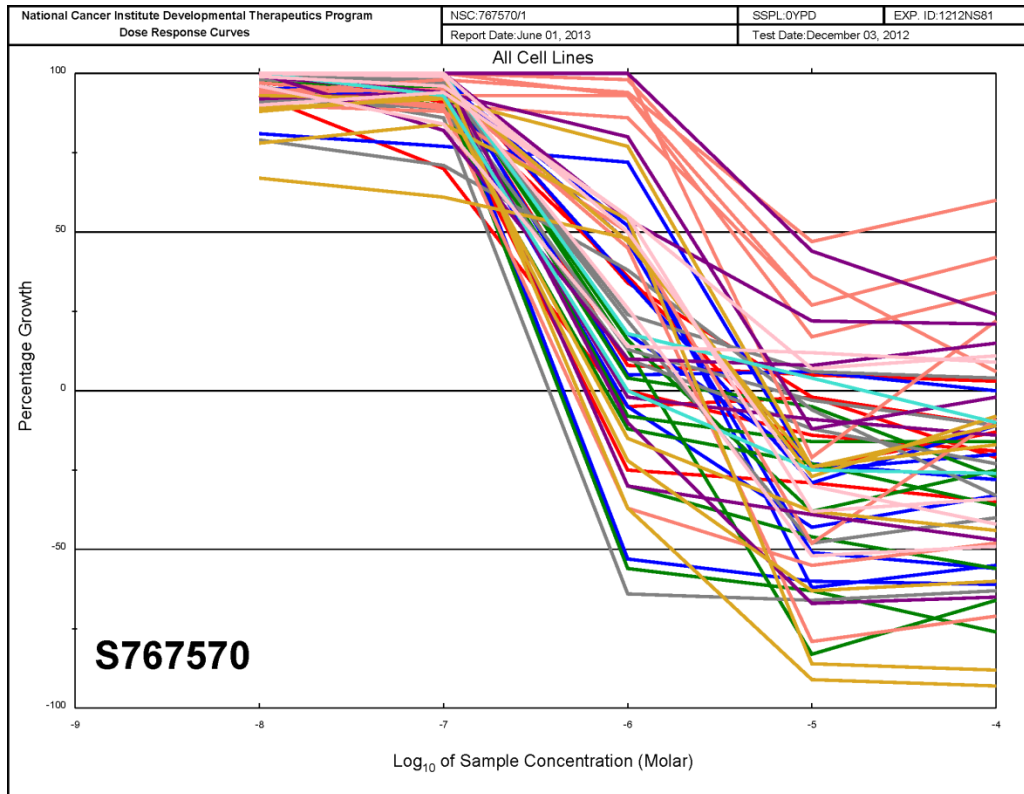
# One dose data of Compound 14



# One dose data of Compound 22



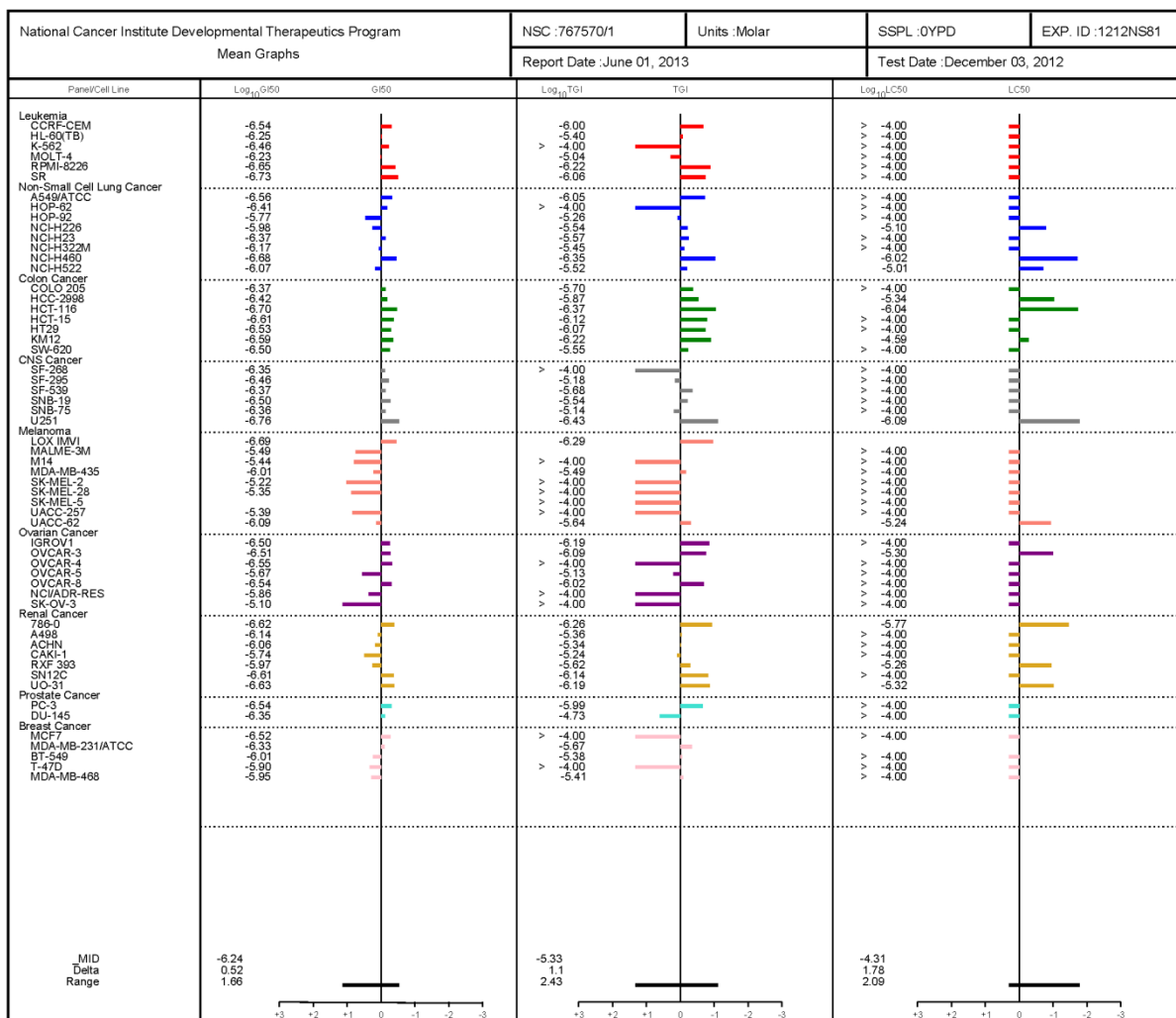
## Five dose data of Compound 22



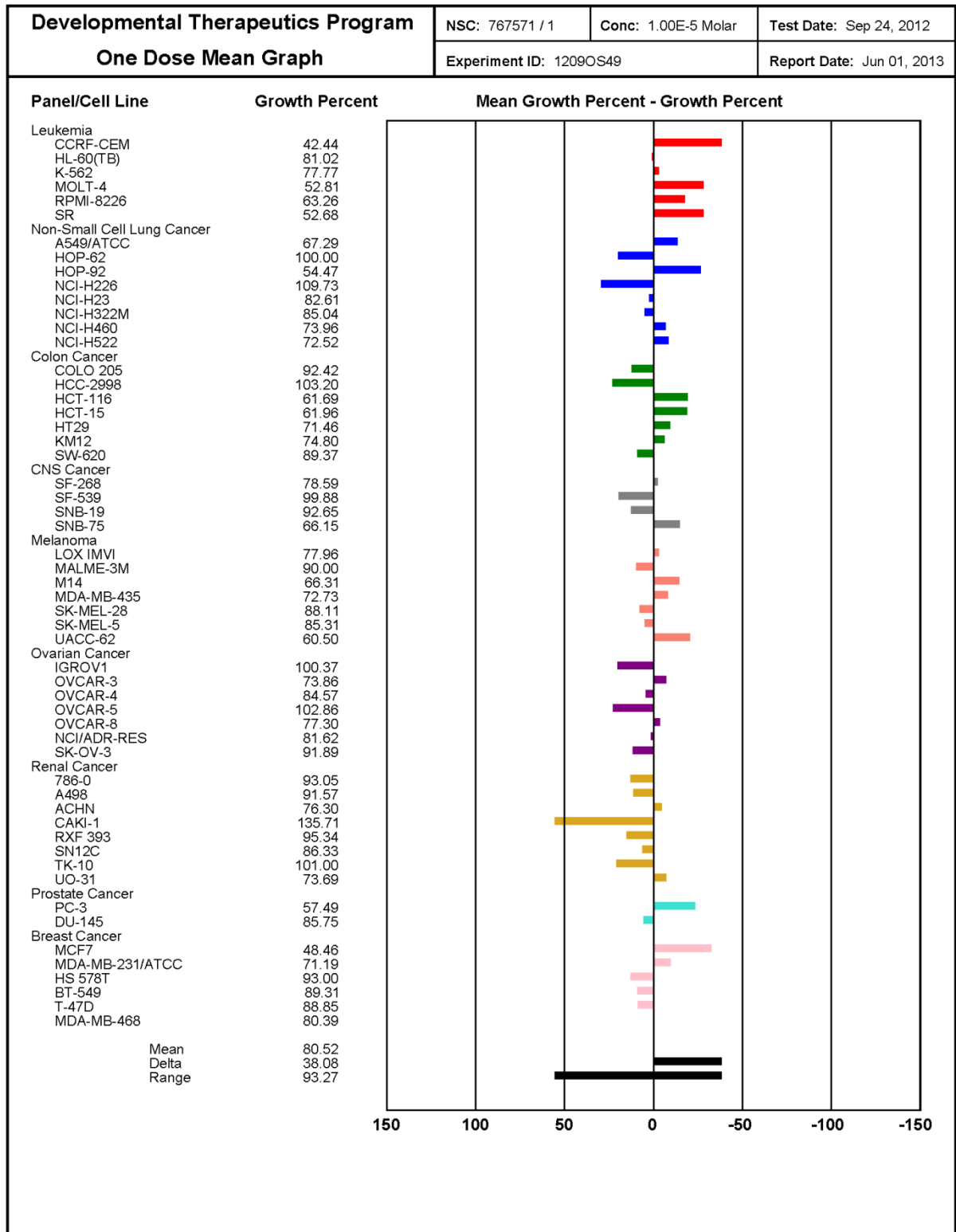


**National Cancer Institute Developmental Therapeutics Program  
In-Vitro Testing Results**

NSC : 767570 / 1			Experiment ID : 1212NS81										Test Type : 08			Units : Molar		
Report Date : June 01, 2013			Test Date : December 03, 2012										QNS :			MC :		
COMI : ATH-78 (120563)			Stain Reagent : SRB Dual-Pass Related										SSPL : 0YPD					
Log10 Concentration																		
Panel/Cell Line	Time Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50			
Leukemia																		
CCRF-CEM	0.596	2.110	2.079	1.991	0.595	0.514	0.485	98	92	.	-14	-19	2.86E-7	9.94E-7	> 1.00E-4			
HL-60(TB)	0.628	2.726	2.666	2.560	1.382	0.477	0.544	97	92	36	-24	-13	5.62E-7	3.97E-6	> 1.00E-4			
K-562	0.230	1.978	2.006	1.969	0.364	0.311	0.282	102	99	8	5	3	3.46E-7	> 1.00E-4	> 1.00E-4			
MOLT-4	0.620	2.092	2.148	2.176	1.116	0.611	0.552	104	106	34	-2	-11	5.94E-7	9.05E-6	> 1.00E-4			
RPMI-8226	1.538	3.079	3.140	2.939	1.147	1.095	1.002	104	91	-25	-29	-35	2.25E-7	6.05E-7	> 1.00E-4			
SR	0.256	0.727	0.694	0.586	0.244	0.251	0.202	93	70	-5	-2	-21	1.85E-7	8.65E-7	> 1.00E-4			
Non-Small Cell Lung Cancer																		
A549/ATCC	0.477	1.955	1.846	1.863	0.453	0.270	0.320	93	94	-5	-43	-33	2.77E-7	8.87E-7	> 1.00E-4			
HOP-62	0.508	1.146	1.167	1.231	0.541	0.544	0.511	103	113	5	6	.	3.85E-7	> 1.00E-4	> 1.00E-4			
HOP-92	1.407	1.960	1.853	1.836	1.807	1.057	1.126	81	77	72	-25	-20	1.70E-6	5.55E-6	> 1.00E-4			
NCH-H226	0.992	2.441	2.326	2.402	1.747	0.382	0.443	92	97	52	-62	-55	1.04E-6	2.87E-6	7.92E-6			
NCH-H23	0.899	2.730	2.789	2.804	1.224	0.690	0.648	103	104	18	-23	-28	4.23E-7	2.71E-6	> 1.00E-4			
NCH-H322M	0.925	1.672	1.726	1.840	1.190	0.659	0.819	107	123	35	-29	-11	6.80E-7	3.56E-6	> 1.00E-4			
NCH-H460	0.366	2.833	2.910	2.783	0.173	0.146	0.143	103	98	-53	-60	-61	2.08E-7	4.47E-7	9.59E-7			
NCH-H522	0.807	1.501	1.467	1.482	1.130	0.394	0.352	95	97	47	-51	-56	8.54E-7	2.99E-6	9.73E-6			
Colon Cancer																		
COLO 205	0.405	1.613	1.689	1.692	0.603	0.253	0.305	106	107	16	-38	-25	4.24E-7	2.01E-6	> 1.00E-4			
HCC-2998	0.837	2.315	2.345	2.345	1.026	0.144	0.288	102	102	13	-83	-66	3.83E-7	1.36E-6	4.54E-6			
HCT-116	0.189	1.785	1.770	1.704	0.083	0.070	0.045	99	95	-56	-63	-76	1.98E-7	4.24E-7	9.08E-7			
HCT-15	0.314	2.285	2.181	2.094	0.276	0.242	0.203	95	90	-12	-23	-36	2.47E-7	7.59E-7	> 1.00E-4			
HT29	0.229	1.309	1.330	1.318	0.211	0.192	0.193	102	101	-8	-16	-16	2.93E-7	8.43E-7	> 1.00E-4			
KM12	0.284	1.558	1.555	1.624	0.200	0.154	0.126	100	105	-30	-46	-56	2.56E-7	6.02E-7	2.57E-5			
SW-620	0.320	2.186	2.126	2.116	0.395	0.304	0.233	97	96	4	-5	-27	3.17E-7	2.79E-6	> 1.00E-4			
CNS Cancer																		
SF-268	0.667	1.855	1.844	1.826	0.958	0.744	0.710	99	98	24	6	4	4.47E-7	> 1.00E-4	> 1.00E-4			
SF-295	0.886	3.186	2.981	3.036	1.178	0.862	0.785	91	93	13	-3	-11	3.45E-7	6.67E-6	> 1.00E-4			
SF-539	0.911	2.512	2.466	2.467	1.263	0.478	0.545	98	97	22	-48	-40	4.24E-7	2.07E-6	> 1.00E-4			
SNB-19	0.681	2.041	1.931	1.898	0.614	0.603	0.525	92	89	10	-12	-23	3.13E-7	2.88E-6	> 1.00E-4			
SNB-75	0.893	1.705	1.531	1.473	1.199	0.840	0.598	79	71	38	-6	-33	4.32E-7	7.29E-6	> 1.00E-4			
U251	0.482	2.040	1.974	1.818	0.173	0.166	0.180	96	86	-64	-66	-63	1.73E-7	3.73E-7	8.05E-7			
Melanoma																		
LOX IMVI	0.291	1.451	1.394	1.319	0.184	0.132	0.150	95	89	-37	-55	-48	2.03E-7	5.08E-7	.			
MALME-3M	0.757	1.437	1.560	1.634	1.591	0.601	0.907	118	129	123	-21	22	3.21E-6	.	> 1.00E-4			
M14	0.505	1.919	1.953	1.982	1.818	0.744	0.942	102	104	93	17	31	3.66E-6	> 1.00E-4	> 1.00E-4			
MDA-MB-435	0.532	2.382	2.193	2.154	1.453	0.274	0.482	90	88	50	-48	-9	9.85E-7	3.21E-6	> 1.00E-4			
SK-MEL-2	1.121	2.018	2.029	2.118	1.997	1.448	1.174	101	111	98	36	6	6.01E-6	> 1.00E-4	> 1.00E-4			
SK-MEL-28	0.662	1.707	1.676	1.629	1.632	0.941	1.099	97	93	93	27	42	4.44E-6	> 1.00E-4	> 1.00E-4			
SK-MEL-5	0.876	3.307	3.168	3.257	3.165	2.025	2.337	94	98	94	47	60	.	> 1.00E-4	> 1.00E-4			
UACC-257	0.834	1.637	1.588	1.560	1.523	1.053	1.169	94	90	86	27	42	4.08E-6	> 1.00E-4	> 1.00E-4			
UACC-62	0.734	2.554	2.453	2.470	1.558	0.151	0.214	94	95	45	-79	-71	8.04E-7	2.31E-6	5.81E-6			
Ovarian Cancer																		
IGROV1	0.670	1.605	1.759	1.890	0.468	0.407	0.352	116	130	-30	-39	-47	3.17E-7	6.49E-7	> 1.00E-4			
OVCAR-3	0.600	1.700	1.828	1.792	0.538	0.198	0.209	112	108	-10	-67	-65	3.10E-7	8.18E-7	5.01E-6			
OVCAR-4	0.621	1.024	1.032	0.951	0.663	0.652	0.680	102	82	10	8	15	2.79E-7	> 1.00E-4	> 1.00E-4			
OVCAR-5	0.624	1.668	1.585	1.605	1.462	0.550	0.615	92	94	80	-12	-2	2.13E-6	7.43E-6	> 1.00E-4			
OVCAR-8	0.590	1.972	1.956	1.883	0.580	0.539	0.505	99	94	-2	-9	-14	2.86E-7	9.58E-7	> 1.00E-4			
NCI/ADR-RES	0.815	2.576	2.656	2.736	1.775	1.199	1.187	105	109	54	22	21	1.37E-6	> 1.00E-4	> 1.00E-4			
SK-OV-3	0.634	1.386	1.456	1.400	1.450	0.962	0.814	109	102	108	44	24	7.95E-6	> 1.00E-4	> 1.00E-4			
Renal Cancer																		
786-0	0.833	2.589	2.609	2.660	0.521	0.073	0.057	101	104	-37	-91	-93	2.41E-7	5.44E-7	1.71E-6			
A498	1.722	2.227	2.062	2.032	1.966	1.261	1.585	67	61	48	-27	-8	7.27E-7	4.39E-6	> 1.00E-4			
ACHN	0.338	1.640	1.626	1.583	0.952	0.256	0.281	99	96	47	-24	-17	8.74E-7	4.56E-6	> 1.00E-4			
CAKI-1	1.171	3.069	2.862	2.917	2.626	0.888	1.043	89	92	77	-24	-11	1.84E-6	5.75E-6	> 1.00E-4			
RXF 393	0.960	1.882	1.676	1.738	1.454	0.138	0.116	78	84	54	-86	-88	1.06E-6	2.42E-6	5.54E-6			
SN12C	0.730	2.680	2.549	2.519	0.618	0.455	0.407	93	92	-15	-38	-44	2.45E-7	7.18E-7	> 1.00E-4			
UO-31	0.865	1.974	1.841	1.896	0.671	0.319	0.348	88	93	-22	-63	-60	2.36E-7	6.39E-7	4.75E-6			
Prostate Cancer																		
PC-3	0.664	1.708	1.703	1.634	0.667	0.501	0.494	100	93	.	-25	-26	2.91E-7	1.03E-6	> 1.00E-4			
DU-145	0.407	1.418	1.481	1.520	0.585	0.446	0.366	106	110	18	4	-10	4.46E-7	1.88E-5	> 1.00E-4			
Breast Cancer																		
MCF7	0.614	2.578	2.502	2.266	0.881	0.846	0.782	96	84	14	12	9	3.05E-7	> 1.00E-4	> 1.00E-4			
MDA-MB-231/ATCC	0.680	1.506	1.522	1.494	0.895	0.329	0.345	102	99	26	-52	-49	4.66E-7	2.16E-6	.			
BT-549	1.189	2.183	2.240	2.287	1.673	0.820	0.673	106	110	50	-30	-42	9.87E-7	4.21E-6	> 1.00E-4			
T-47D	0.598	1.662	1.647	1.616	1.182	0.676	0.710	99	96	55	7	11	1.27E-6	> 1.00E-4	> 1.00E-4			
MDA-MB-468	1.003	2.440	2.302	2.349	1.795	0.620	0.659	90	94	55	-38	-34	1.13E-6	3.89E-6	> 1.00E-4			



# One dose data of Compound 23



**NMR spectra (<sup>1</sup>H, <sup>13</sup>C) of compound (8-25)**

