

SUPPORTING INFORMATION

Structure-based design, synthesis and biological testing of etoposide analog epipodophyllotoxin-N-mustard hybrid compounds designed to covalently bind to topoisomerase II and DNA

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Arun A. Yadav, Xing Wu, Daywin Patel, Jack C. Yalowich and Brian B. Hasinoff*

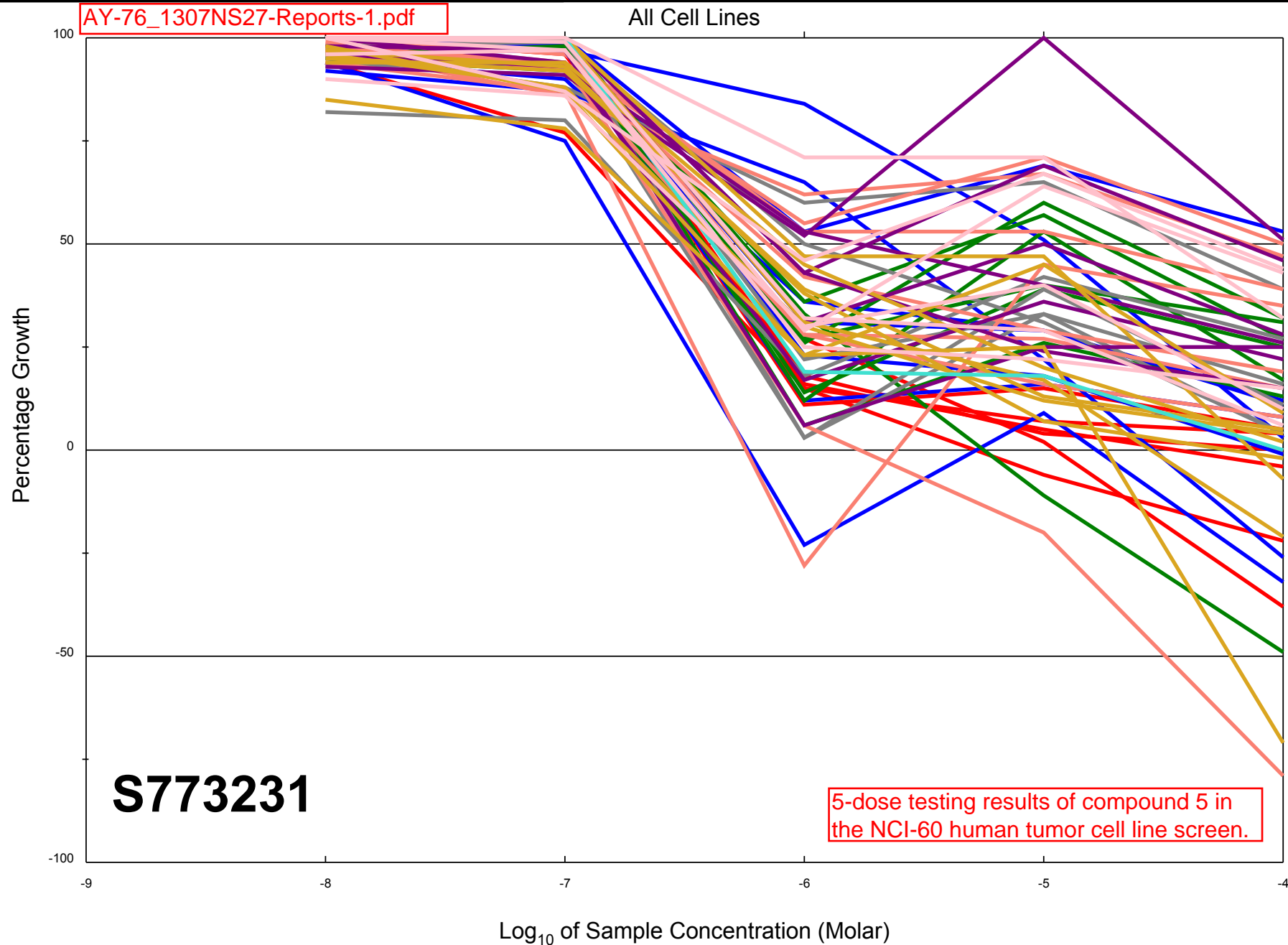
AUTHOR INFORMATION

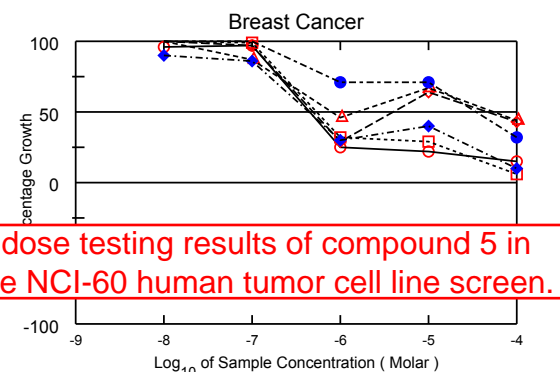
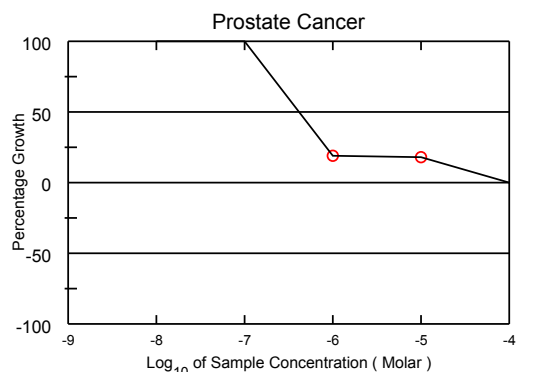
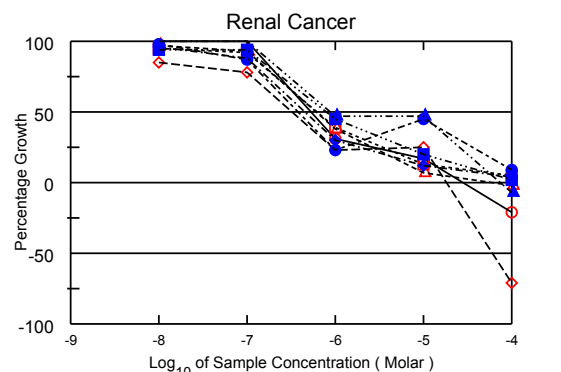
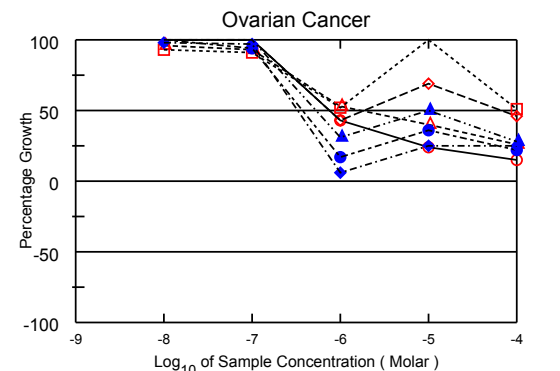
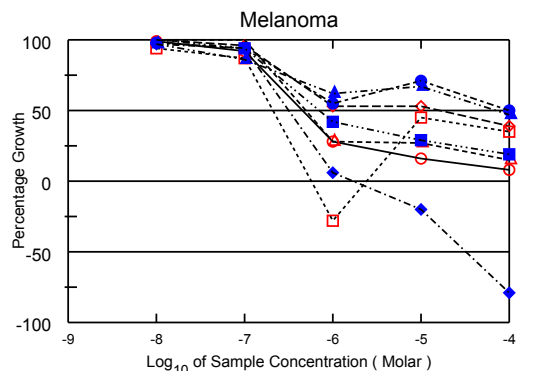
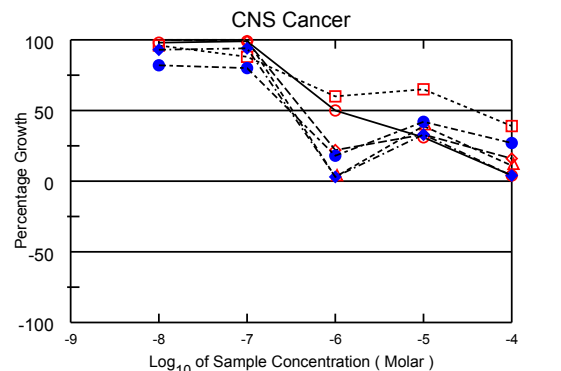
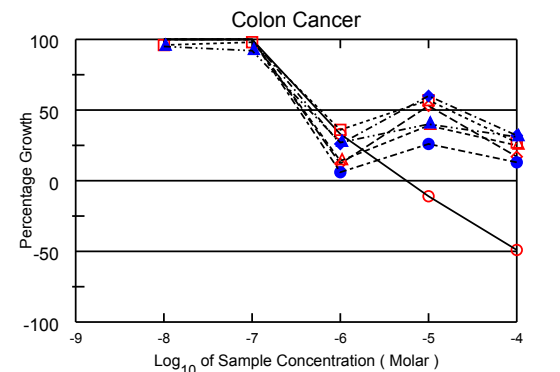
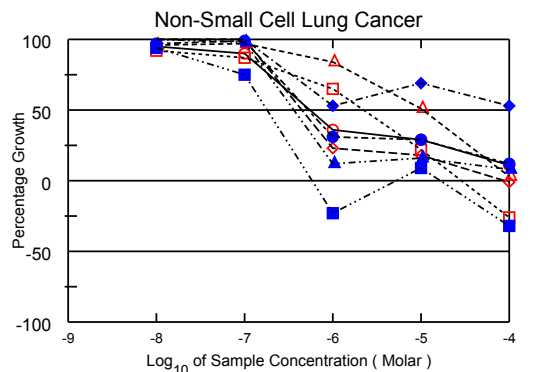
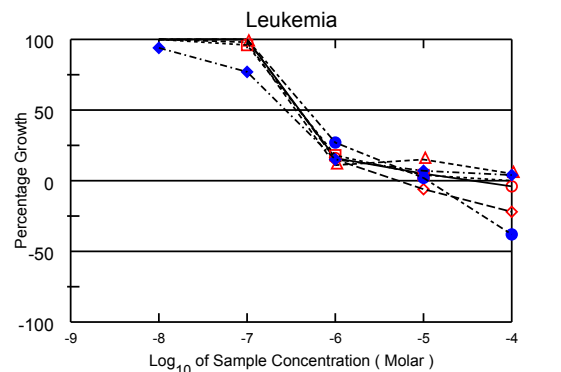
*Corresponding author

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5-dose testing results of compound 5 in the NCI-60 human tumor cell line screen.

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

NSC : D - 773231 / 1	Experiment ID : 1307NS27	Test Type : 08	Units : Molar
Report Date : September 19, 2013	Test Date : July 08, 2013	QNS :	MC :
COMI : AY-76 (128357)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0XMP	

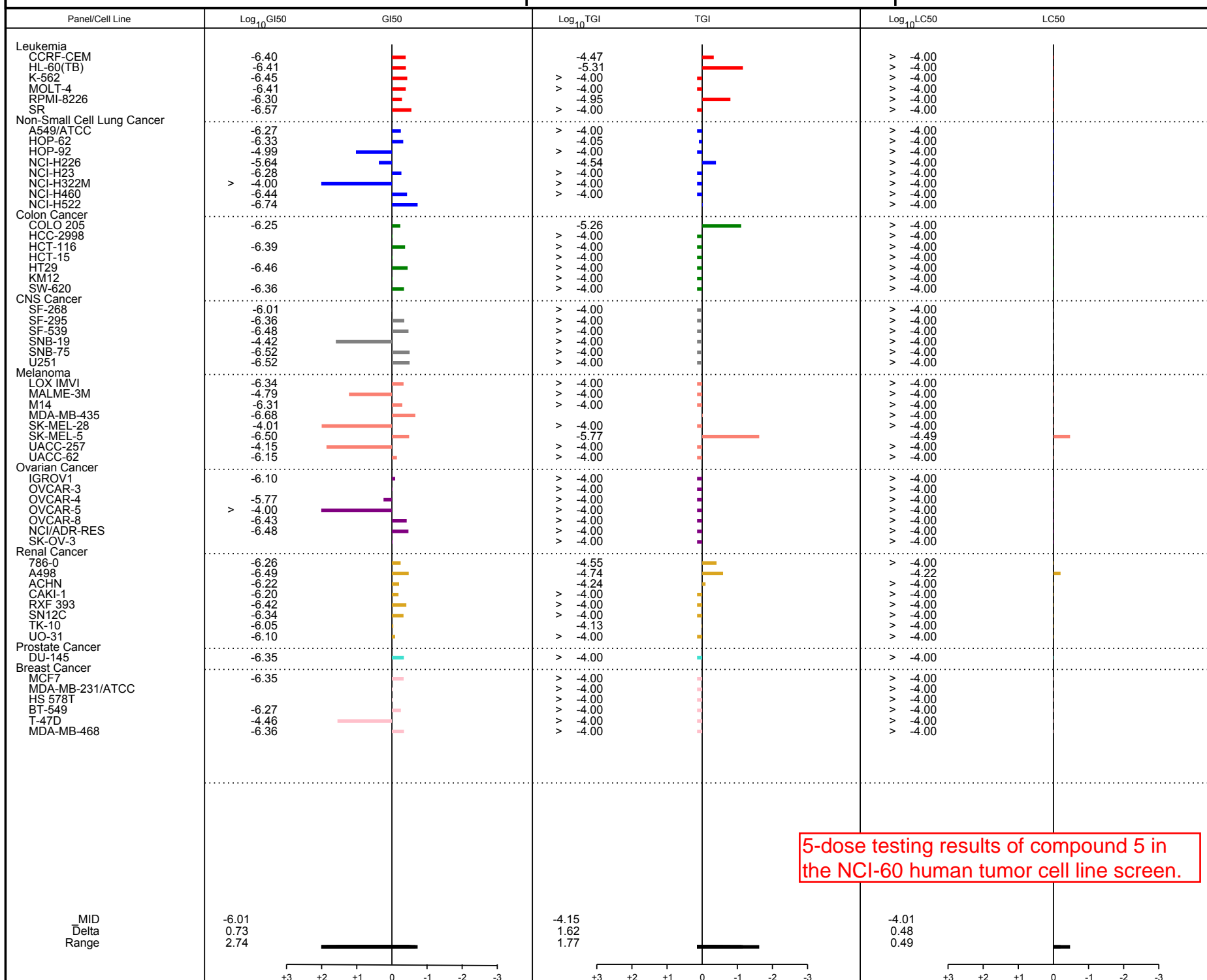
Panel/Cell Line	Log10 Concentration												GI50	TGI	LC50
	Time Zero	Ctrl	Mean Optical Densities					Percent Growth							
			-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0			
Leukemia															
CCRF-CEM	0.510	2.258	2.306	2.254	0.795	0.592	0.489	103	100	16	5	-4	3.95E-7	3.35E-5	> 1.00E-4
HL-60(TB)	1.003	3.414	3.455	3.437	1.358	0.938	0.785	102	101	15	-6	-22	3.90E-7	4.94E-6	> 1.00E-4
K-562	0.201	2.175	2.167	2.140	0.415	0.490	0.307	100	98	11	15	5	3.56E-7	> 1.00E-4	> 1.00E-4
MOLT-4	0.677	2.809	2.887	2.732	1.066	0.756	0.688	104	96	18	4	.	3.92E-7	> 1.00E-4	> 1.00E-4
RPMI-8226	0.757	2.212	2.310	2.267	1.153	0.787	0.469	107	104	27	2	-38	5.04E-7	1.12E-5	> 1.00E-4
SR	0.694	2.643	2.518	2.194	0.983	0.824	0.765	94	77	15	7	4	2.72E-7	> 1.00E-4	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.325	1.568	1.501	1.444	0.767	0.686	0.464	95	90	36	29	11	5.42E-7	> 1.00E-4	> 1.00E-4
HOP-62	0.354	0.991	1.020	1.021	0.498	0.471	0.351	105	105	23	18	-1	4.64E-7	8.89E-5	> 1.00E-4
HOP-92	1.159	1.632	1.614	1.618	1.558	1.398	1.172	96	97	84	51	3	1.03E-5	> 1.00E-4	> 1.00E-4
NCI-H226	0.795	2.104	1.998	1.929	1.652	1.089	0.588	92	87	65	22	-26	2.29E-6	2.90E-5	> 1.00E-4
NCI-H23	0.686	2.118	2.075	2.105	1.126	1.094	0.863	97	99	31	29	12	5.23E-7	> 1.00E-4	> 1.00E-4
NCI-H322M	0.742	1.809	1.815	1.845	1.307	1.483	1.312	101	103	53	69	53	> 1.00E-4	> 1.00E-4	> 1.00E-4
NCI-H460	0.330	3.123	3.134	3.060	0.666	0.766	0.553	100	98	12	16	8	5.61E-7	> 1.00E-4	> 1.00E-4
NCI-H522	0.637	1.303	1.260	1.138	0.491	0.694	0.436	94	75	-23	9	-32	1.80E-7	.	> 1.00E-4
Colon Cancer															
COLO 205	0.595	2.376	2.388	2.402	1.179	0.528	0.305	101	101	33	-11	-49	5.62E-7	5.53E-6	> 1.00E-4
HCC-2998	0.521	2.026	2.025	2.038	0.695	1.315	0.781	100	101	12	53	17	.	> 1.00E-4	> 1.00E-4
HCT-116	0.304	2.248	2.300	2.397	0.569	1.062	0.799	103	108	14	39	25	4.10E-7	> 1.00E-4	> 1.00E-4
HCT-15	0.248	1.749	1.694	1.713	0.787	1.107	0.655	96	98	36	57	27	.	> 1.00E-4	> 1.00E-4
HT29	0.248	1.256	1.263	1.279	0.304	0.514	0.380	101	102	6	26	13	3.47E-7	> 1.00E-4	> 1.00E-4
KM12	0.589	2.698	2.711	2.790	1.139	1.844	1.274	101	104	26	60	32	.	> 1.00E-4	> 1.00E-4
SW-620	0.282	2.307	2.207	2.152	0.821	1.086	0.901	95	92	27	40	31	4.41E-7	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	0.910	2.469	2.434	2.448	1.686	1.396	0.976	98	99	50	31	4	9.88E-7	> 1.00E-4	> 1.00E-4
SF-295	0.726	2.372	2.415	2.354	1.089	1.267	0.984	103	99	22	33	16	4.33E-7	> 1.00E-4	> 1.00E-4
SF-539	1.133	2.856	2.907	2.853	1.191	1.807	1.320	103	100	3	39	11	3.28E-7	> 1.00E-4	> 1.00E-4
SNB-19	0.825	2.257	2.206	2.079	1.682	1.757	1.388	96	88	60	65	39	3.84E-5	> 1.00E-4	> 1.00E-4
SNB-75	0.908	1.800	1.637	1.621	1.070	1.279	1.152	82	80	18	42	27	3.04E-7	> 1.00E-4	> 1.00E-4
U251	0.372	1.555	1.472	1.483	0.410	0.760	0.419	93	94	3	33	4	3.05E-7	> 1.00E-4	> 1.00E-4
Melanoma															
LOX IMVI	0.358	2.446	2.425	2.270	0.949	0.701	0.521	99	92	28	16	8	4.54E-7	> 1.00E-4	> 1.00E-4
MALME-3M	0.902	1.908	1.968	1.870	1.436	1.435	1.293	106	96	53	53	39	1.62E-5	> 1.00E-4	> 1.00E-4
M14	0.460	1.849	1.867	1.850	0.846	0.841	0.663	101	100	28	27	15	4.92E-7	> 1.00E-4	> 1.00E-4
MDA-MB-435	0.621	2.481	2.377	2.240	0.446	1.451	1.281	94	87	-28	45	35	2.10E-7	.	> 1.00E-4
SK-MEL-28	0.549	1.801	1.774	1.724	1.238	1.443	1.172	98	94	55	71	50	9.73E-5	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.725	3.118	3.056	2.968	0.867	0.582	0.156	97	94	6	-20	-79	3.15E-7	1.70E-6	3.27E-5
UACC-257	0.819	1.713	1.685	1.591	1.370	1.422	1.239	97	86	62	67	47	7.09E-5	> 1.00E-4	> 1.00E-4
UACC-62	0.928	2.805	2.820	2.688	1.717	1.472	1.279	101	94	42	29	19	7.01E-7	> 1.00E-4	> 1.00E-4
Ovarian Cancer															
IGROV1	0.717	2.099	2.240	2.235	1.312	1.052	0.931	110	110	43	24	15	7.86E-7	> 1.00E-4	> 1.00E-4
OVCAR-3	0.685	1.901	1.985	2.000	1.206	1.520	1.239	107	108	43	69	46	.	> 1.00E-4	> 1.00E-4
OVCAR-4	0.721	1.434	1.403	1.386	1.098	1.010	0.906	96	93	53	40	26	1.69E-6	> 1.00E-4	> 1.00E-4
OVCAR-5	0.704	1.487	1.433	1.418	1.111	1.532	1.103	93	91	52	106	51	> 1.00E-4	> 1.00E-4	> 1.00E-4
OVCAR-8	0.422	1.841	1.867	1.753	0.658	0.928	0.736	102	94	17	36	22	3.69E-7	> 1.00E-4	> 1.00E-4
NCI/ADR-RES	0.614	2.092	2.061	2.050	0.704	0.988	0.981	98	97	6	25	25	3.29E-7	> 1.00E-4	> 1.00E-4
SK-OV-3	0.807	1.994	2.042	2.047	1.174	1.406	1.141	104	104	31	50	28	.	> 1.00E-4	> 1.00E-4
Renal Cancer															
786-0	0.909	2.655	2.728	2.716	1.453	1.208	0.715	104	103	31	17	-21	5.49E-7	2.79E-5	> 1.00E-4
A498	1.589	2.523	2.383	2.315	1.808	1.821	0.469	85	78	23	25	-71	3.24E-7	1.82E-5	6.09E-5
ACHN	0.492	2.266	2.219	2.150	1.168	0.617	0.481	97	93	38	7	-2	6.09E-7	5.74E-5	> 1.00E-4
CAKI-1	0.741	2.494	2.405	2.359	1.433	0.964	0.825	95	92	39	13	5	6.32E-7	> 1.00E-4	> 1.00E-4
RXF 393	1.048	1.725	1.710	1.638	1.202	1.355	1.108	98	87	23	45	9	3.78E-7	> 1.00E-4	> 1.00E-4
SN12C	0.533	1.974	1.920	1.802	0.969	0.709	0.594	96	88	30	12	4	4.55E-7	> 1.00E-4	> 1.00E-4
TK-10	0.647	1.360	1.426	1.369	0.984	0.981	0.602	109	101	47	47	-7	8.89E-7	7.40E-5	> 1.00E-4
UO-31	0.822	2.198	2.122	2.114	1.441	1.102	0.848	94	94	45	20	2	7.89E-7	> 1.00E-4	> 1.00E-4
Prostate Cancer															
DU-145	0.499	1.911	2.002	1.998	0.774	0.748	0.504	106	106	19	18	.	4.44E-7	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.418	2.063	1.999	2.008	0.835	0.781	0.658	96	97	25	22	15	4.51E-7	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.593	1.465	1.473	1.435	0.846	1.155	0.971	101	97	29	64	43	.	> 1.00E-4	> 1.00E-4
HS 578T	1.412	2.666	2.691	2.508	1.992	2.252	1.966	102	87	46	67	44	.	> 1.00E-4	> 1.00E-4
BT-549	1.069	2.023	2.077	2.013	1.376	1.349	1.125	106	99	32	29	6	5.41E-7	> 1.00E-4	> 1.00E-4
T-47D	0.732	1.443	1.467	1.447	1.234	1.237	0.960	103	101	71	71	32	3.45E-5	> 1.00E-4	> 1.00E-4
MDA-MB-468	0.931	1.685	1.609	1.582	1.157	1.233	1.004	90	86	30	40	10	4.41E-7	> 1.00E-4	> 1.00E-4

5-dose testing results of compound 5 in the NCI-60 human tumor cell line screen.

Mean Graphs

Report Date :September 19, 2013

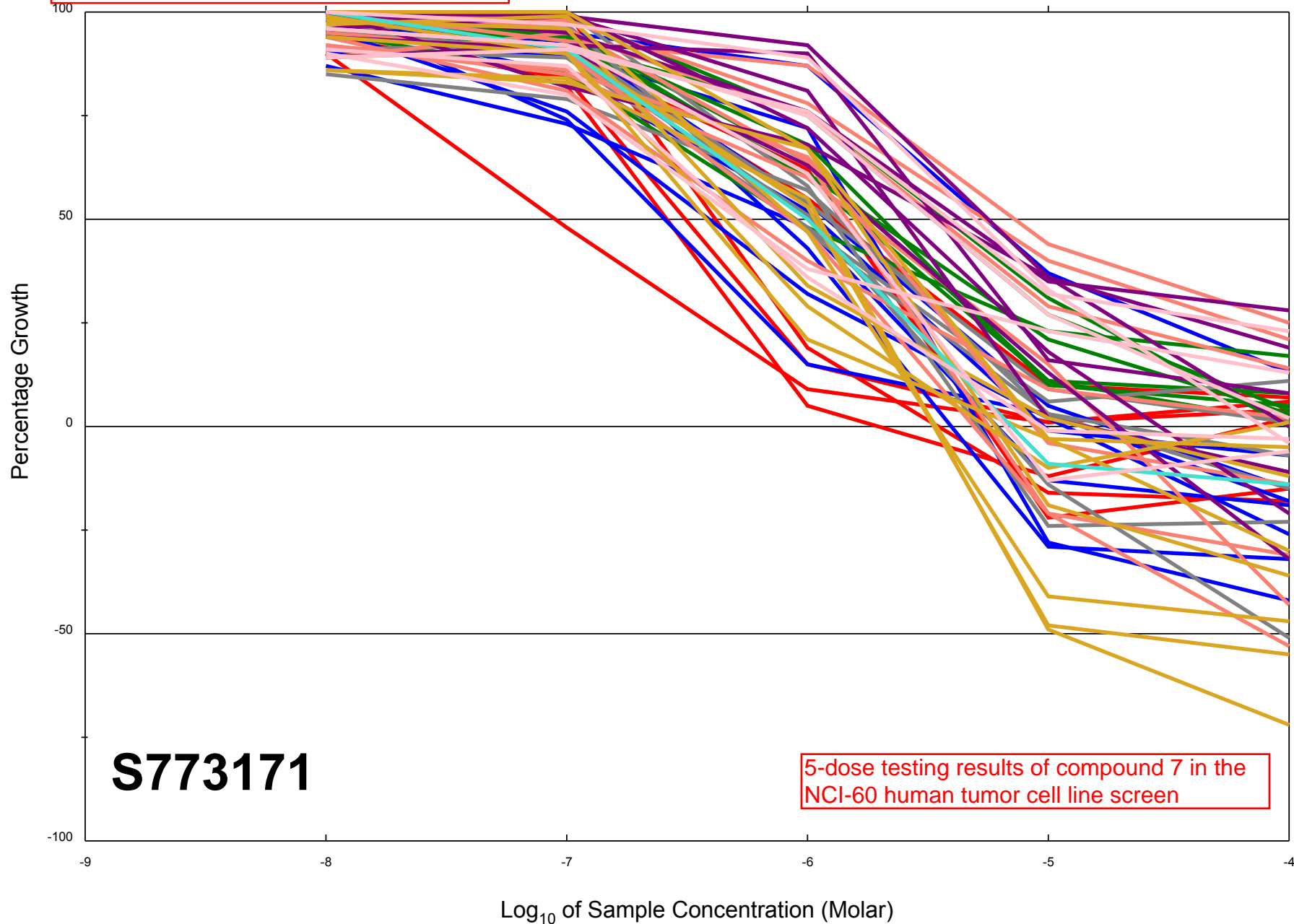
Test Date :July 08, 2013



5-dose testing results of compound 5 in the NCI-60 human tumor cell line screen.

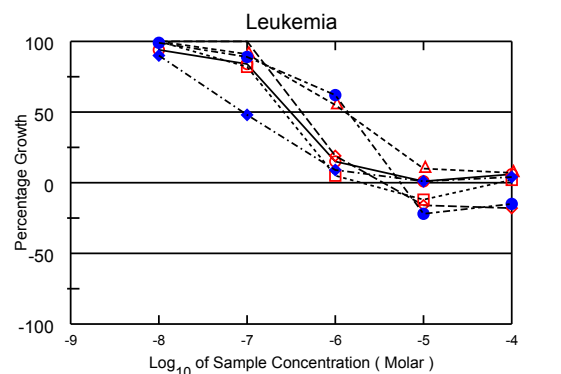
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All Cell Lines

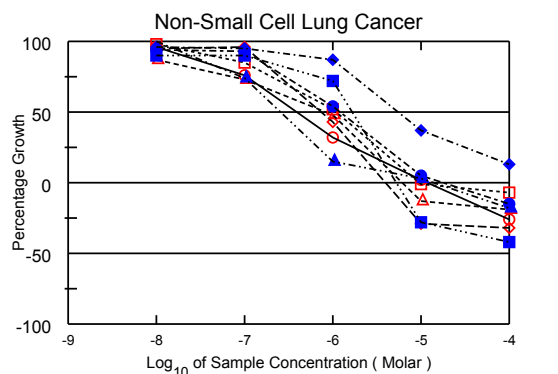


S773171

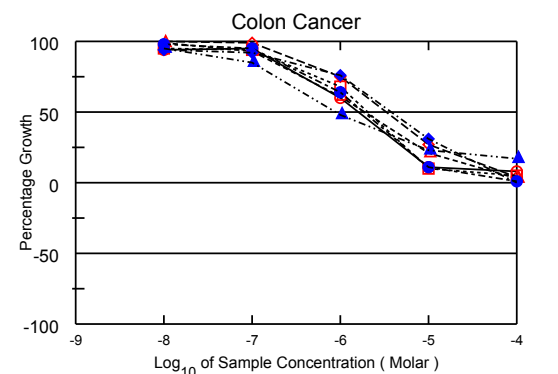
5-dose testing results of compound 7 in the
NCI-60 human tumor cell line screen



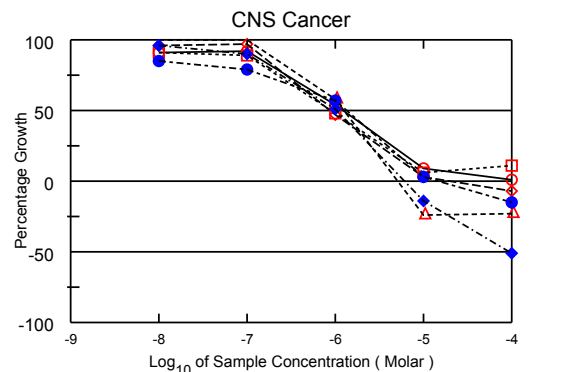
CCRF-CEM —○— HL-60(TB) —◇— K-562 —△—
MOLT-4 —□— RPMI-8226 —●— SR —◆—



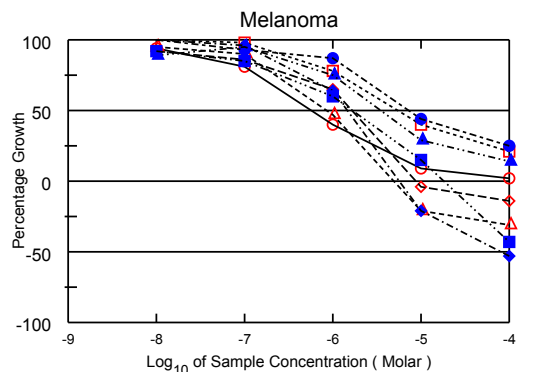
A549/ATCC —○— HOP-62 —◇— HOP-92 —△—
NCI-H226 —□— NCI-H23 —●— NCI-H322M —◆—
NCI-H460 —▲— NCI-H522 —■—



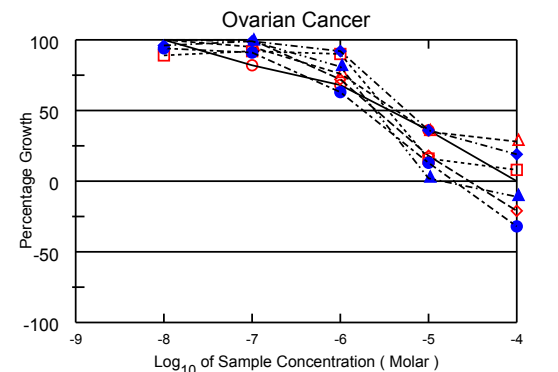
COLO 205 —○— HCC-2998 —◇— HCT-116 —△—
HCT-15 —□— HT29 —●— KM12 —◆—
SW-620 —▲—



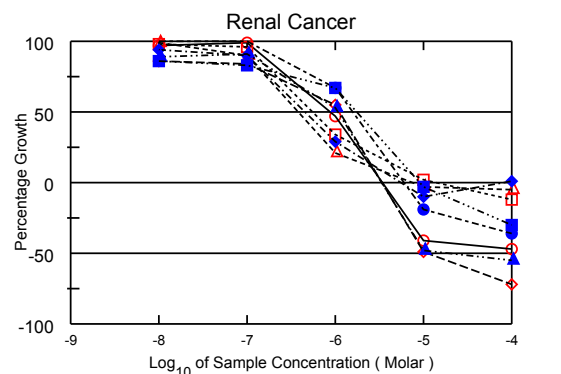
SF-268 —○— SF-295 —◇— SF-539 —△—
SNB-19 —□— SNB-75 —●— U251 —◆—



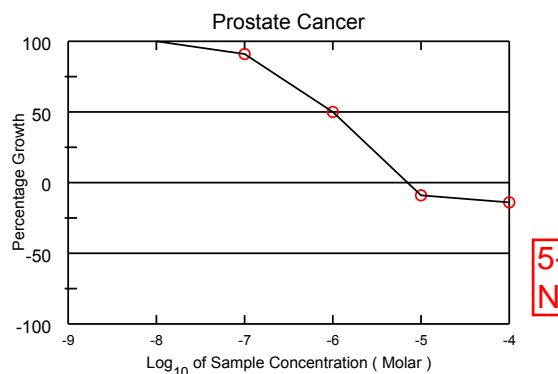
LOX IMVI —○— MALME-3M —◇— M14 —△—
MDA-MB-435 —□— SK-MEL-28 —●— SK-MEL-5 —◆—
UACC-257 —▲— UACC-62 —■—



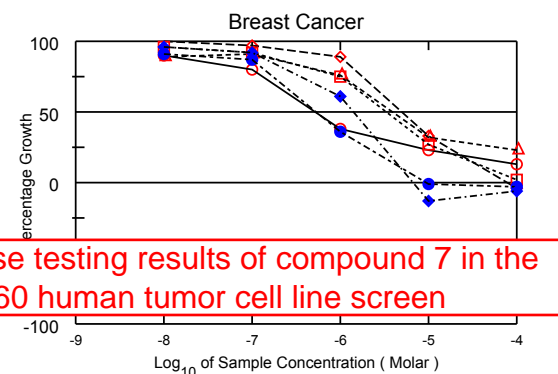
IGROV1 —○— OVCAR-3 —◇— OVCAR-4 —△—
OVCAR-5 —□— OVCAR-8 —●— NCI/ADR-RES —◆—
SK-OV-3 —▲—



786-0 —○— A498 —◇— ACHN —△—
CAKI-1 —□— RXF 393 —●— SN12C —◆—
TK-10 —▲— UO-31 —■—



DU-145 —○—



MCF7 —○— MDA-MB-231 —◇— HS 578T —△—
BT-549 —□— T-47D —●— MDA-MB-468 —◆—

5-dose testing results of compound 7 in the NCI-60 human tumor cell line screen

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

NSC : D - 773171 / 1	Experiment ID : 1307NS27	Test Type : 08	Units : Molar
Report Date : September 19, 2013	Test Date : July 08, 2013	QNS :	MC :
COMI : AY-54-chlorambucil (127849)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0XMP	

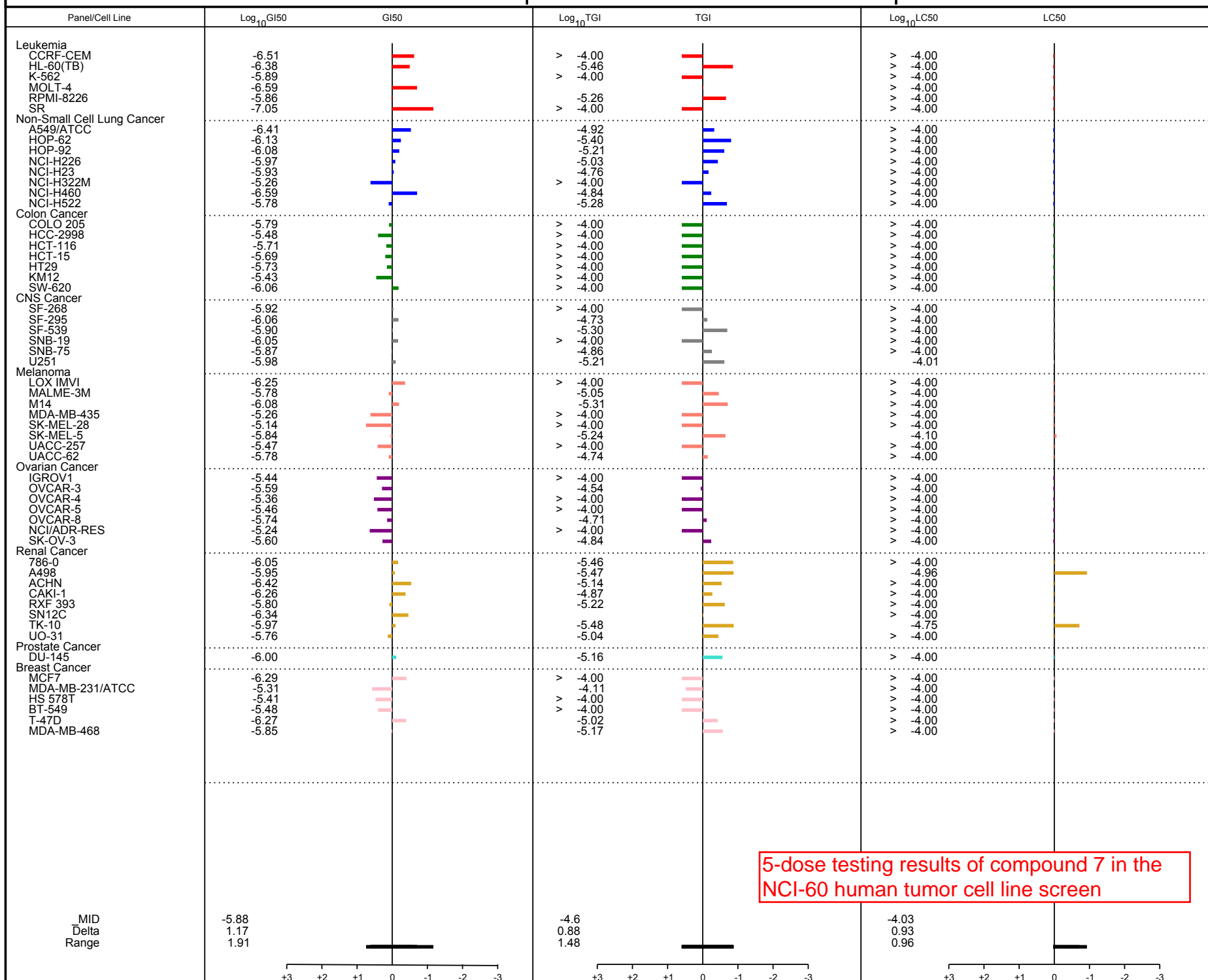
Panel/Cell Line	Log10 Concentration												GI50	TGI	LC50
	Time Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0			
Leukemia															
CCRF-CEM	0.510	2.242	2.137	1.965	0.774	0.522	0.613	94	84	15	1	6	3.12E-7	> 1.00E-4	> 1.00E-4
HL-60(TB)	1.003	3.415	3.469	3.416	1.468	0.841	0.819	102	100	19	-16	-18	4.16E-7	3.50E-6	> 1.00E-4
K-562	0.201	2.254	2.262	2.069	1.332	0.411	0.336	100	91	55	10	7	1.30E-6	> 1.00E-4	> 1.00E-4
MOLT-4	0.677	2.831	2.837	2.436	0.782	0.595	0.726	100	82	5	-12	2	2.58E-7	.	> 1.00E-4
RPMI-8226	0.757	2.278	2.262	2.112	1.697	0.594	0.644	99	89	62	-22	-15	1.39E-6	5.52E-6	> 1.00E-4
SR	0.694	2.640	2.437	1.624	0.870	0.719	0.764	90	48	9	1	4	8.85E-8	> 1.00E-4	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.325	1.558	1.503	1.262	0.715	0.352	0.240	96	76	32	2	-26	3.85E-7	1.19E-5	> 1.00E-4
HOP-62	0.354	0.973	0.942	0.945	0.622	0.251	0.240	95	96	43	-29	-32	7.42E-7	3.95E-6	> 1.00E-4
HOP-92	1.159	1.598	1.541	1.480	1.370	1.012	0.944	87	73	48	-13	-19	8.28E-7	6.18E-6	> 1.00E-4
NCI-H226	0.795	2.035	2.013	1.844	1.435	0.784	0.737	98	85	52	-1	-7	1.07E-6	9.39E-6	> 1.00E-4
NCI-H23	0.686	2.121	2.036	2.014	1.455	0.755	0.581	94	93	54	5	-15	1.19E-6	1.73E-5	> 1.00E-4
NCI-H322M	0.742	1.887	1.841	1.828	1.741	1.162	0.890	96	95	87	37	13	5.45E-6	> 1.00E-4	> 1.00E-4
NCI-H460	0.330	3.144	3.139	2.422	0.752	0.428	0.271	100	74	15	3	-18	2.57E-7	1.45E-5	> 1.00E-4
NCI-H522	0.637	1.371	1.295	1.296	1.164	0.457	0.370	90	90	72	-28	-42	1.65E-6	5.21E-6	> 1.00E-4
Colon Cancer															
COLO 205	0.595	2.354	2.250	2.261	1.656	0.789	0.737	94	95	60	11	8	1.62E-6	> 1.00E-4	> 1.00E-4
HCC-2998	0.521	2.060	2.110	2.049	1.671	0.942	0.589	103	99	75	27	4	3.32E-6	> 1.00E-4	> 1.00E-4
HCT-116	0.304	2.262	2.247	2.120	1.507	0.723	0.353	99	93	61	21	3	1.93E-6	> 1.00E-4	> 1.00E-4
HCT-15	0.248	1.736	1.663	1.642	1.265	0.396	0.330	95	94	68	10	5	2.06E-6	> 1.00E-4	> 1.00E-4
HT29	0.248	1.253	1.230	1.205	0.894	0.364	0.262	98	95	64	11	1	1.86E-6	> 1.00E-4	> 1.00E-4
KM12	0.589	2.672	2.547	2.511	2.168	1.229	0.595	94	92	76	31	.	3.74E-6	> 1.00E-4	> 1.00E-4
SW-620	0.282	2.281	2.178	1.975	1.235	0.751	0.618	95	85	48	23	17	8.66E-7	> 1.00E-4	> 1.00E-4
CNS Cancer															
SF-268	0.910	2.503	2.364	2.380	1.766	1.047	0.919	91	92	54	9	1	1.21E-6	> 1.00E-4	> 1.00E-4
SF-295	0.726	2.386	2.324	2.341	1.505	0.772	0.673	96	97	47	3	-7	8.70E-7	1.88E-5	> 1.00E-4
SF-539	1.133	2.922	2.958	2.939	2.171	0.858	0.869	102	101	58	-24	-23	1.25E-6	5.07E-6	> 1.00E-4
SNB-19	0.825	2.202	2.079	2.056	1.485	0.911	0.975	91	89	48	6	11	8.91E-7	> 1.00E-4	> 1.00E-4
SNB-75	0.908	1.797	1.662	1.610	1.416	0.931	0.770	85	79	57	3	-15	1.35E-6	1.39E-5	> 1.00E-4
U251	0.372	1.517	1.471	1.405	0.959	0.321	0.184	96	90	51	-14	-51	1.05E-6	6.15E-6	9.67E-5
Melanoma															
LOX IMVI	0.358	2.567	2.441	2.139	1.240	0.552	0.412	94	81	40	9	2	5.65E-7	> 1.00E-4	> 1.00E-4
MALME-3M	0.902	1.937	1.856	1.796	1.572	0.869	0.775	92	86	65	-4	-14	1.64E-6	8.84E-6	> 1.00E-4
M14	0.460	1.880	1.809	1.744	1.123	0.364	0.317	95	90	47	-21	-31	8.39E-7	4.91E-6	> 1.00E-4
MDA-MB-435	0.621	2.448	2.457	2.405	2.041	1.355	1.011	101	98	78	40	21	5.47E-6	> 1.00E-4	> 1.00E-4
SK-MEL-28	0.549	1.772	1.767	1.691	1.616	1.088	0.850	100	93	87	44	25	7.28E-6	> 1.00E-4	> 1.00E-4
SK-MEL-5	0.725	3.122	3.127	3.025	2.254	0.575	0.340	100	96	64	-21	-53	1.46E-6	5.69E-6	8.02E-5
UACC-257	0.819	1.706	1.611	1.660	1.481	1.073	0.941	89	95	75	29	14	3.42E-6	> 1.00E-4	> 1.00E-4
UACC-62	0.928	2.813	2.660	2.533	2.054	1.213	0.531	92	85	60	15	-43	1.65E-6	1.82E-5	> 1.00E-4
Ovarian Cancer															
IGROV1	0.717	2.121	2.138	1.872	1.671	1.219	0.719	101	82	68	36	.	3.61E-6	> 1.00E-4	> 1.00E-4
OVCAR-3	0.685	1.874	1.948	1.988	1.540	0.904	0.539	106	110	72	18	-21	2.56E-6	2.90E-5	> 1.00E-4
OVCAR-4	0.721	1.436	1.457	1.398	1.264	0.974	0.925	103	95	76	35	28	4.34E-6	> 1.00E-4	> 1.00E-4
OVCAR-5	0.704	1.516	1.423	1.449	1.434	0.834	0.772	89	92	90	16	8	3.46E-6	> 1.00E-4	> 1.00E-4
OVCAR-8	0.422	1.863	1.780	1.732	1.333	0.611	0.287	94	91	63	13	-32	1.84E-6	1.95E-5	> 1.00E-4
NCI/ADR-RES	0.614	2.138	2.081	2.121	2.022	1.170	0.909	96	99	92	36	19	5.72E-6	> 1.00E-4	> 1.00E-4
SK-OV-3	0.807	2.009	2.037	2.001	1.783	0.834	0.715	102	99	81	2	-11	2.48E-6	1.45E-5	> 1.00E-4
Renal Cancer															
786-0	0.909	2.722	2.665	2.697	1.770	0.536	0.478	97	99	47	-41	-47	8.93E-7	3.44E-6	> 1.00E-4
A498	1.589	2.518	2.391	2.371	2.098	0.809	0.444	86	84	55	-49	-72	1.11E-6	3.37E-6	1.10E-5
ACHN	0.492	2.133	2.121	1.964	0.833	0.476	0.466	99	90	21	-3	-5	3.76E-7	7.26E-6	> 1.00E-4
CAKI-1	0.741	2.456	2.428	2.383	1.321	0.772	0.653	98	96	34	2	-12	5.47E-7	1.35E-5	> 1.00E-4
RXF 393	1.048	1.727	1.739	1.726	1.504	0.845	0.675	102	100	67	-19	-36	1.58E-6	5.97E-6	> 1.00E-4
SN12C	0.533	1.916	1.836	1.772	0.940	0.482	0.547	94	90	29	-10	1	4.55E-7	.	> 1.00E-4
TK-10	0.647	1.365	1.288	1.301	1.026	0.335	0.291	89	91	53	-48	-55	1.06E-6	3.32E-6	1.79E-5
UO-31	0.822	2.329	2.111	2.068	1.835	0.796	0.579	86	83	67	-3	-30	1.75E-6	9.02E-6	> 1.00E-4
Prostate Cancer															
DU-145	0.499	1.905	1.915	1.783	1.204	0.453	0.427	101	91	50	-9	-14	1.00E-6	6.97E-6	> 1.00E-4
Breast Cancer															
MCF7	0.418	2.079	1.920	1.754	1.045	0.795	0.641	90	80	38	23	13	5.16E-7	> 1.00E-4	> 1.00E-4
MDA-MB-231/ATCC	0.593	1.409	1.436	1.382	1.317	0.861	0.569	103	97	89	33	-4	4.93E-6	7.73E-5	> 1.00E-4
HS 578T	1.412	2.681	2.543	2.566	2.379	1.819	1.703	89	91	76	32	23	3.92E-6	> 1.00E-4	> 1.00E-4
BT-549	1.069	2.116	2.072	2.031	1.857	1.349	1.088	96	92	75	27	2	3.31E-6	> 1.00E-4	> 1.00E-4
T-47D	0.732	1.498	1.429	1.398	1.008	0.726	0.714	91	87	36	-1	-3	5.31E-7	9.50E-6	> 1.00E-4
MDA-MB-468	0.931	1.577	1.553	1.528	1.327	0.814	0.876	96	92	61	-13	-6	1.42E-6	6.75E-6	> 1.00E-4

5-dose testing results of compound 7 in the
NCI-60 human tumor cell line screen

Mean Graphs

Report Date :September 19, 2013

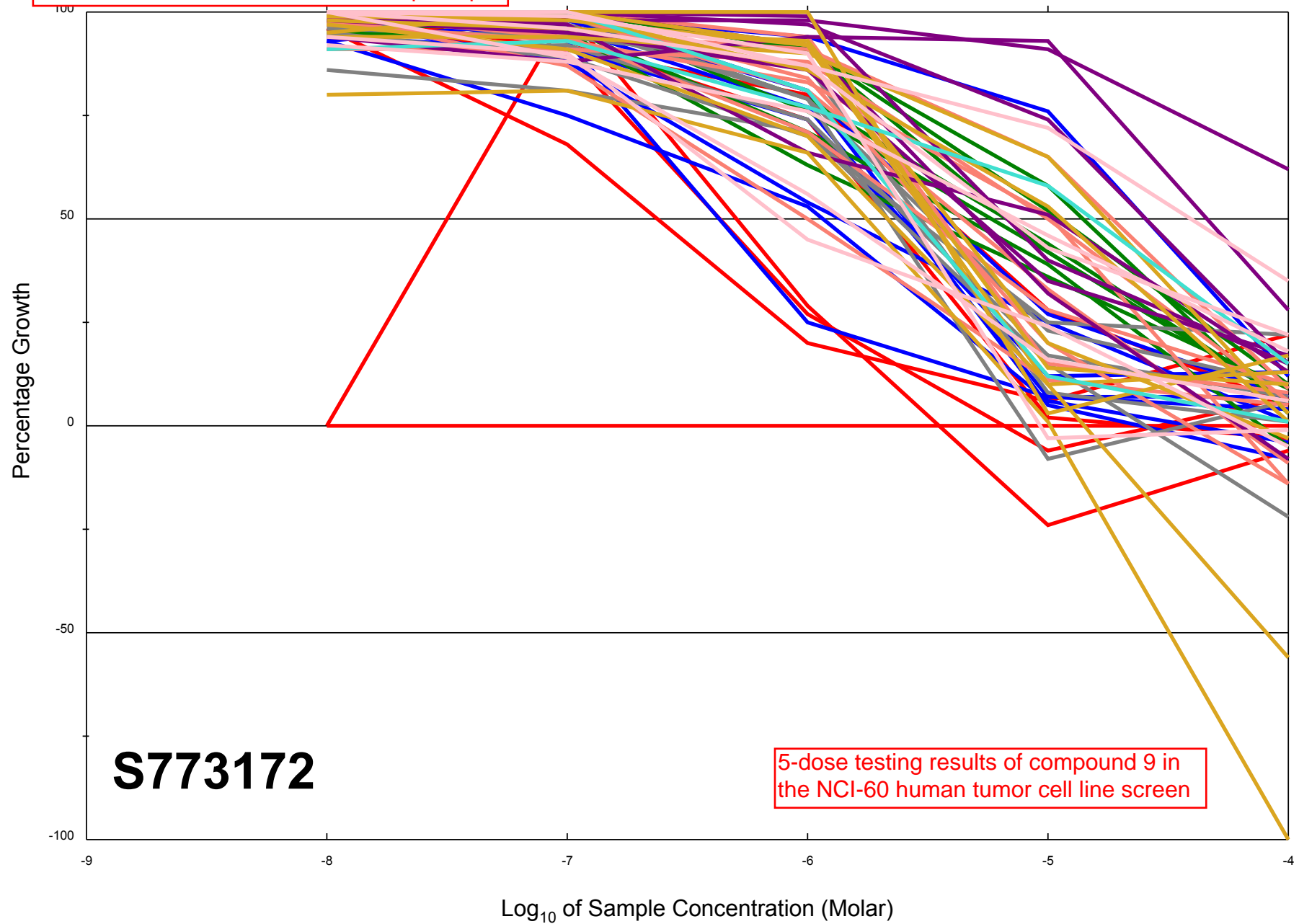
Test Date :July 08, 2013

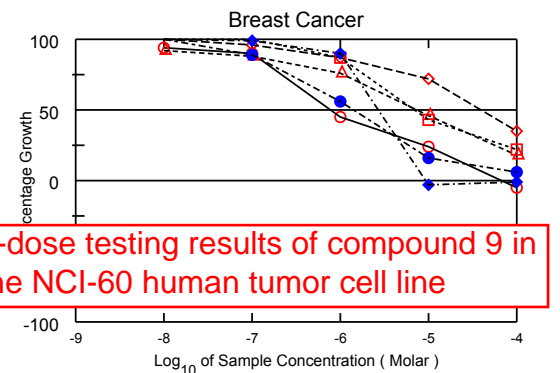
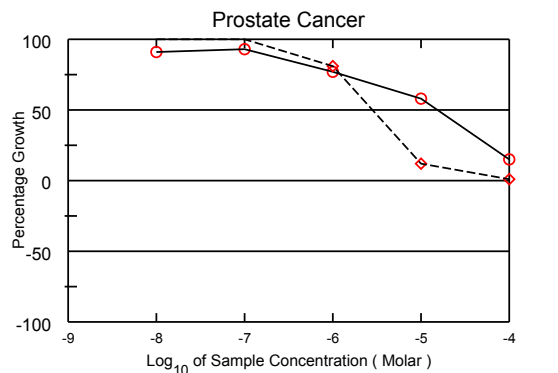
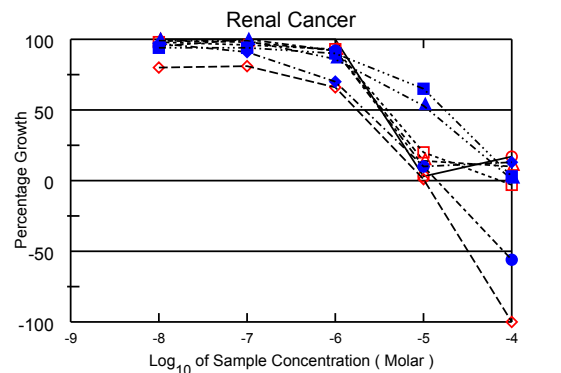
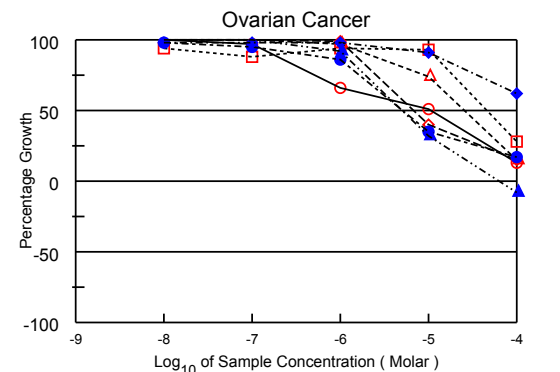
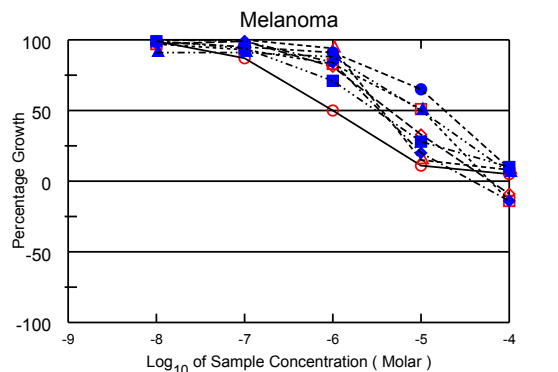
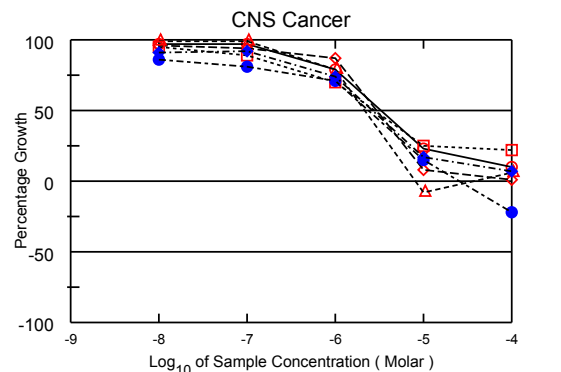
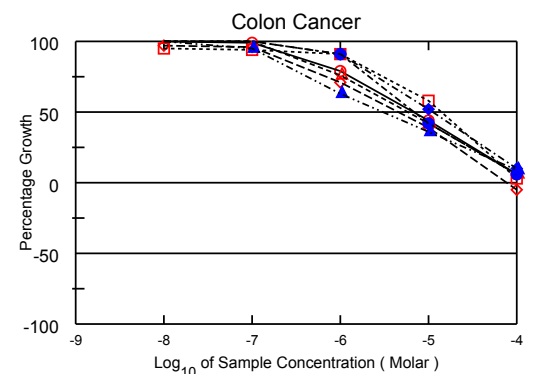
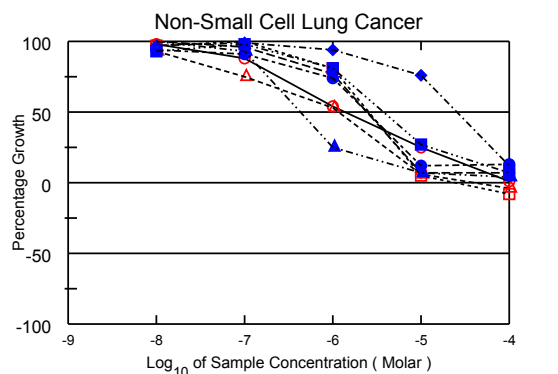
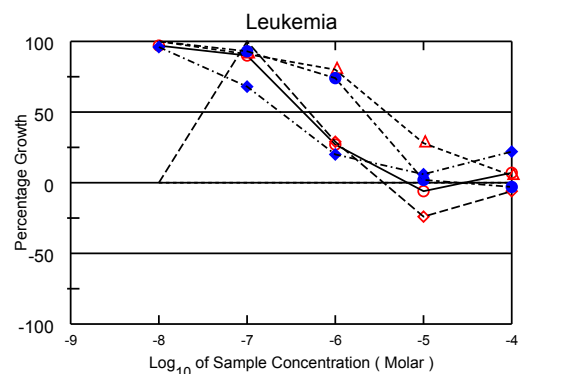


5-dose testing results of compound 7 in the NCI-60 human tumor cell line screen

AY-68-bendamustine_1307NS30-Reports.pdf

All Cell Lines





5-dose testing results of compound 9 in the NCI-60 human tumor cell line

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

NSC : D - 773172 / 1	Experiment ID : 1307NS30	Test Type : 08	Units : Molar
Report Date : September 19, 2013	Test Date : July 15, 2013	QNS :	MC :
COMI : AY-68-bendamustine (127850)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0XMP	

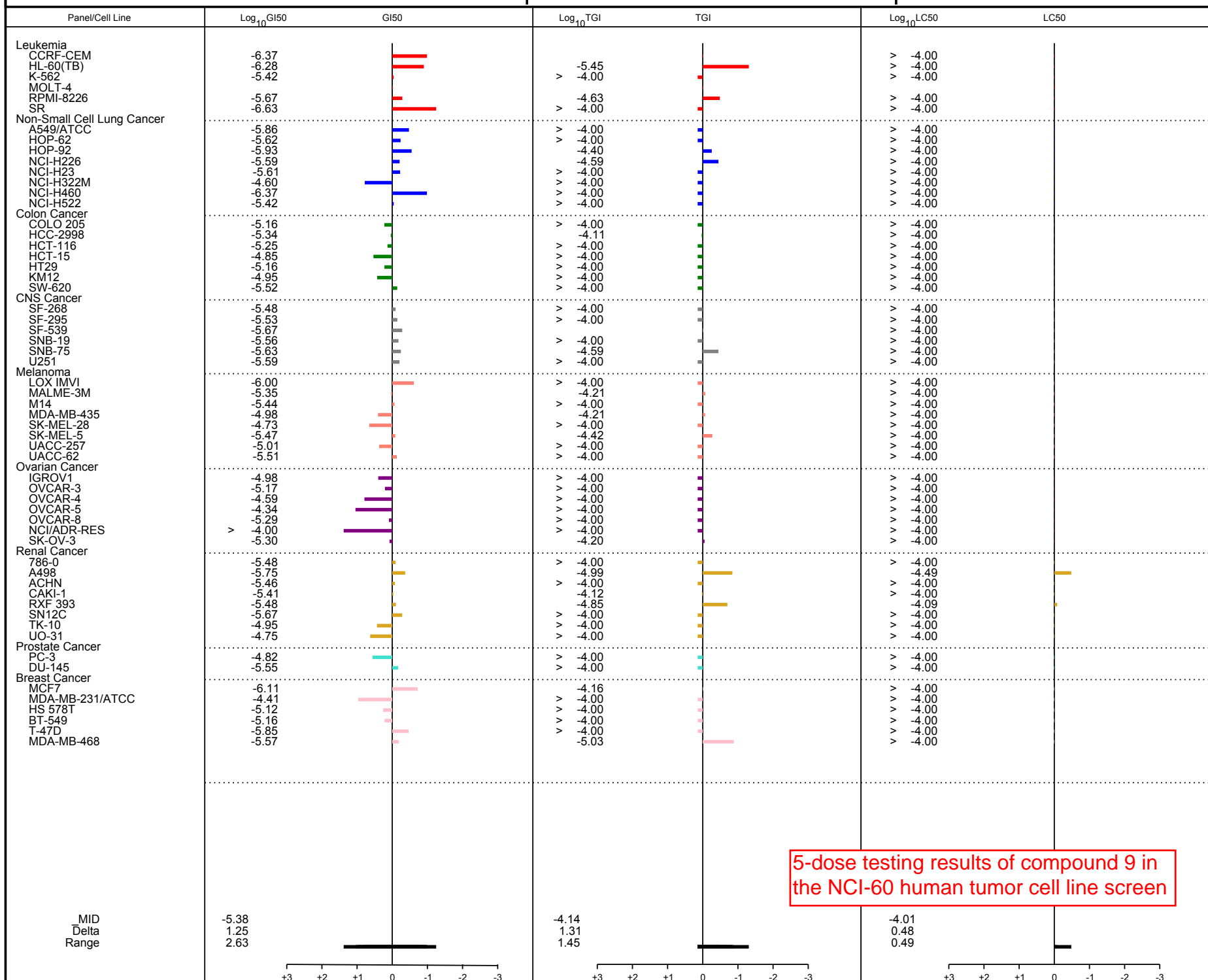
Panel/Cell Line	Time Zero	Log10 Concentration											GI50	TGI	LC50	
		Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0				
Leukemia																
CCRF-CEM	0.357	1.855	1.807	1.702	0.755	0.336	0.462	97	90	27	-6	7	4.26E-7	.	.	> 1.00E-4
HL-60(TB)	0.775	1.967	.	2.014	1.118	0.589	0.732	.	104	29	-24	-6	5.22E-7	3.51E-6	.	> 1.00E-4
K-562	0.261	2.311	2.405	2.122	1.909	0.829	0.371	105	91	80	28	5	3.77E-6	> 1.00E-4	> 1.00E-4	
MOLT-4	0.770	2.818
RPMI-8226	0.835	2.615	2.623	2.491	2.148	0.872	0.806	100	93	74	2	-3	2.15E-6	2.35E-5	.	> 1.00E-4
SR	0.258	1.079	1.047	0.814	0.420	0.311	0.441	96	68	20	6	22	2.34E-7	> 1.00E-4	> 1.00E-4	
Non-Small Cell Lung Cancer																
A549/ATCC	0.375	1.878	1.843	1.704	1.190	0.745	0.389	98	88	54	25	1	1.39E-6	> 1.00E-4	> 1.00E-4	
HOP-62	0.280	0.742	0.745	0.724	0.635	0.310	0.314	101	96	77	7	7	2.41E-6	> 1.00E-4	> 1.00E-4	
HOP-92	1.014	1.498	1.465	1.377	1.271	1.043	0.974	93	75	53	6	-4	1.17E-6	3.97E-5	.	> 1.00E-4
NCI-H226	0.871	2.068	2.037	2.092	1.838	0.936	0.803	97	102	81	5	-8	2.56E-6	2.57E-5	.	> 1.00E-4
NCI-H23	0.737	2.287	2.199	2.147	1.890	0.929	0.946	94	91	74	12	13	2.47E-6	> 1.00E-4	> 1.00E-4	
NCI-H322M	0.530	1.605	1.576	1.594	1.546	1.343	0.654	97	99	94	76	12	2.51E-5	> 1.00E-4	> 1.00E-4	
NCI-H460	0.267	2.801	2.839	2.636	0.891	0.445	0.360	102	93	25	7	4	4.28E-7	> 1.00E-4	> 1.00E-4	
NCI-H522	0.743	1.833	1.755	1.812	1.626	1.039	0.819	93	98	81	27	7	3.76E-6	> 1.00E-4	> 1.00E-4	
Colon Cancer																
COLO 205	0.523	2.133	2.140	2.120	1.800	1.239	0.614	100	99	79	44	6	6.94E-6	> 1.00E-4	> 1.00E-4	
HCC-2998	0.960	3.072	3.007	2.986	2.458	1.789	0.913	97	96	71	39	-5	4.58E-6	7.73E-5	.	> 1.00E-4
HCT-116	0.283	2.193	2.351	2.311	1.732	1.076	0.397	108	106	76	42	6	5.66E-6	> 1.00E-4	> 1.00E-4	
HCT-15	0.342	2.224	2.127	2.111	2.048	1.442	0.405	95	94	91	58	3	1.42E-5	> 1.00E-4	> 1.00E-4	
HT29	0.226	1.424	1.420	1.487	1.314	0.732	0.300	100	105	91	42	6	6.91E-6	> 1.00E-4	> 1.00E-4	
KM12	0.573	2.808	2.881	2.867	2.611	1.734	0.795	103	103	91	52	10	1.11E-5	> 1.00E-4	> 1.00E-4	
SW-620	0.386	2.747	2.756	2.624	1.872	1.231	0.599	100	95	63	36	9	2.99E-6	> 1.00E-4	> 1.00E-4	
CNS Cancer																
SF-268	0.734	2.205	2.166	2.158	1.903	1.073	0.885	97	97	79	23	10	3.33E-6	> 1.00E-4	> 1.00E-4	
SF-295	0.677	2.091	2.028	2.002	1.911	0.796	0.693	96	94	87	8	1	2.97E-6	> 1.00E-4	> 1.00E-4	
SF-539	1.065	2.837	2.819	2.826	2.464	0.985	1.179	99	99	79	-8	6	2.16E-6	.	> 1.00E-4	
SNB-19	0.790	2.178	2.109	2.021	1.762	1.132	1.099	95	89	70	25	22	2.76E-6	> 1.00E-4	> 1.00E-4	
SNB-75	0.774	1.464	1.365	1.334	1.261	0.879	0.604	86	81	71	15	-22	2.36E-6	2.57E-5	.	> 1.00E-4
U251	0.406	1.700	1.578	1.600	1.357	0.620	0.499	91	92	74	17	7	2.59E-6	> 1.00E-4	> 1.00E-4	
Melanoma																
LOX IMVI	0.305	2.223	2.198	1.965	1.265	0.510	0.408	99	87	50	11	5	1.00E-6	> 1.00E-4	> 1.00E-4	
MALME-3M	0.509	1.249	1.230	1.239	1.109	0.757	0.463	97	99	81	33	-9	4.49E-6	6.10E-5	.	> 1.00E-4
M14	0.578	2.334	2.370	2.351	2.233	0.835	0.715	102	101	94	15	8	3.59E-6	> 1.00E-4	> 1.00E-4	
MDA-MB-435	0.538	2.205	2.154	2.091	1.927	1.396	0.465	97	93	83	51	-14	1.05E-5	6.17E-5	.	> 1.00E-4
SK-MEL-28	0.542	1.781	1.768	1.716	1.663	1.350	0.653	99	95	91	65	9	1.87E-5	> 1.00E-4	> 1.00E-4	
SK-MEL-5	0.757	2.650	2.682	2.638	2.350	1.136	0.649	102	99	84	20	-14	3.41E-6	3.83E-5	.	> 1.00E-4
UACC-257	0.880	1.944	1.854	1.844	1.817	1.408	0.946	91	91	88	50	6	9.75E-6	> 1.00E-4	> 1.00E-4	
UACC-62	0.900	2.705	2.684	2.599	2.184	1.406	1.081	99	94	71	28	10	3.09E-6	> 1.00E-4	> 1.00E-4	
Ovarian Cancer																
IGROV1	0.339	1.458	1.484	1.420	1.082	0.906	0.480	102	97	66	51	13	1.04E-5	> 1.00E-4	> 1.00E-4	
OVCAR-3	0.767	2.075	2.128	2.166	2.064	1.285	0.962	104	107	99	40	15	6.69E-6	> 1.00E-4	> 1.00E-4	
OVCAR-4	0.957	1.440	1.469	1.470	1.425	1.317	1.028	106	106	97	74	15	2.56E-5	> 1.00E-4	> 1.00E-4	
OVCAR-5	0.663	1.384	1.342	1.300	1.338	1.332	0.868	94	88	94	93	28	4.62E-5	> 1.00E-4	> 1.00E-4	
OVCAR-8	0.483	2.161	2.133	2.077	1.924	1.079	0.774	98	95	86	35	17	5.15E-6	> 1.00E-4	> 1.00E-4	
NCI/ADR-RES	0.727	2.206	2.173	2.175	2.182	2.066	1.645	98	98	98	91	62	> 1.00E-4	> 1.00E-4	> 1.00E-4	
SK-OV-3	0.491	1.001	1.029	1.028	0.960	0.652	0.453	106	105	92	32	-8	4.96E-6	6.36E-5	.	> 1.00E-4
Renal Cancer																
786-0	0.934	2.797	2.818	2.916	2.830	0.982	1.247	101	106	102	3	17	3.32E-6	> 1.00E-4	> 1.00E-4	
A498	1.622	2.546	2.361	2.368	2.235	1.634	-0.005	80	81	66	1	-100	1.78E-6	1.03E-5	.	3.21E-5
ACHN	0.337	1.845	1.827	1.808	1.728	0.555	0.482	99	98	92	14	10	3.49E-6	> 1.00E-4	> 1.00E-4	
CAKI-1	0.684	2.443	2.402	2.367	2.323	1.031	0.666	98	96	93	20	-3	3.87E-6	7.57E-5	.	> 1.00E-4
RXF 393	0.920	1.521	1.489	1.542	1.475	0.982	0.404	95	103	92	10	-56	3.28E-6	1.43E-5	.	8.10E-5
SN12C	0.746	2.558	2.502	2.402	2.014	0.929	0.979	97	91	70	10	13	2.16E-6	> 1.00E-4	> 1.00E-4	
TK-10	0.742	1.768	1.758	1.762	1.622	1.284	0.749	99	99	86	53	1	1.13E-5	> 1.00E-4	> 1.00E-4	
UO-31	0.533	1.960	1.875	1.872	1.814	1.467	0.574	94	94	90	65	3	1.76E-5	> 1.00E-4	> 1.00E-4	
Prostate Cancer																
PC-3	0.537	1.485	1.398	1.415	1.263	1.085	0.675	91	93	77	58	15	1.51E-5	> 1.00E-4	> 1.00E-4	
DU-145	0.390	1.560	1.651	1.627	1.332	0.536	0.405	108	106	81	12	1	2.81E-6	> 1.00E-4	> 1.00E-4	
Breast Cancer																
MCF7	0.461	2.120	2.018	1.949	1.211	0.865	0.440	94	90	45	24	-5	7.81E-7	6.95E-5	.	> 1.00E-4
MDA-MB-231/ATCC	0.505	1.212	1.217	1.186	1.121	1.014	0.749	101	96	87	72	35	3.87E-5	> 1.00E-4	> 1.00E-4	
HS 578T	1.186	2.364	2.271	2.220	2.084	1.733	1.395	92	88	76	46	18	7.58E-6	> 1.00E-4	> 1.00E-4	
BT-549	1.186	2.141	2.171	2.187	2.019	1.595	1.401	103	105	87	43	22	6.87E-6	> 1.00E-4	> 1.00E-4	
T-47D	0.584	1.370	1.372	1.280	1.026	0.707	0.629	100	89	56	16	6	1.43E-6	> 1.00E-4	> 1.00E-4	
MDA-MB-468	0.766	1.275	1.283	1.269	1.225	0.745	0.760	101	99	90	-3	-1	2.70E-6	9.33E-6	.	> 1.00E-4

5-dose testing results of compound 9 in the
NCI-60 human tumor cell line screen

Mean Graphs

Report Date :September 19, 2013

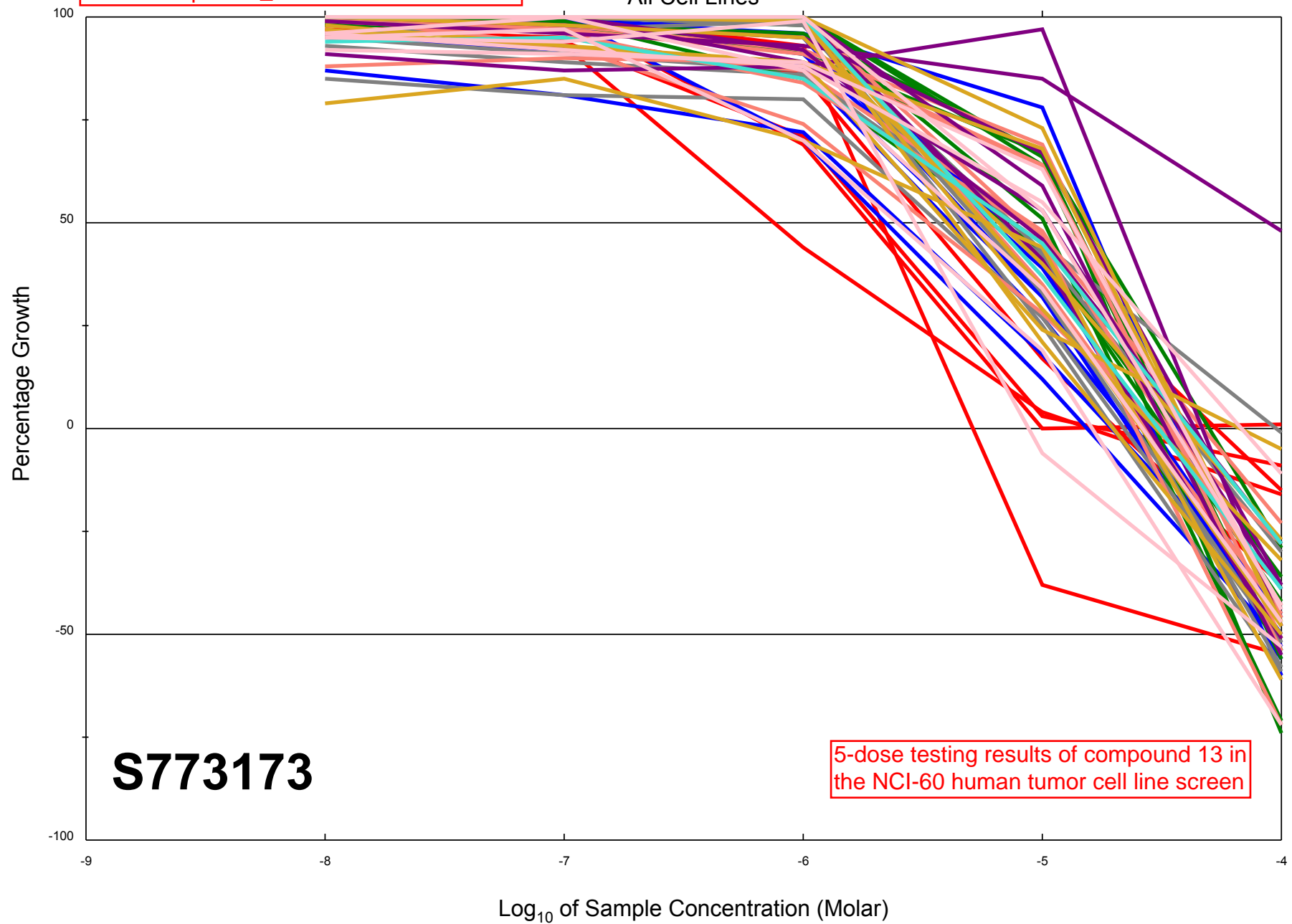
Test Date :July 15, 2013



5-dose testing results of compound 9 in the NCI-60 human tumor cell line screen

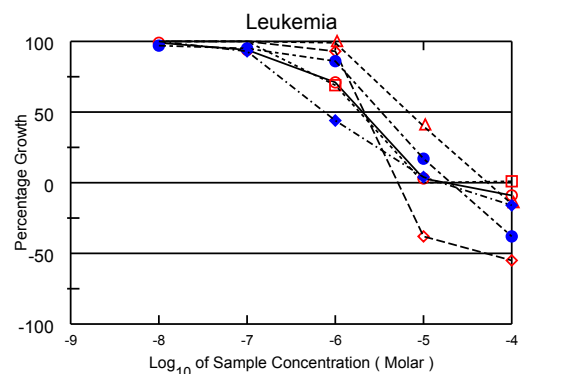
AY-70-melphalan_1307NS30-

All Cell Lines

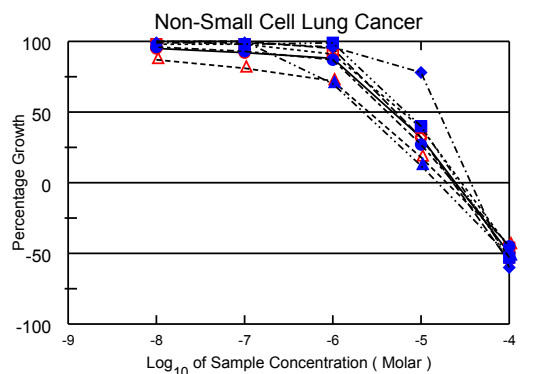


S773173

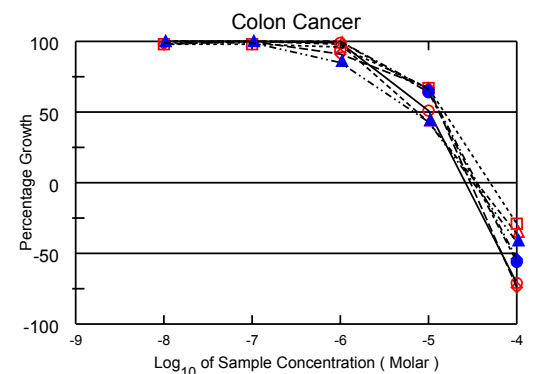
5-dose testing results of compound 13 in the NCI-60 human tumor cell line screen



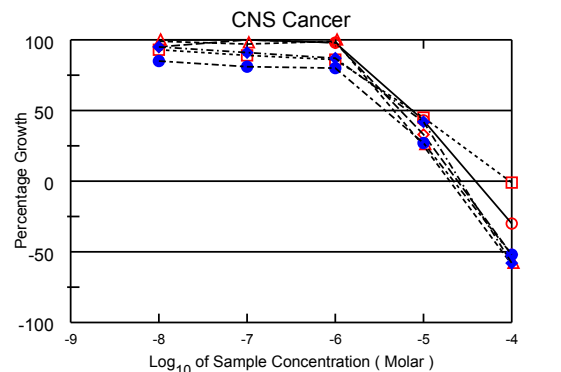
CCRF-CEM —○— HL-60(TB) —◇— K-562 —△—
MOLT-4 —□— RPMI-8226 —●— SR —◆—



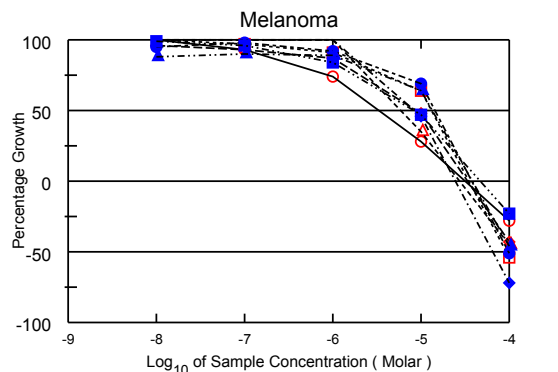
A549/ATCC —○— HOP-62 —◇— HOP-92 —△—
NCI-H226 —□— NCI-H23 —●— NCI-H322M —◆—
NCI-H460 —▲— NCI-H522 —■—



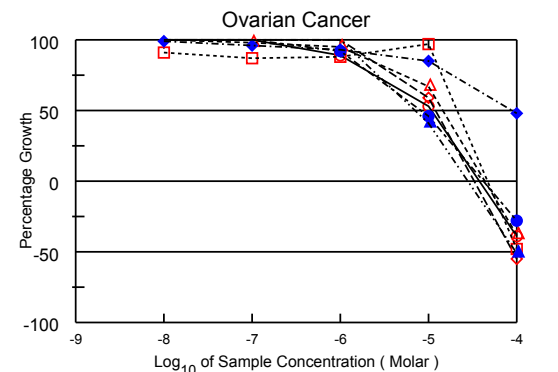
COLO 205 —○— HCC-2998 —◇— HCT-116 —△—
HCT-15 —□— HT29 —●— KM12 —◆—
SW-620 —▲—



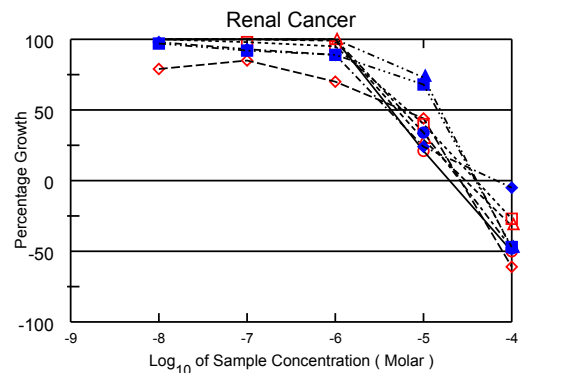
SF-268 —○— SF-295 —◇— SF-539 —△—
SNB-19 —□— SNB-75 —●— U251 —◆—



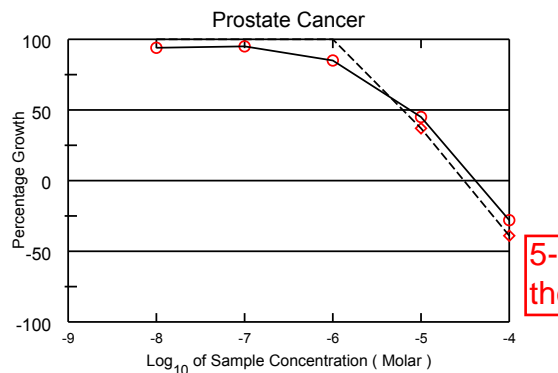
LOX IMVI —○— MALME-3M —◇— M14 —△—
MDA-MB-435 —□— SK-MEL-28 —●— SK-MEL-5 —◆—
UACC-257 —▲— UACC-62 —■—



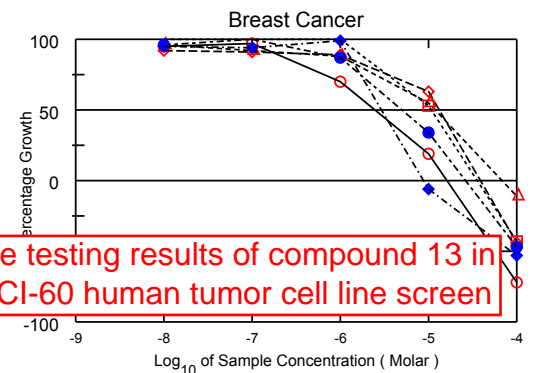
IGROV1 —○— OVCAR-3 —◇— OVCAR-4 —△—
OVCAR-5 —□— OVCAR-8 —●— NCI/ADR-RES —◆—
SK-OV-3 —▲—



786-0 —○— A498 —◇— ACHN —△—
CAKI-1 —□— RXF 393 —●— SN12C —◆—
TK-10 —▲— UO-31 —■—



PC-3 —○— DU-145 —◇—



MCF7 —○— MDA-MB-231 —◇— HS 578T —△—
BT-549 —□— T-47D —●— MDA-MB-468 —◆—

5-dose testing results of compound 13 in the NCI-60 human tumor cell line screen

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

NSC : D - 773173 / 1	Experiment ID : 1307NS30	Test Type : 08	Units : Molar
Report Date : September 19, 2013	Test Date : July 15, 2013	QNS :	MC :
COMI : AY-70-melphalan (127851)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0XMP	

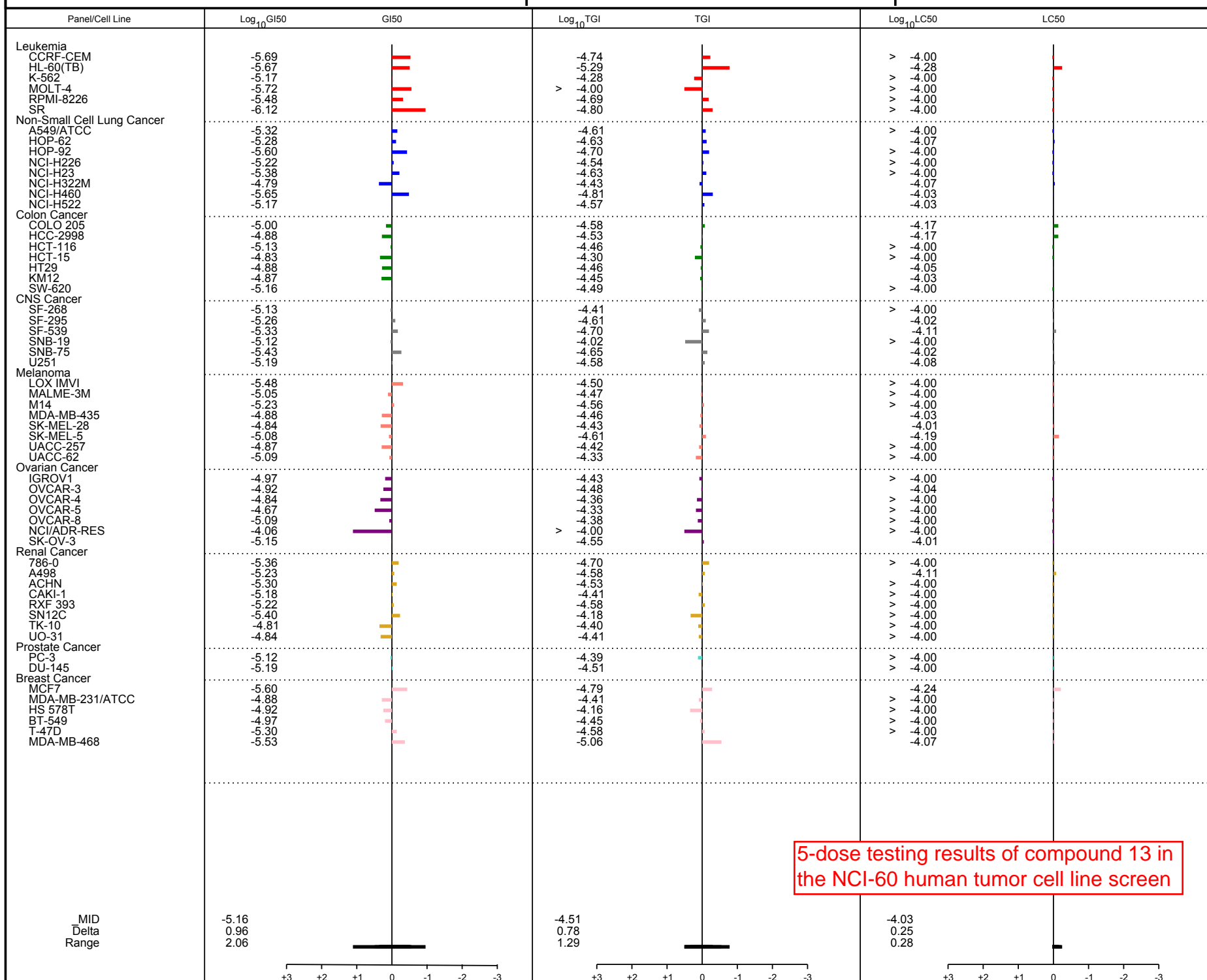
Panel/Cell Line	Log10 Concentration												GI50	TGI	LC50
	Time Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0			
Leukemia															
CCRF-CEM	0.357	1.930	1.920	1.841	1.468	0.409	0.324	99	94	71	3	-9	2.02E-6	1.82E-5	> 1.00E-4
HL-60(TB)	0.775	2.054	2.160	2.102	1.959	0.484	0.350	108	104	93	-38	-55	2.12E-6	5.15E-6	5.25E-5
K-562	0.261	2.328	2.478	2.440	2.314	1.084	0.221	107	105	99	40	-15	6.75E-6	5.27E-5	> 1.00E-4
MOLT-4	0.770	2.872	3.021	2.974	2.227	0.770	0.787	107	105	69	.	1	1.90E-6	> 1.00E-4	> 1.00E-4
RPMI-8226	0.835	2.716	2.661	2.626	2.447	1.151	0.521	97	95	86	17	-38	3.30E-6	2.04E-5	> 1.00E-4
SR	0.258	1.109	1.107	1.046	0.633	0.290	0.218	100	93	44	4	-16	7.54E-7	1.57E-5	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.375	1.935	1.852	1.804	1.753	0.874	0.189	95	92	88	32	-50	4.79E-6	2.46E-5	> 1.00E-4
HOP-62	0.280	0.714	0.731	0.713	0.692	0.420	0.124	104	100	95	32	-56	5.21E-6	2.32E-5	8.57E-5
HOP-92	1.014	1.541	1.474	1.442	1.391	1.111	0.571	87	81	72	18	-44	2.54E-6	1.97E-5	> 1.00E-4
NCI-H226	0.871	2.143	2.123	2.124	2.033	1.363	0.474	98	98	91	39	-46	6.09E-6	2.88E-5	> 1.00E-4
NCI-H23	0.737	2.379	2.315	2.265	2.173	1.183	0.403	96	93	87	27	-45	4.18E-6	2.37E-5	> 1.00E-4
NCI-H322M	0.530	1.631	1.622	1.625	1.590	1.392	0.214	99	99	96	78	-60	1.60E-5	3.69E-5	8.50E-5
NCI-H460	0.267	2.744	2.804	2.840	2.009	0.567	0.129	102	104	70	12	-52	2.23E-6	1.55E-5	9.41E-5
NCI-H522	0.743	1.751	1.774	1.733	1.744	1.146	0.349	102	98	99	40	-53	6.78E-6	2.69E-5	9.26E-5
Colon Cancer															
COLO 205	0.523	2.153	2.260	2.248	2.136	1.348	0.154	107	106	99	51	-71	1.01E-5	2.61E-5	6.76E-5
HCC-2998	0.960	3.115	3.069	3.115	2.928	2.403	0.249	98	100	91	67	-74	1.32E-5	2.98E-5	6.75E-5
HCT-116	0.283	2.276	2.425	2.357	2.243	1.140	0.181	107	104	98	43	-36	7.46E-6	3.50E-5	> 1.00E-4
HCT-15	0.342	2.243	2.201	2.198	2.174	1.609	0.245	98	98	96	67	-29	1.50E-5	5.02E-5	> 1.00E-4
HT29	0.226	1.426	1.517	1.468	1.435	0.994	0.101	108	103	101	64	-56	1.31E-5	3.43E-5	8.99E-5
KM12	0.573	2.766	2.811	2.880	2.863	2.013	0.265	102	105	104	66	-54	1.35E-5	3.55E-5	9.30E-5
SW-620	0.386	2.711	2.679	2.690	2.372	1.395	0.224	99	99	85	43	-42	6.97E-6	3.22E-5	> 1.00E-4
CNS Cancer															
SF-268	0.734	2.162	2.175	2.204	2.139	1.348	0.512	101	103	98	43	-30	7.48E-6	3.86E-5	> 1.00E-4
SF-295	0.677	2.143	2.067	2.144	2.118	1.159	0.328	95	100	98	33	-52	5.48E-6	2.45E-5	9.59E-5
SF-539	1.065	2.822	2.797	2.769	2.811	1.509	0.437	99	97	99	25	-59	4.64E-6	2.00E-5	7.83E-5
SNB-19	0.790	2.299	2.192	2.139	2.083	1.468	0.782	93	89	86	45	-1	7.50E-6	9.48E-5	> 1.00E-4
SNB-75	0.774	1.525	1.412	1.383	1.372	0.979	0.374	85	81	80	27	-52	3.67E-6	2.21E-5	9.52E-5
U251	0.406	1.728	1.665	1.605	1.551	0.956	0.173	95	91	87	42	-58	6.51E-6	2.63E-5	8.40E-5
Melanoma															
LOX IMVI	0.305	2.444	2.452	2.300	1.886	0.899	0.221	100	93	74	28	-28	3.30E-6	3.18E-5	> 1.00E-4
MALME-3M	0.509	1.302	1.270	1.243	1.199	0.889	0.290	96	93	87	48	-43	8.86E-6	3.36E-5	> 1.00E-4
M14	0.578	2.310	2.344	2.362	2.313	1.189	0.320	102	103	100	35	-45	5.92E-6	2.76E-5	> 1.00E-4
MDA-MB-435	0.538	2.219	2.219	2.169	2.069	1.621	0.249	100	97	91	64	-54	1.32E-5	3.51E-5	9.28E-5
SK-MEL-28	0.542	1.792	1.732	1.767	1.694	1.402	0.263	95	98	92	69	-51	1.43E-5	3.73E-5	9.72E-5
SK-MEL-5	0.757	2.678	2.678	2.720	2.677	1.635	0.210	100	102	100	46	-72	8.33E-6	2.44E-5	6.47E-5
UACC-257	0.880	2.002	1.869	1.885	1.876	1.598	0.474	88	90	89	64	-46	1.34E-5	3.81E-5	> 1.00E-4
UACC-62	0.900	2.864	2.843	2.787	2.547	1.814	0.697	99	96	84	47	-23	8.07E-6	4.72E-5	> 1.00E-4
Ovarian Cancer															
IGROV1	0.339	1.466	1.522	1.479	1.346	0.932	0.207	105	101	89	53	-39	1.07E-5	3.75E-5	> 1.00E-4
OVCAR-3	0.767	2.066	2.177	2.277	2.191	1.534	0.346	109	116	110	59	-55	1.20E-5	3.30E-5	9.05E-5
OVCAR-4	0.957	1.483	1.554	1.471	1.459	1.311	0.597	113	98	95	67	-38	1.46E-5	4.37E-5	> 1.00E-4
OVCAR-5	0.663	1.423	1.357	1.327	1.331	1.402	0.346	91	87	88	97	-48	2.12E-5	4.68E-5	> 1.00E-4
OVCAR-8	0.483	2.182	2.175	2.196	2.054	1.262	0.346	100	101	92	46	-28	8.15E-6	4.15E-5	> 1.00E-4
NCI/ADR-RES	0.727	2.360	2.341	2.288	2.244	2.120	1.510	99	96	93	85	48	8.80E-5	> 1.00E-4	> 1.00E-4
SK-OV-3	0.491	1.014	1.038	1.034	1.021	0.706	0.240	105	104	101	41	-51	7.12E-6	2.79E-5	9.72E-5
Renal Cancer															
786-0	0.934	2.751	2.771	2.830	2.795	1.313	0.470	101	104	102	21	-50	4.39E-6	1.97E-5	> 1.00E-4
A498	1.622	2.649	2.437	2.498	2.342	2.074	0.629	79	85	70	44	-61	5.88E-6	2.62E-5	7.82E-5
ACHN	0.337	1.795	1.811	1.790	1.787	0.754	0.229	101	100	99	29	-32	4.99E-6	2.95E-5	> 1.00E-4
CAKI-1	0.684	2.417	2.437	2.390	2.337	1.375	0.497	101	98	95	40	-27	6.57E-6	3.92E-5	> 1.00E-4
RXF 393	0.920	1.535	1.532	1.556	1.573	1.131	0.480	100	103	106	34	-48	6.05E-6	2.62E-5	> 1.00E-4
SN12C	0.746	2.675	2.634	2.550	2.467	1.214	0.707	98	93	89	24	-5	4.01E-6	6.65E-5	> 1.00E-4
TK-10	0.742	1.776	1.813	1.832	1.831	1.493	0.390	104	105	105	73	-48	1.54E-5	4.02E-5	> 1.00E-4
UO-31	0.533	1.997	1.948	1.883	1.838	1.530	0.281	97	92	89	68	-47	1.43E-5	3.89E-5	> 1.00E-4
Prostate Cancer															
PC-3	0.537	1.543	1.480	1.489	1.396	0.990	0.385	94	95	85	45	-28	7.51E-6	4.10E-5	> 1.00E-4
DU-145	0.390	1.624	1.670	1.710	1.687	0.850	0.236	104	107	105	37	-39	6.49E-6	3.06E-5	> 1.00E-4
Breast Cancer															
MCF7	0.461	2.096	2.015	2.046	1.612	0.775	0.129	95	97	70	19	-72	2.50E-6	1.62E-5	5.72E-5
MDA-MB-231/ATCC	0.505	1.310	1.246	1.239	1.218	1.013	0.281	92	91	89	63	-44	1.32E-5	3.87E-5	> 1.00E-4
HS 578T	1.186	2.332	2.288	2.236	2.200	1.821	1.059	96	92	88	55	-11	1.21E-5	6.88E-5	> 1.00E-4
BT-549	1.186	2.088	2.110	2.152	2.102	1.665	0.678	102	107	102	53	-43	1.08E-5	3.58E-5	> 1.00E-4
T-47D	0.584	1.323	1.291	1.338	1.223	0.836	0.312	96	102	87	34	-47	4.98E-6	2.65E-5	> 1.00E-4
MDA-MB-468	0.766	1.336	1.305	1.300	1.331	0.720	0.358	95	94	99	-6	-53	2.93E-6	8.77E-6	8.50E-5

5-dose testing results of compound 13 in the NCI-60 human tumor cell line screen

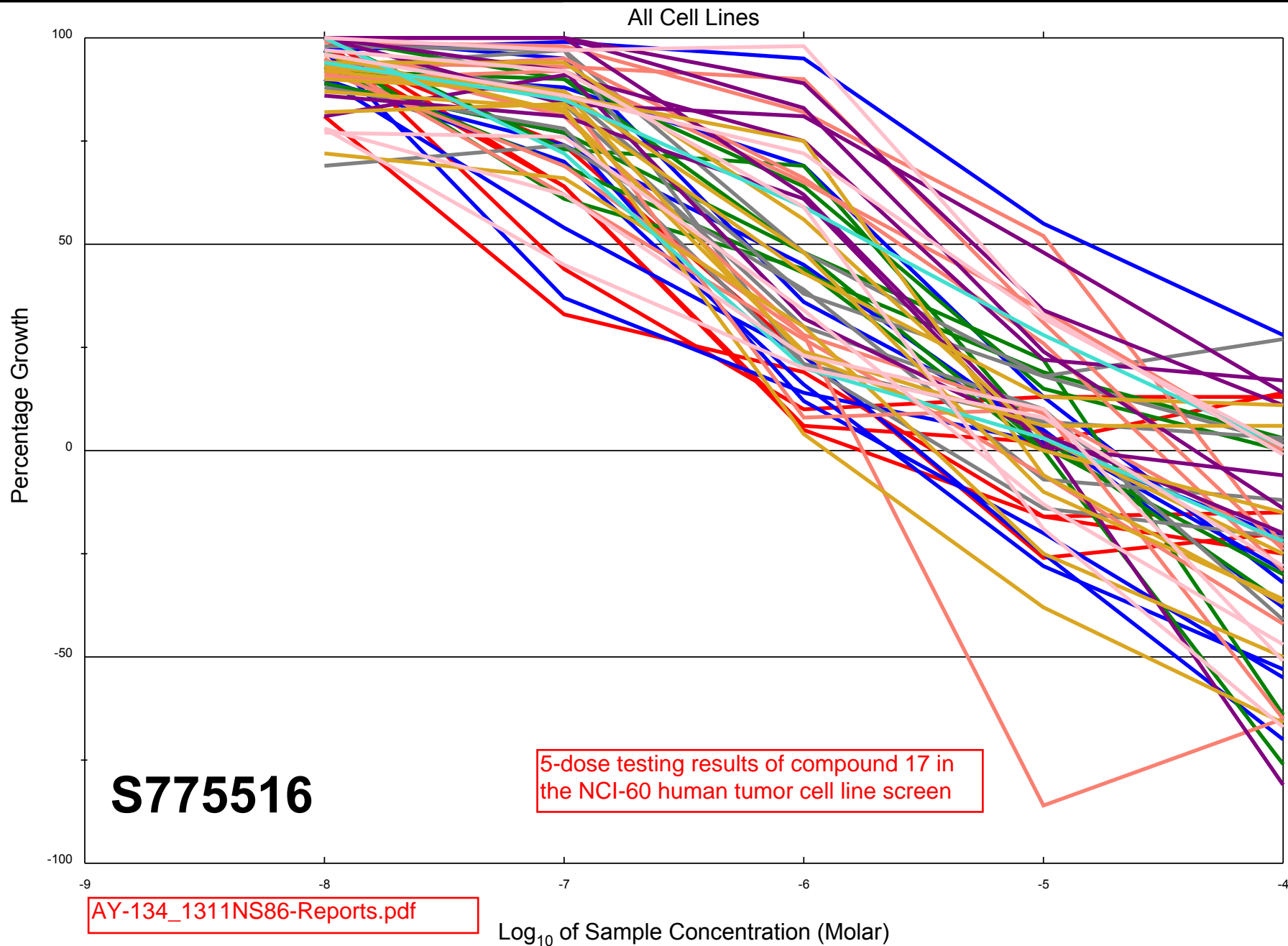
Mean Graphs

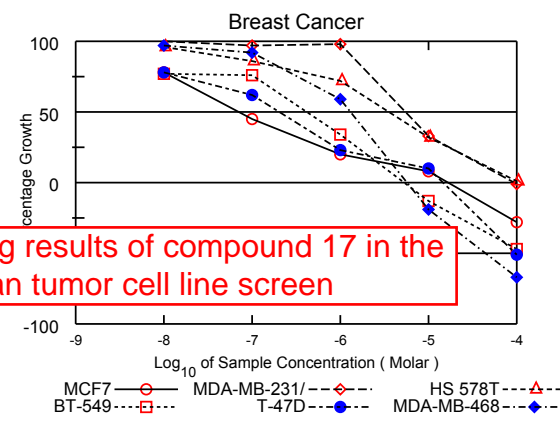
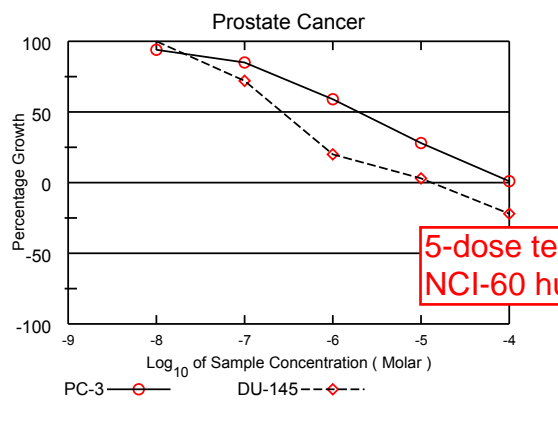
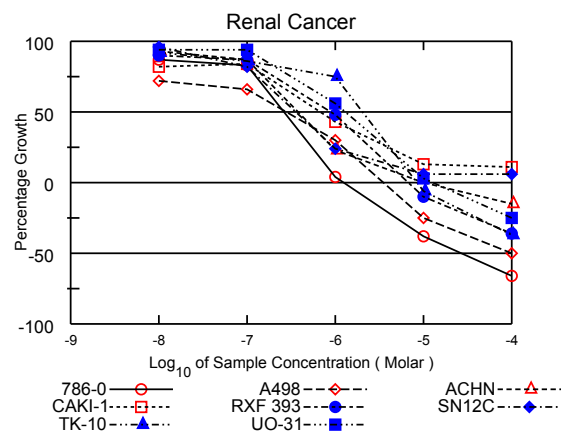
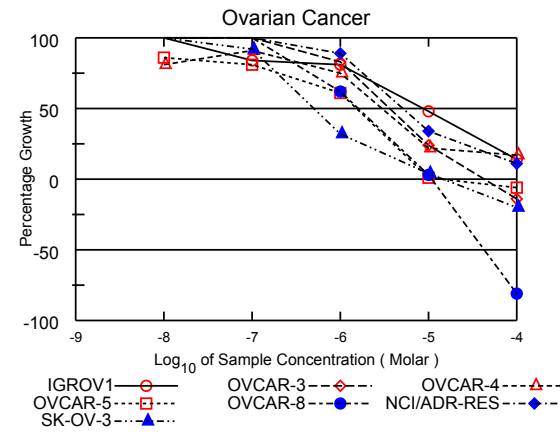
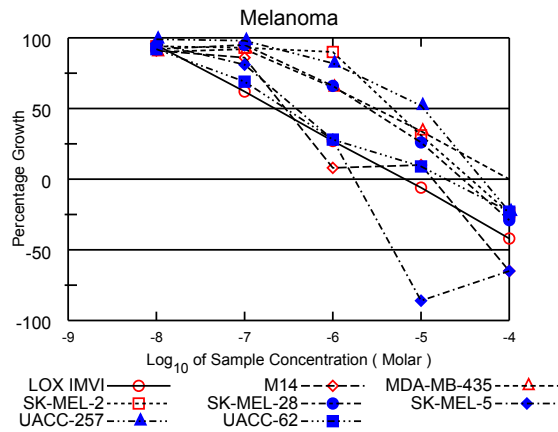
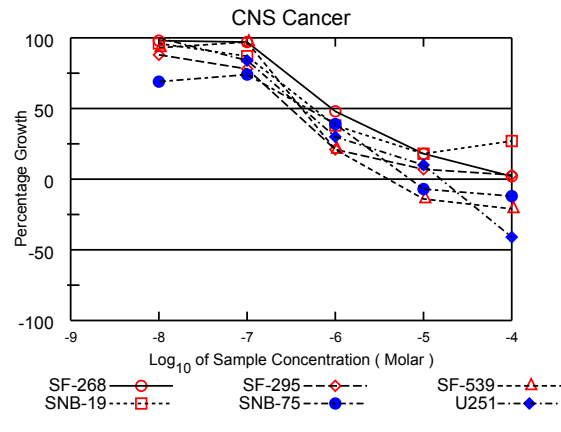
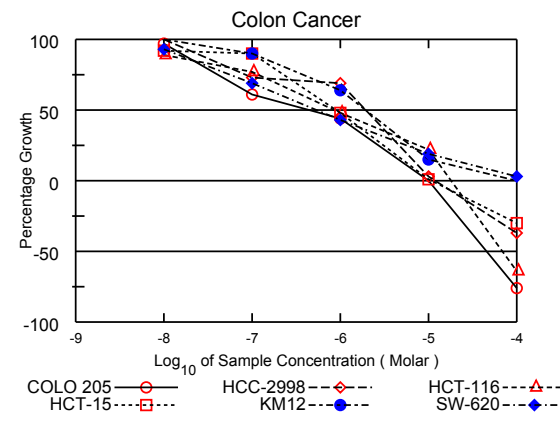
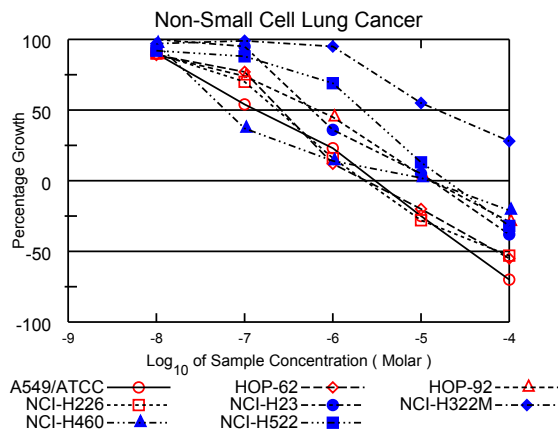
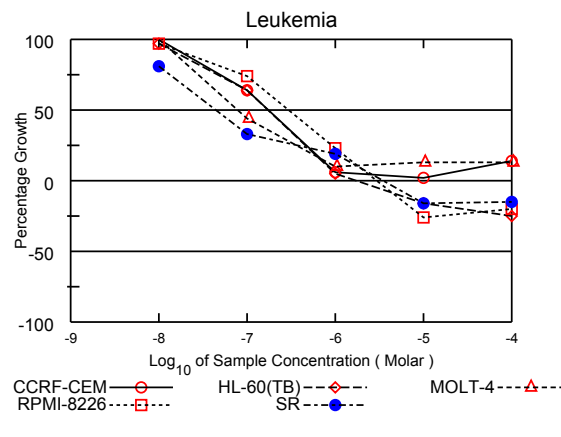
Report Date :September 19, 2013

Test Date :July 15, 2013



5-dose testing results of compound 13 in the NCI-60 human tumor cell line screen





5-dose testing results of compound 17 in the NCI-60 human tumor cell line screen

National Cancer Institute Developmental Therapeutics Program In-Vitro Testing Results

NSC : D - 775516 / 1	Experiment ID : 1311NS86	Test Type : 08	Units : Molar
Report Date : January 15, 2014	Test Date : November 12, 2013	QNS :	MC :
COMI : AY-134 (130531)	Stain Reagent : SRB Dual-Pass Related	SSPL : 0XMP	

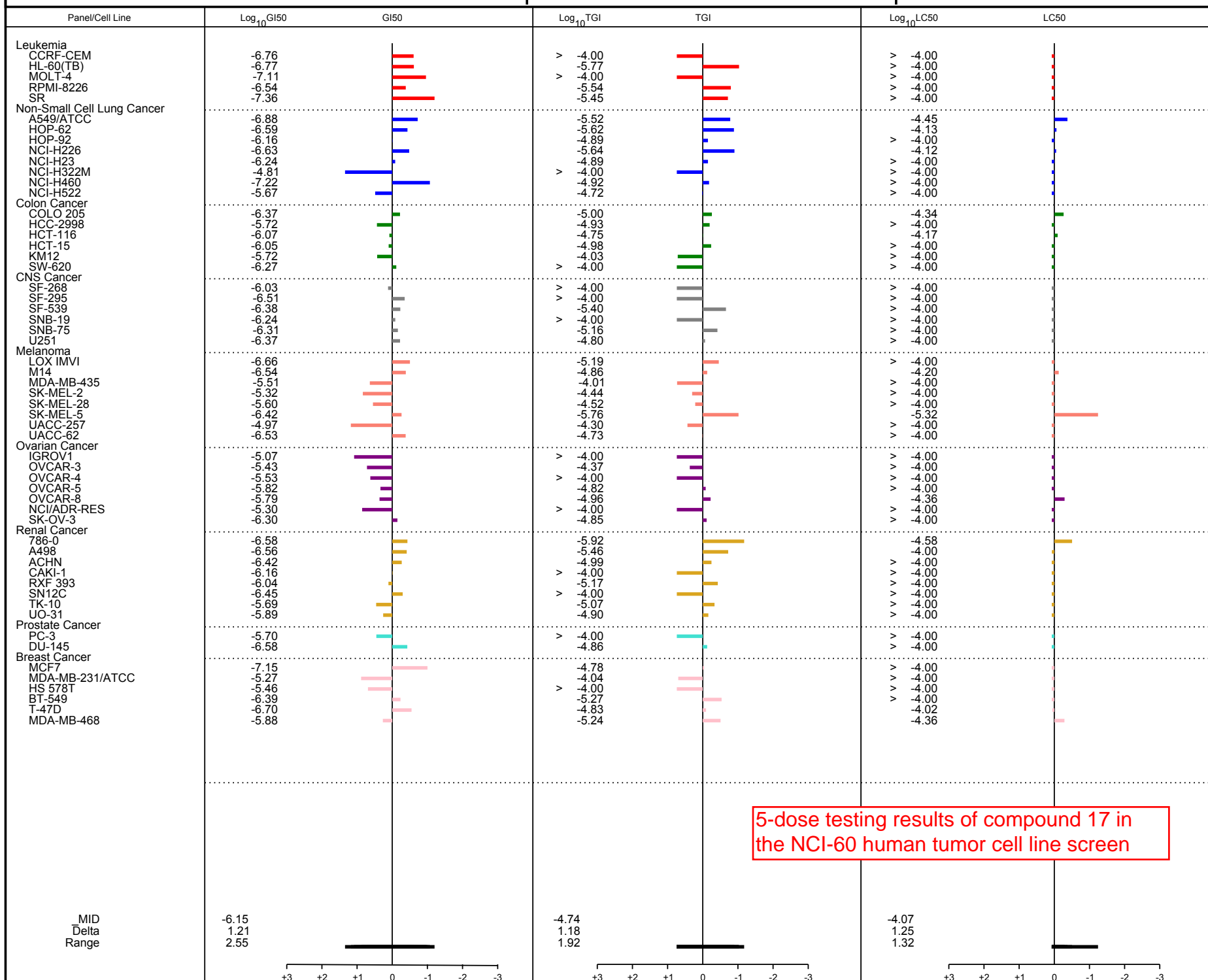
Panel/Cell Line	Time Zero	Log10 Concentration							Percent Growth					GI50	TGI	LC50
		Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0				
Leukemia																
CCRF-CEM	0.539	1.789	1.841	1.337	0.617	0.569	0.713	104	64	6	2	14	1.74E-7	> 1.00E-4	> 1.00E-4	
HL-60(TB)	0.667	2.690	2.639	1.956	0.764	0.561	0.498	97	64	5	-16	-25	1.71E-7	1.70E-6	> 1.00E-4	
MOLT-4	0.612	2.091	2.103	1.257	0.762	0.799	0.810	101	44	10	13	13	7.73E-8	> 1.00E-4	> 1.00E-4	
RPMI-8226	0.957	2.305	2.261	1.950	1.262	0.707	0.764	97	74	23	-26	-20	2.91E-7	2.91E-6	> 1.00E-4	
SR	0.252	1.022	0.879	0.504	0.398	0.213	0.214	81	33	19	-16	-15	4.41E-8	3.52E-6	> 1.00E-4	
Non-Small Cell Lung Cancer																
A549/ATCC	0.398	1.448	1.346	0.964	0.639	0.300	0.118	90	54	23	-25	-70	1.33E-7	3.02E-6	3.58E-5	
HOP-62	0.830	1.874	1.760	1.631	0.958	0.661	0.377	89	77	12	-20	-55	2.60E-7	2.37E-6	7.35E-5	
HOP-92	0.944	1.483	1.421	1.341	1.189	0.965	0.666	89	74	45	4	-29	6.90E-7	1.30E-5	> 1.00E-4	
NCI-H226	0.851	2.230	2.086	1.811	1.070	0.612	0.399	90	70	16	-28	-53	2.32E-7	2.29E-6	7.50E-5	
NCI-H23	0.672	2.020	2.017	1.959	1.157	0.738	0.416	100	95	36	5	-38	5.81E-7	1.30E-5	> 1.00E-4	
NCI-H322M	0.888	2.264	2.220	2.256	2.197	1.648	1.269	97	99	95	55	28	1.55E-5	> 1.00E-4	> 1.00E-4	
NCI-H460	0.386	3.194	3.096	1.416	0.780	0.439	0.307	97	37	14	2	-21	5.99E-8	1.21E-5	> 1.00E-4	
NCI-H522	1.103	2.243	2.152	2.110	1.887	1.246	0.745	92	88	69	13	-32	2.16E-6	1.90E-5	> 1.00E-4	
Colon Cancer																
COLO 205	0.527	1.474	1.443	1.102	0.940	0.529	0.129	97	61	44	.	-76	4.24E-7	1.01E-5	4.60E-5	
HCC-2998	0.568	1.952	1.999	1.576	1.519	0.605	0.358	103	73	69	3	-37	1.92E-6	1.17E-5	> 1.00E-4	
HCT-116	0.207	1.644	1.483	1.315	0.896	0.522	0.074	89	77	48	22	-64	8.50E-7	1.79E-5	6.80E-5	
HCT-15	0.284	2.198	2.049	2.012	1.200	0.298	0.200	92	90	48	1	-30	8.90E-7	1.05E-5	> 1.00E-4	
KM12	0.508	2.572	2.566	2.372	1.820	0.810	0.506	100	90	64	15	.	1.89E-6	9.41E-5	> 1.00E-4	
SW-620	0.314	2.556	2.402	1.854	1.282	0.749	0.390	93	69	43	19	3	5.40E-7	> 1.00E-4	> 1.00E-4	
CNS Cancer																
SF-268	0.564	1.961	1.928	1.915	1.240	0.816	0.591	98	97	48	18	2	9.26E-7	> 1.00E-4	> 1.00E-4	
SF-295	0.641	2.665	2.416	2.221	1.072	0.780	0.700	88	78	21	7	3	3.12E-7	> 1.00E-4	> 1.00E-4	
SF-539	0.954	2.574	2.465	2.525	1.295	0.822	0.752	93	97	21	-14	-21	4.15E-7	4.00E-6	> 1.00E-4	
SNB-19	0.705	2.297	2.231	2.097	1.315	0.989	1.138	96	87	38	18	27	5.77E-7	> 1.00E-4	> 1.00E-4	
SNB-75	0.763	1.519	1.285	1.319	1.060	0.708	0.671	69	74	39	-7	-12	4.87E-7	7.00E-6	> 1.00E-4	
U251	0.597	2.006	2.013	1.775	1.018	0.740	0.350	101	84	30	10	-41	4.22E-7	1.57E-5	> 1.00E-4	
Melanoma																
LOX IMVI	0.316	2.107	2.022	1.428	0.799	0.296	0.182	95	62	27	-6	-42	2.21E-7	6.40E-6	> 1.00E-4	
M14	0.452	1.628	1.518	1.459	0.551	0.571	0.159	91	86	8	10	-65	2.90E-7	1.36E-5	6.34E-5	
MDA-MB-435	0.554	2.501	2.299	2.348	1.818	1.220	0.553	90	92	65	34	.	3.06E-6	9.82E-5	> 1.00E-4	
SK-MEL-2	1.069	2.165	2.098	2.086	2.058	1.414	0.810	94	93	90	31	-24	4.83E-6	3.67E-5	> 1.00E-4	
SK-MEL-28	0.627	1.924	1.818	1.860	1.477	0.969	0.446	92	95	66	26	-29	2.49E-6	3.00E-5	> 1.00E-4	
SK-MEL-5	0.621	2.415	2.336	2.072	1.122	0.087	0.219	96	81	28	-86	-65	3.83E-7	1.76E-6	4.83E-6	
UACC-257	1.042	1.991	1.979	1.973	1.819	1.535	0.808	99	98	82	52	-23	1.06E-5	4.98E-5	> 1.00E-4	
UACC-62	0.774	2.982	2.811	2.304	1.390	0.964	0.595	92	69	28	9	-23	2.92E-7	1.86E-5	> 1.00E-4	
Ovarian Cancer																
IGROV1	0.763	2.310	2.356	2.068	2.022	1.501	0.981	103	84	81	48	14	8.56E-6	> 1.00E-4	> 1.00E-4	
OVCAR-3	0.513	1.684	1.768	1.690	1.490	0.799	0.440	107	100	83	24	-14	3.68E-6	4.28E-5	> 1.00E-4	
OVCAR-4	0.665	1.425	1.281	1.357	1.232	0.835	0.792	81	91	75	22	17	2.96E-6	> 1.00E-4	> 1.00E-4	
OVCAR-5	0.693	1.575	1.451	1.411	1.231	0.705	0.652	86	81	61	1	-6	1.52E-6	1.51E-5	> 1.00E-4	
OVCAR-8	0.632	2.053	2.195	2.178	1.519	0.679	0.123	110	109	62	3	-81	1.62E-6	1.09E-5	4.32E-5	
NCI/ADR-RES	0.494	1.782	1.837	1.865	1.638	0.928	0.630	104	106	89	34	11	5.05E-6	> 1.00E-4	> 1.00E-4	
SK-OV-3	0.933	1.627	1.629	1.573	1.155	0.958	0.745	100	92	32	4	-20	5.02E-7	1.42E-5	> 1.00E-4	
Renal Cancer																
786-0	0.506	1.919	1.731	1.680	0.556	0.313	0.172	87	83	4	-38	-66	2.61E-7	1.22E-6	2.64E-5	
A498	1.386	2.280	2.031	1.973	1.652	1.034	0.692	72	66	30	-25	-50	2.73E-7	3.46E-6	9.93E-5	
ACHN	0.448	1.883	1.779	1.695	0.779	0.451	0.383	93	87	23	.	-15	3.78E-7	1.03E-5	> 1.00E-4	
CAKI-1	0.613	2.660	2.298	2.336	1.501	0.877	0.833	82	84	43	13	11	6.87E-7	> 1.00E-4	> 1.00E-4	
RXF 393	0.735	1.307	1.248	1.233	1.011	0.665	0.467	90	87	48	-10	-36	9.03E-7	6.83E-6	> 1.00E-4	
SN12C	0.945	3.091	3.012	2.714	1.451	1.069	1.083	96	82	24	6	6	3.55E-7	> 1.00E-4	> 1.00E-4	
TK-10	0.971	2.214	2.119	2.042	1.898	0.915	0.612	92	86	75	-6	-37	2.02E-6	8.46E-6	> 1.00E-4	
UO-31	0.831	2.304	2.217	2.210	1.650	0.873	0.627	94	94	56	3	-25	1.28E-6	1.27E-5	> 1.00E-4	
Prostate Cancer																
PC-3	0.671	1.600	1.547	1.463	1.223	0.932	0.679	94	85	59	28	1	2.00E-6	> 1.00E-4	> 1.00E-4	
DU-145	0.354	1.578	1.629	1.230	0.602	0.396	0.277	104	72	20	3	-22	2.63E-7	1.37E-5	> 1.00E-4	
Breast Cancer																
MCF7	0.349	1.961	1.612	1.072	0.674	0.480	0.252	78	45	20	8	-28	7.01E-8	1.68E-5	> 1.00E-4	
MDA-MB-231/ATCC	0.612	1.400	1.437	1.379	1.384	0.869	0.604	105	97	98	33	-1	5.41E-6	9.10E-5	> 1.00E-4	
HS 578T	1.009	2.066	2.019	1.914	1.765	1.343	1.017	96	86	72	32	1	3.46E-6	> 1.00E-4	> 1.00E-4	
BT-549	0.820	1.452	1.307	1.300	1.033	0.716	0.439	77	76	34	-13	-47	4.11E-7	5.33E-6	> 1.00E-4	
T-47D	0.857	1.526	1.377	1.269	1.010	0.927	0.419	78	62	23	10	-51	1.99E-7	1.48E-5	9.59E-5	
MDA-MB-468	0.681	1.181	1.167	1.143	0.976	0.552	0.222	97	92	59	-19	-67	1.30E-6	5.70E-6	4.36E-5	

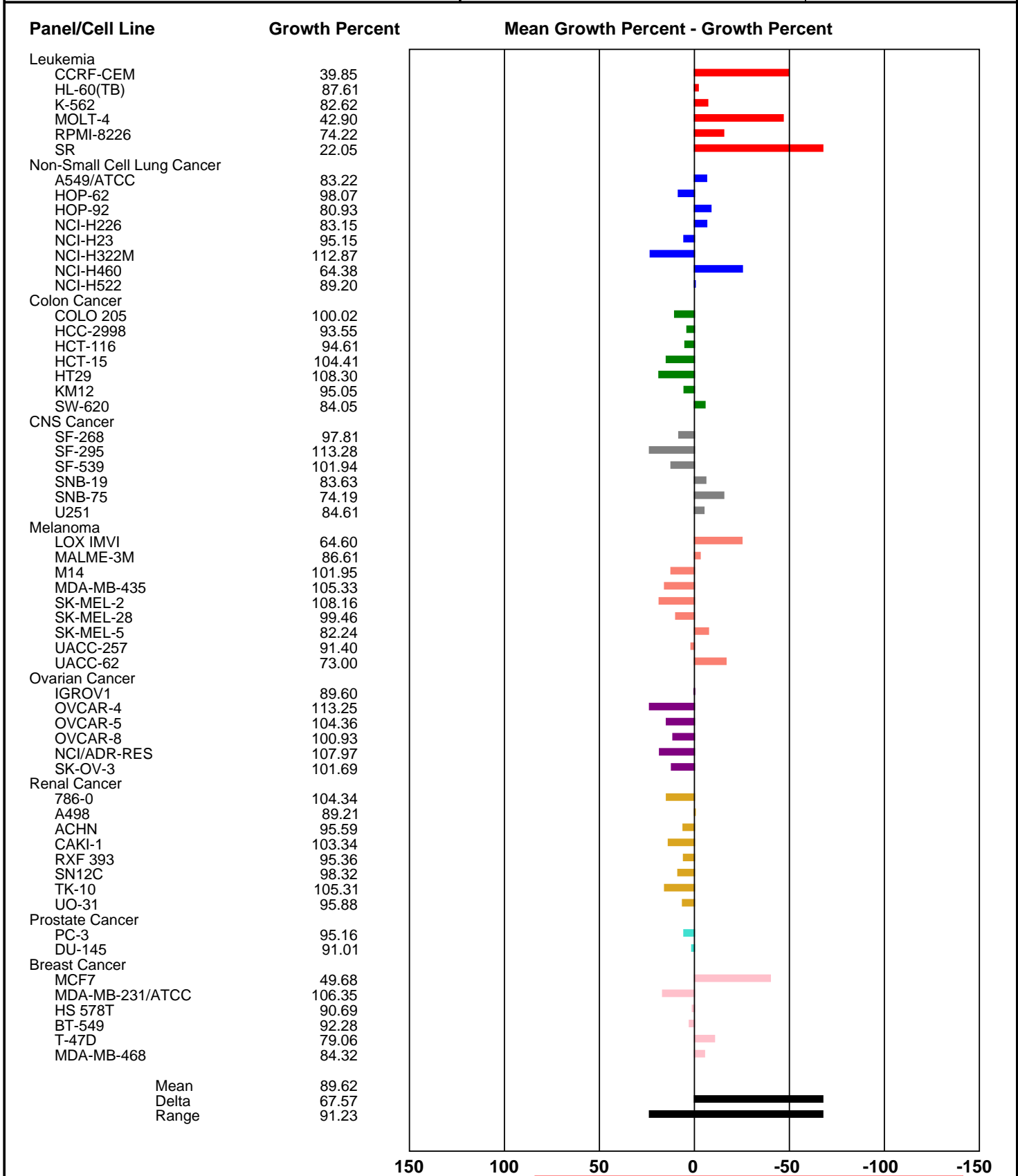
5-dose testing results of compound 17 in
the NCI-60 human tumor cell line screen

Mean Graphs

Report Date :January 15, 2014

Test Date :November 12, 2013

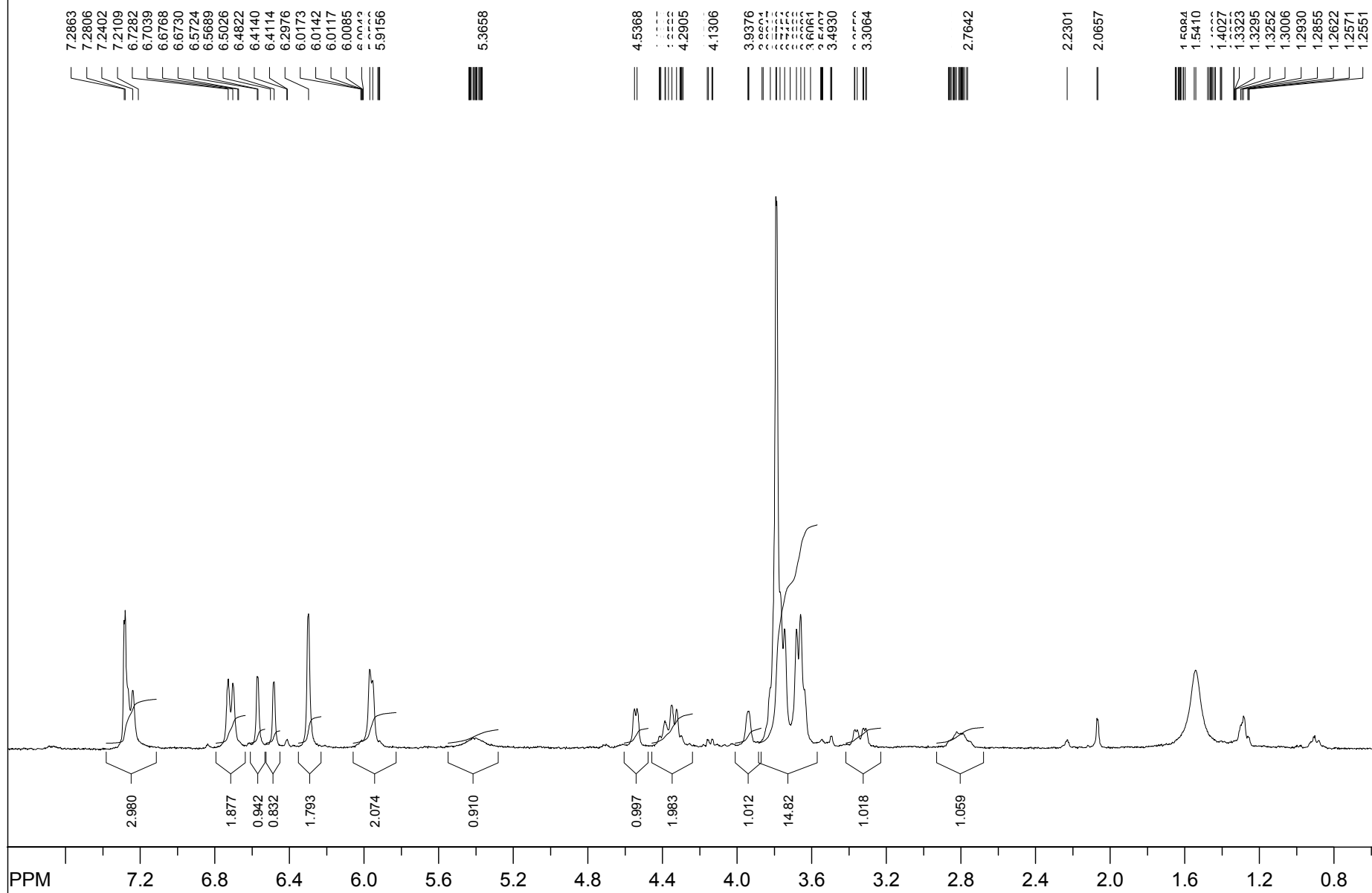




AY138_NCI_1305OS04-775517-
OneDose[1].pdf

1-dose testing results of compound 19 in
the NCI-60 human tumor cell line screen

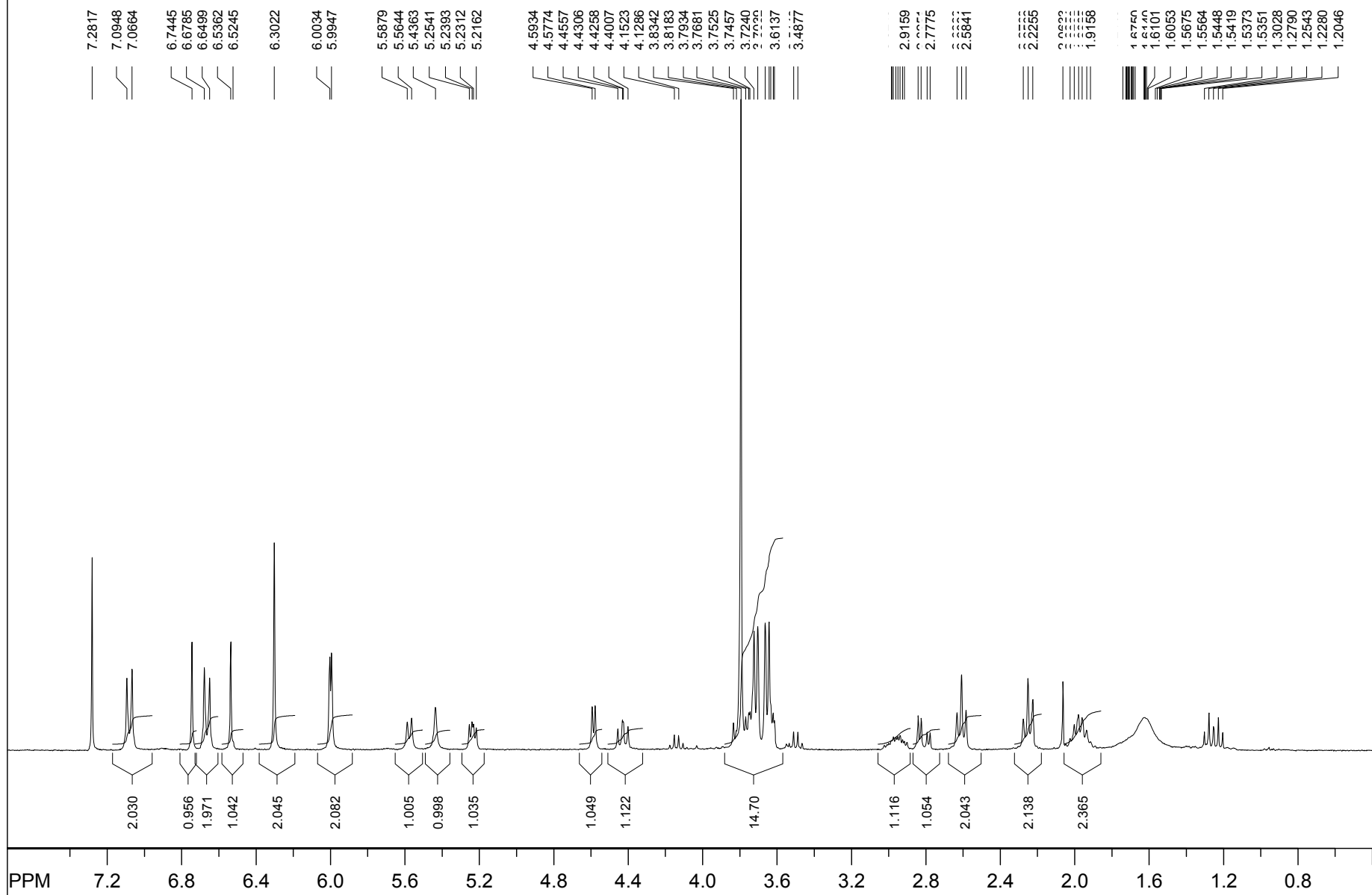
SpinWorks 2.5: Sample AY-76 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\lc-ay-76\lc-ay-76\1\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 32768 points
width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 16384 complex points
LB: 0.300 GB: 0.0000
Hz/cm: 87.919 ppm/cm: 0.29293

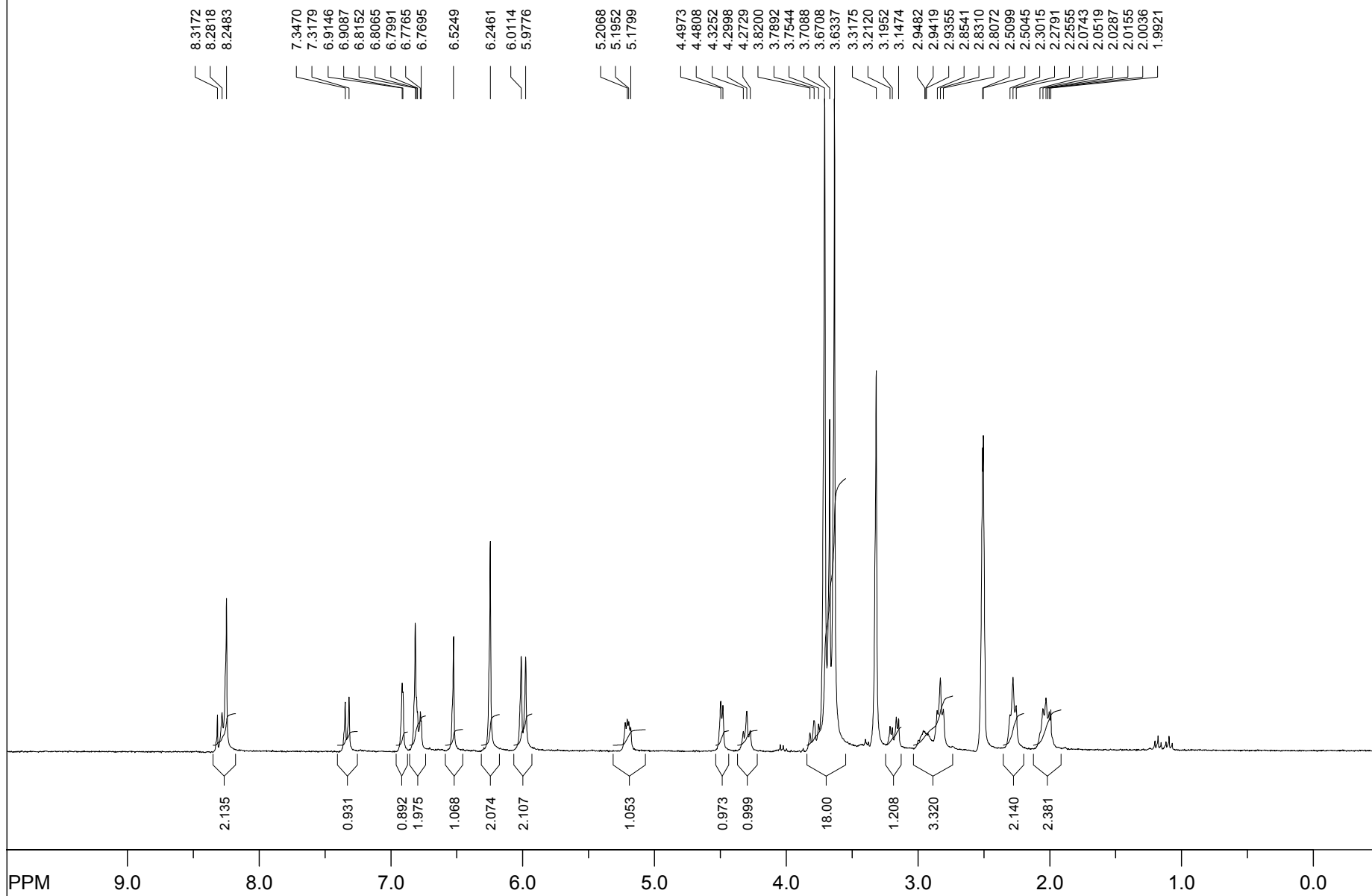
SpinWorks 2.5: Sample AY-54 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\lc-ay-54\lc-ay-54\1\fid exp: <zg30>
 transmitter freq.: 300.131853 MHz
 time domain size: 32768 points
 width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.130006 MHz
 processed size: 16384 complex points
 LB: 0.300 GB: 0.0000
 Hz/cm: 88.402 ppm/cm: 0.29455

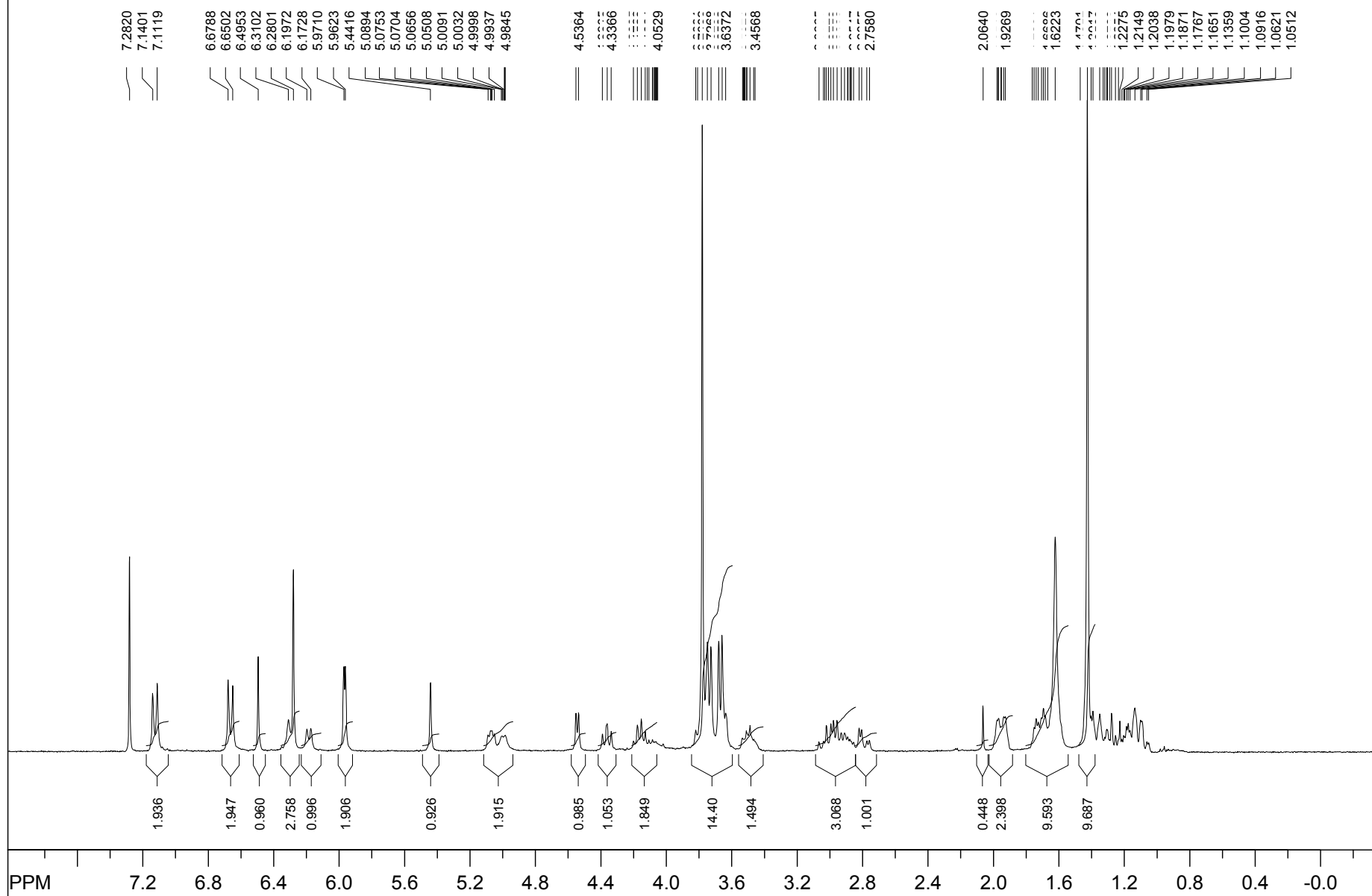
SpinWorks 2.5: Sample AY-68 1-H at 300 MHz in dms0-d6



file: C:\Arun\NMR\lc-ay-68\lc-ay-68\1\fid exp: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 32768 points
width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 16384 complex points
LB: 0.300 GB: 0.0000
Hz/cm: 125.040 ppm/cm: 0.41662

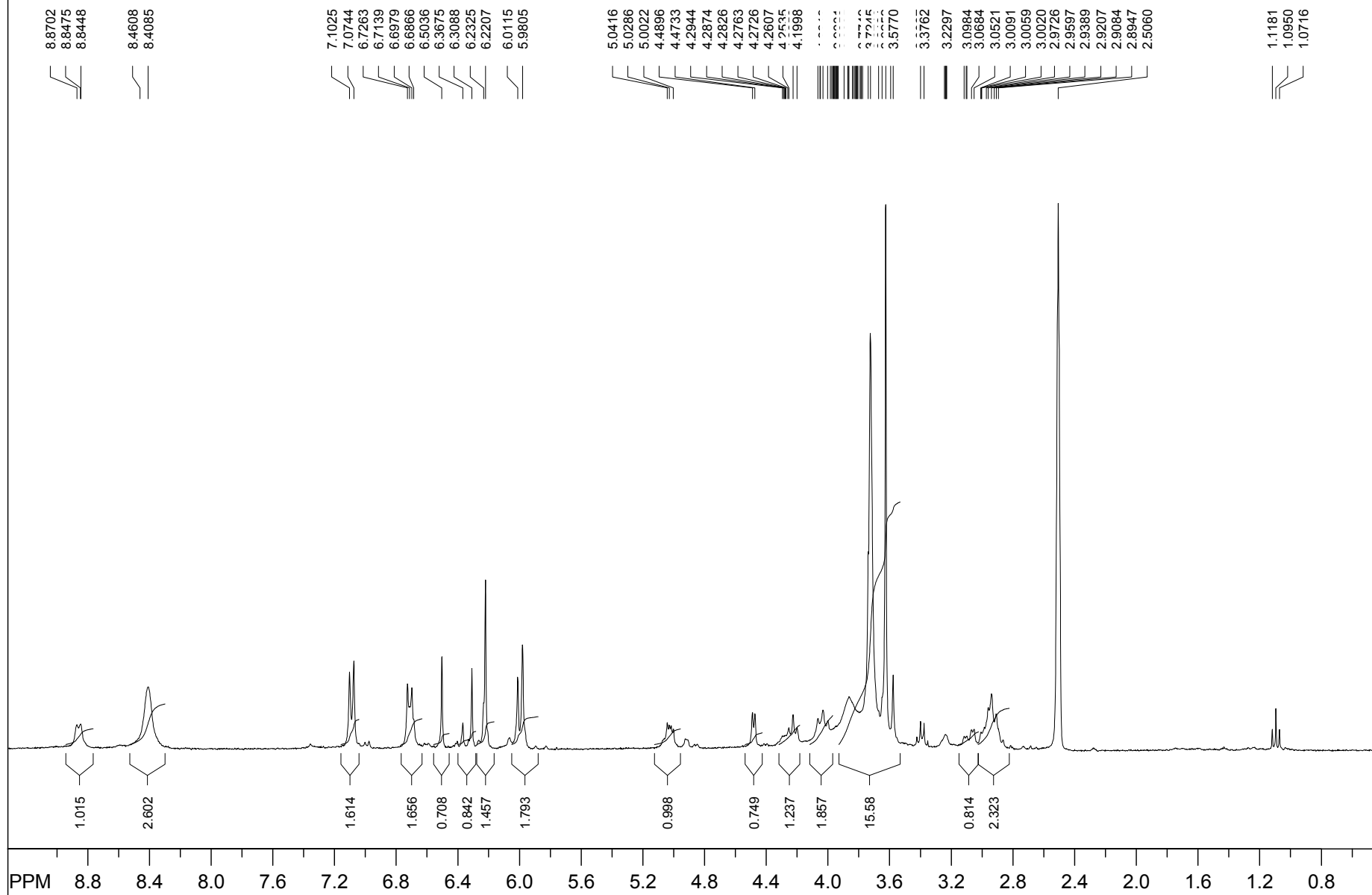
SpinWorks 2.5: Sample AY-64 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\lc-ay-64\lc-ay-64\1\fid exp: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 32768 points
width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130006 MHz
processed size: 16384 complex points
LB: 0.000 GB: 0.0000
Hz/cm: 100.582 ppm/cm: 0.33513

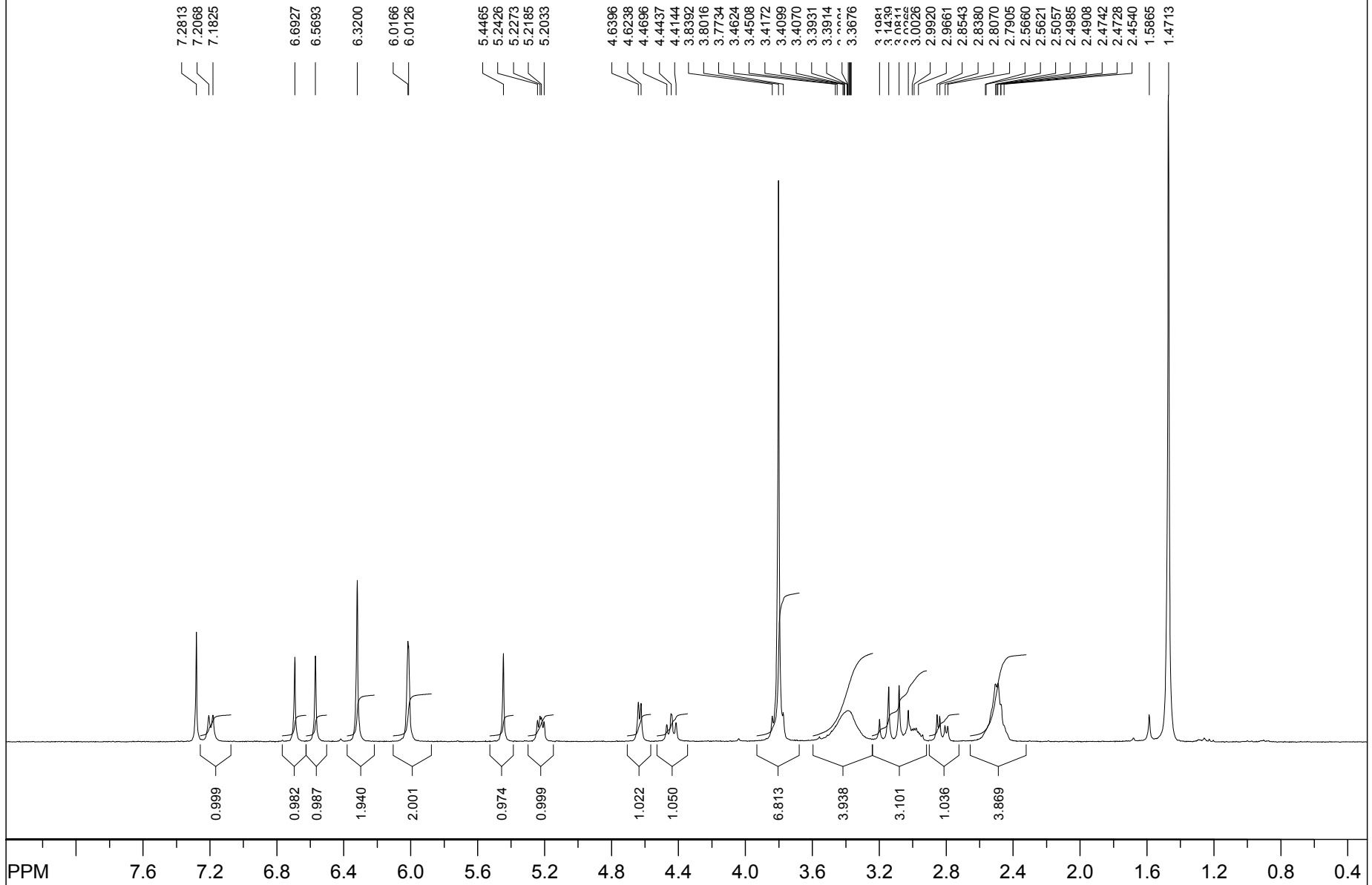
SpinWorks 2.5: Sample AY-70 1-H at 300 MHz in dms0-d6



file: C:\Arun\NMR\lc-ay-70\lc-ay-70\1\fid exp: <zg30>
 transmitter freq.: 300.131853 MHz
 time domain size: 32768 points
 width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.130000 MHz
 processed size: 16384 complex points
 LB: 0.300 GB: 0.0000
 Hz/cm: 106.701 ppm/cm: 0.35551

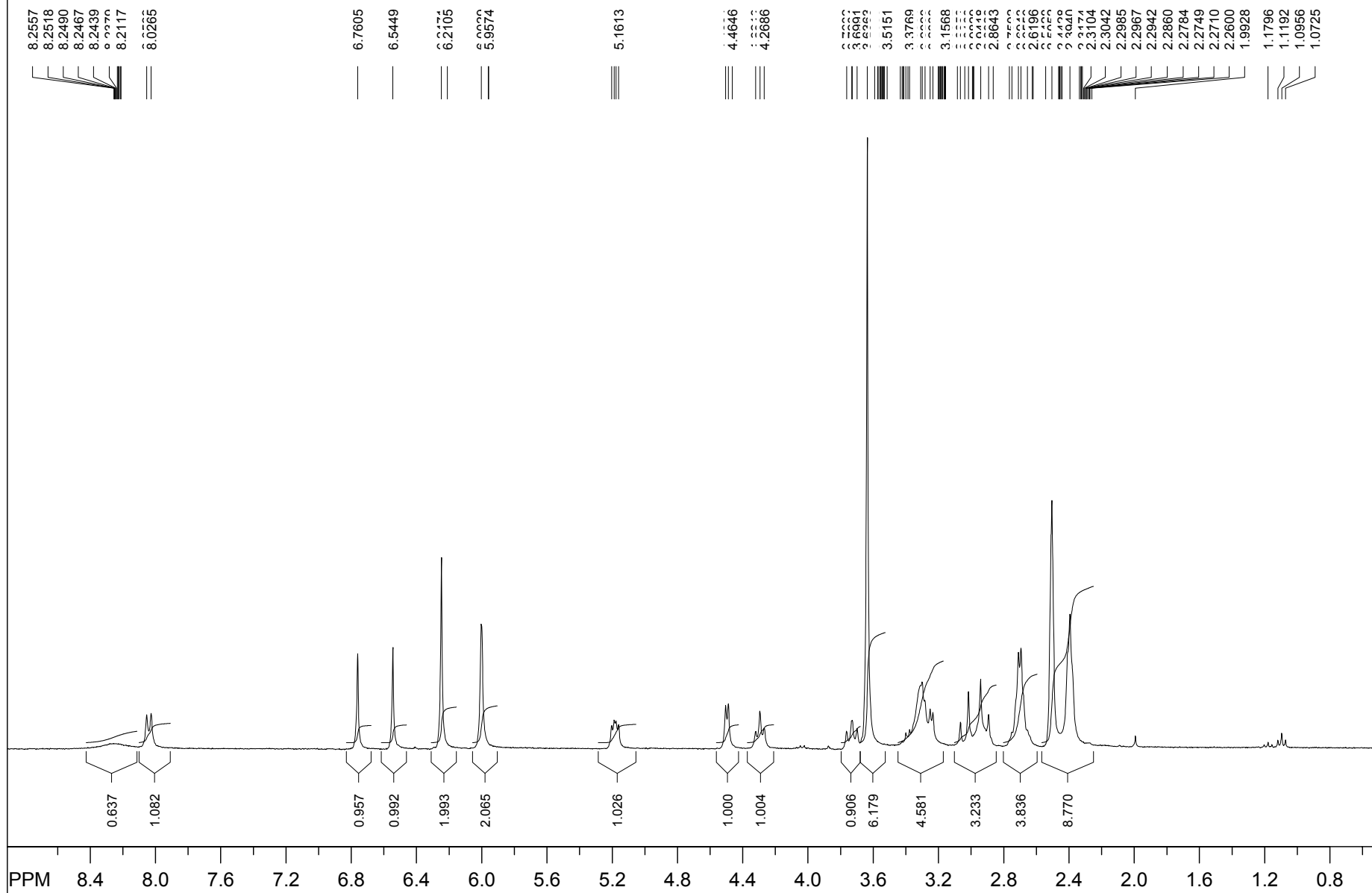
SpinWorks 2.5: Sample AY130 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\ay-130\1\fid exp: <zg30>
 transmitter freq.: 300.131853 MHz
 time domain size: 32768 points
 width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.130006 MHz
 processed size: 16384 complex points
 LB: 0.300 GB: 0.0000
 Hz/cm: 97.656 ppm/cm: 0.32538

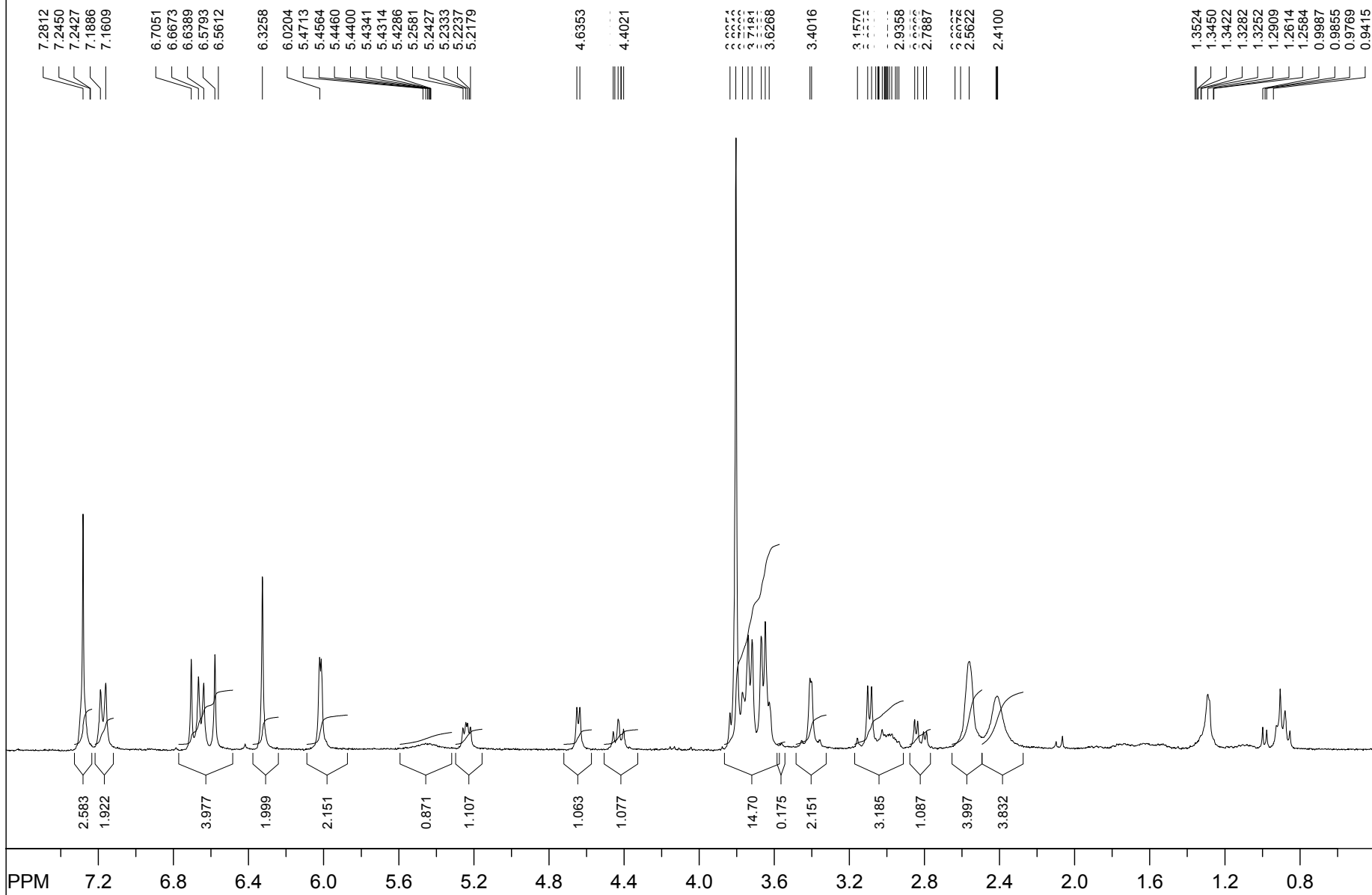
SpinWorks 2.5: Sample Ay-132 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\ay-132\2\fid expt: <zg30>
transmitter freq.: 300.131853 MHz
time domain size: 32768 points
width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 16384 complex points
LB: 0.300 GB: 0.0000
Hz/cm: 100.582 ppm/cm: 0.33513

SpinWorks 2.5: Sample AY-134 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\ay-134\1\fid exp: <zg30>

transmitter freq.: 300.131853 MHz

time domain size: 32768 points

width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt

number of scans: 16

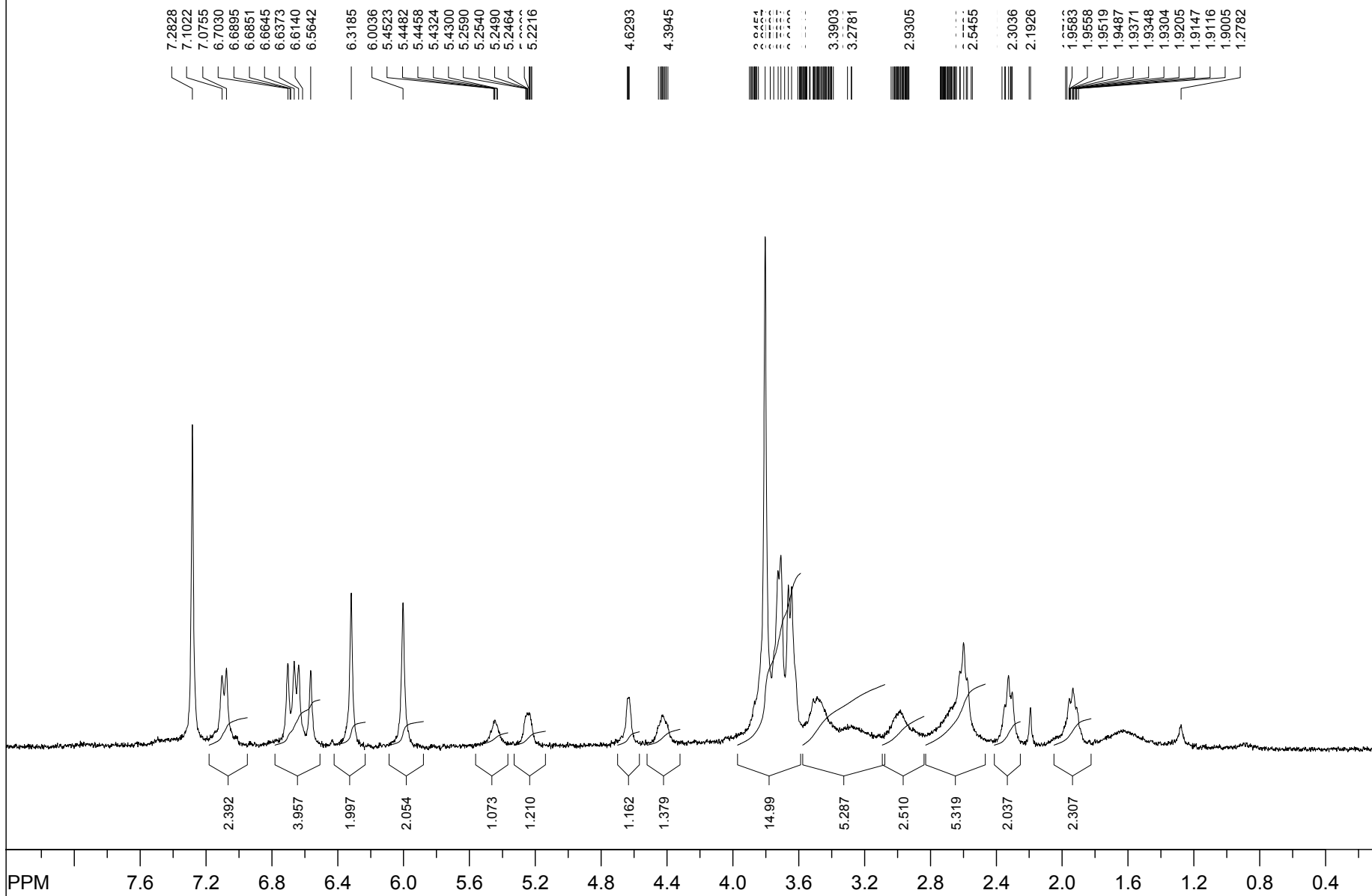
freq. of 0 ppm: 300.130006 MHz

processed size: 16384 complex points

LB: 0.000 GB: 0.0000

Hz/cm: 87.626 ppm/cm: 0.29196

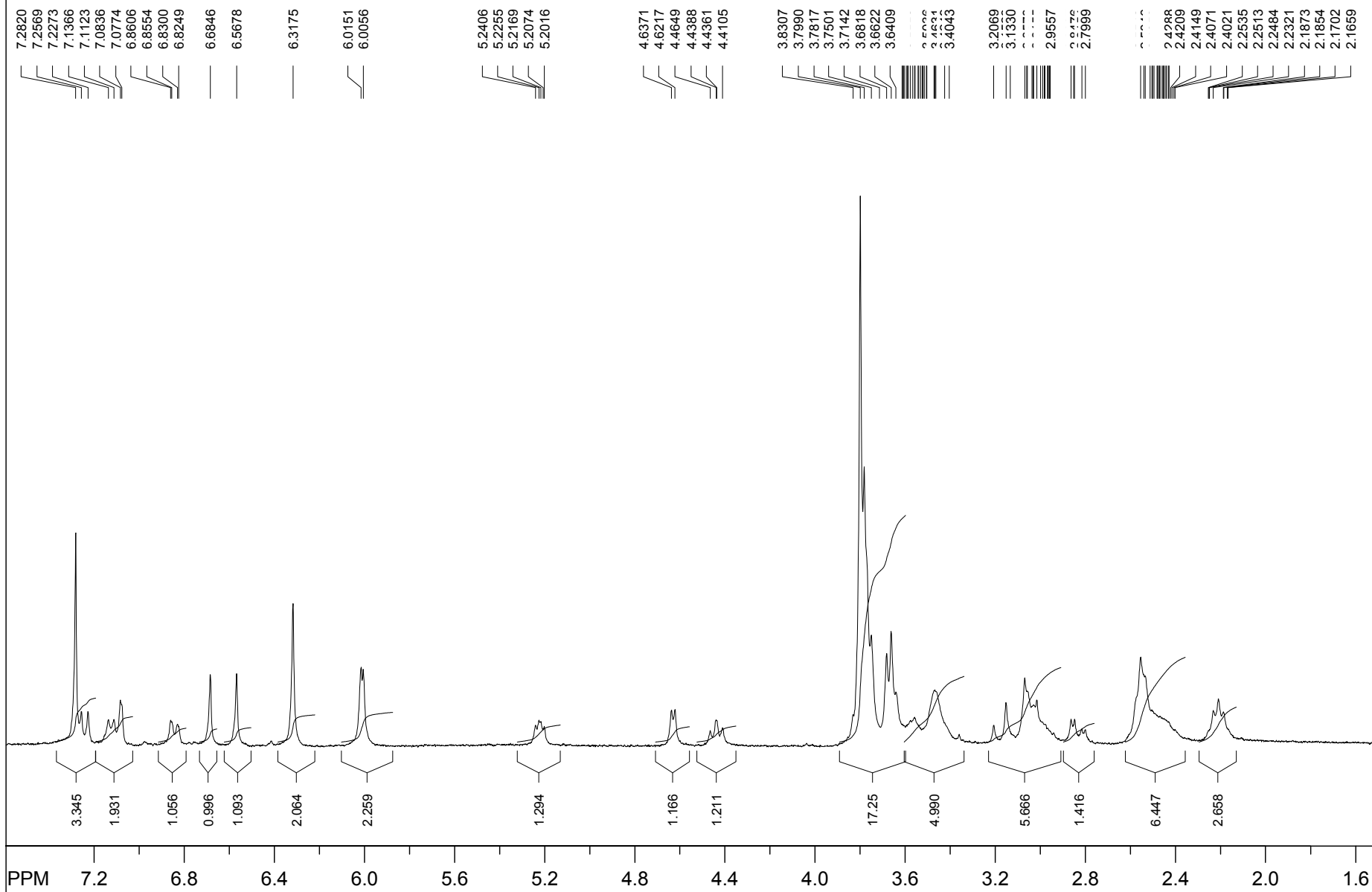
SpinWorks 2.5: Sample Ay-136 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\lh-ay-136\lh-ay-136\1\fid expt: <zg30>
 transmitter freq.: 300.131853 MHz
 time domain size: 32768 points
 width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.130006 MHz
 processed size: 16384 complex points
 LB: 0.000 GB: 0.0000
 Hz/cm: 100.032 ppm/cm: 0.33329

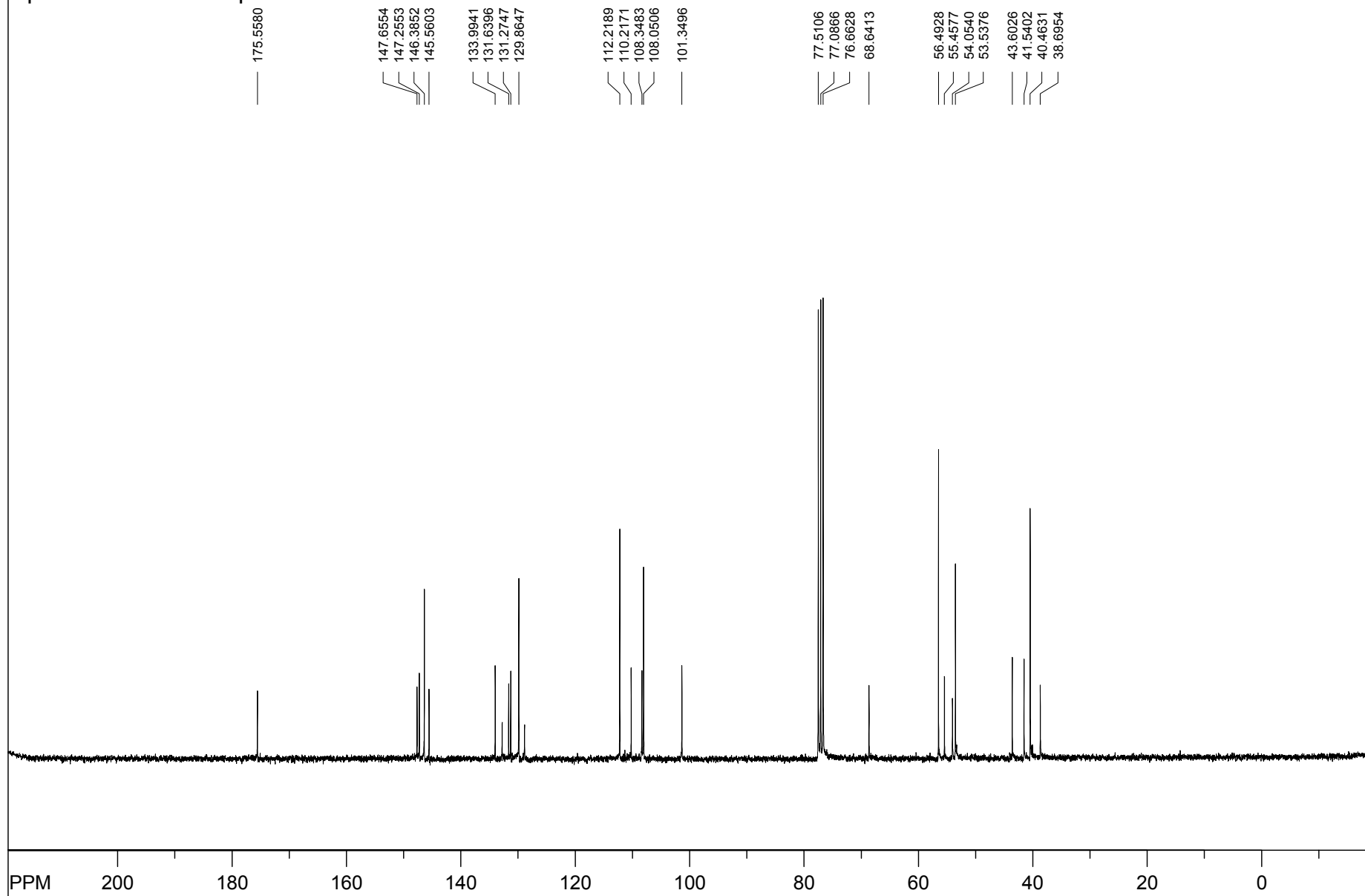
SpinWorks 2.5: Sample AY-138 1-H at 300 MHz in CDCl3



file: C:\Arun\NMR\bh-ay-138\bh-ay-138\1\fid exp: <zg30>
 transmitter freq.: 300.131853 MHz
 time domain size: 32768 points
 width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.130006 MHz
 processed size: 16384 complex points
 LB: 0.000 GB: 0.0000
 Hz/cm: 72.841 ppm/cm: 0.24270

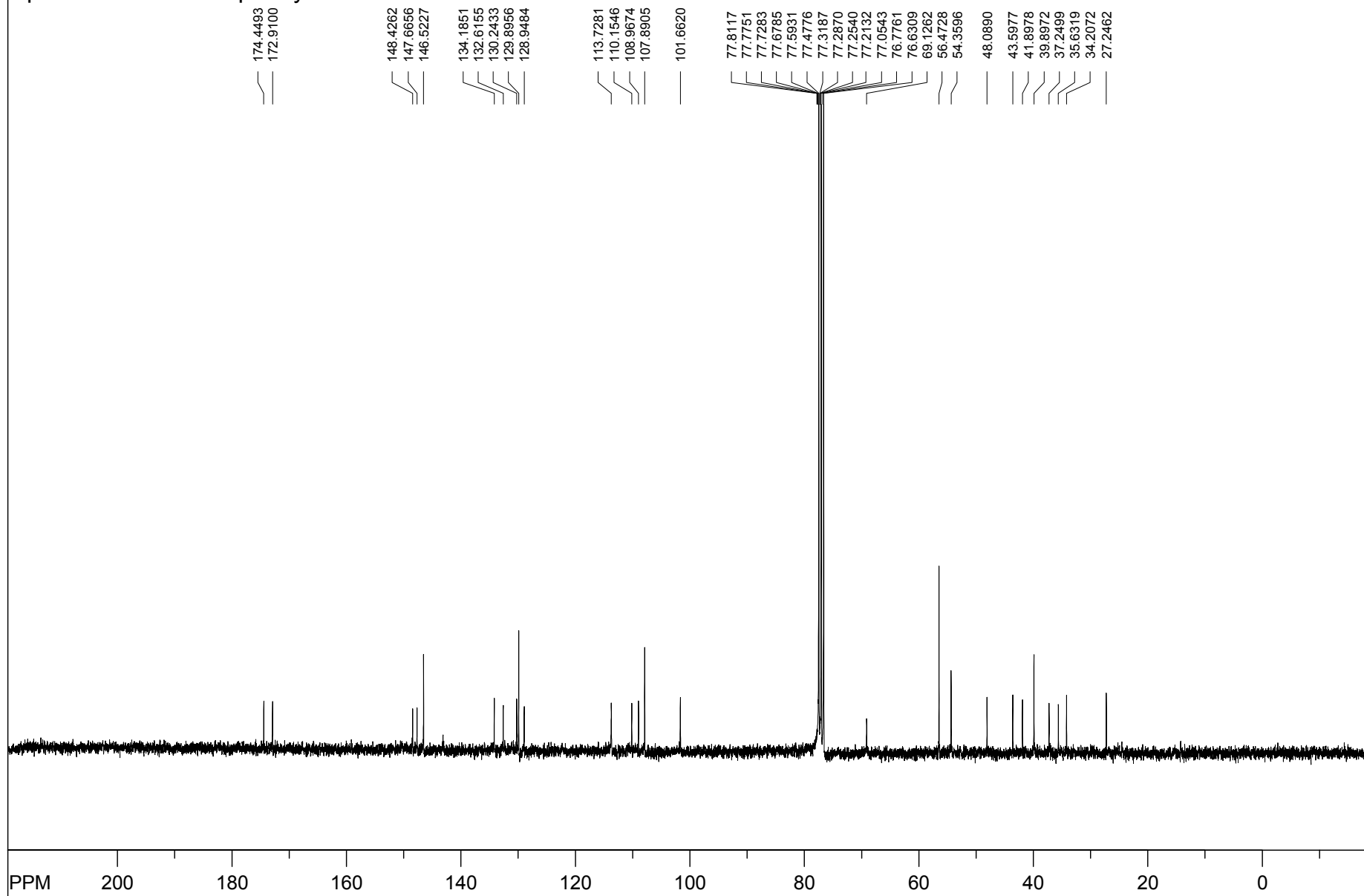
SpinWorks 2.5: Sample AY-76 13-C nmr in CDCl3



file: C:\Arun\NMR\lh-ay-76\lh-ay-76\1\fid exp: <zpgg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000
Hz/cm: 719.353 ppm/cm: 9.53097

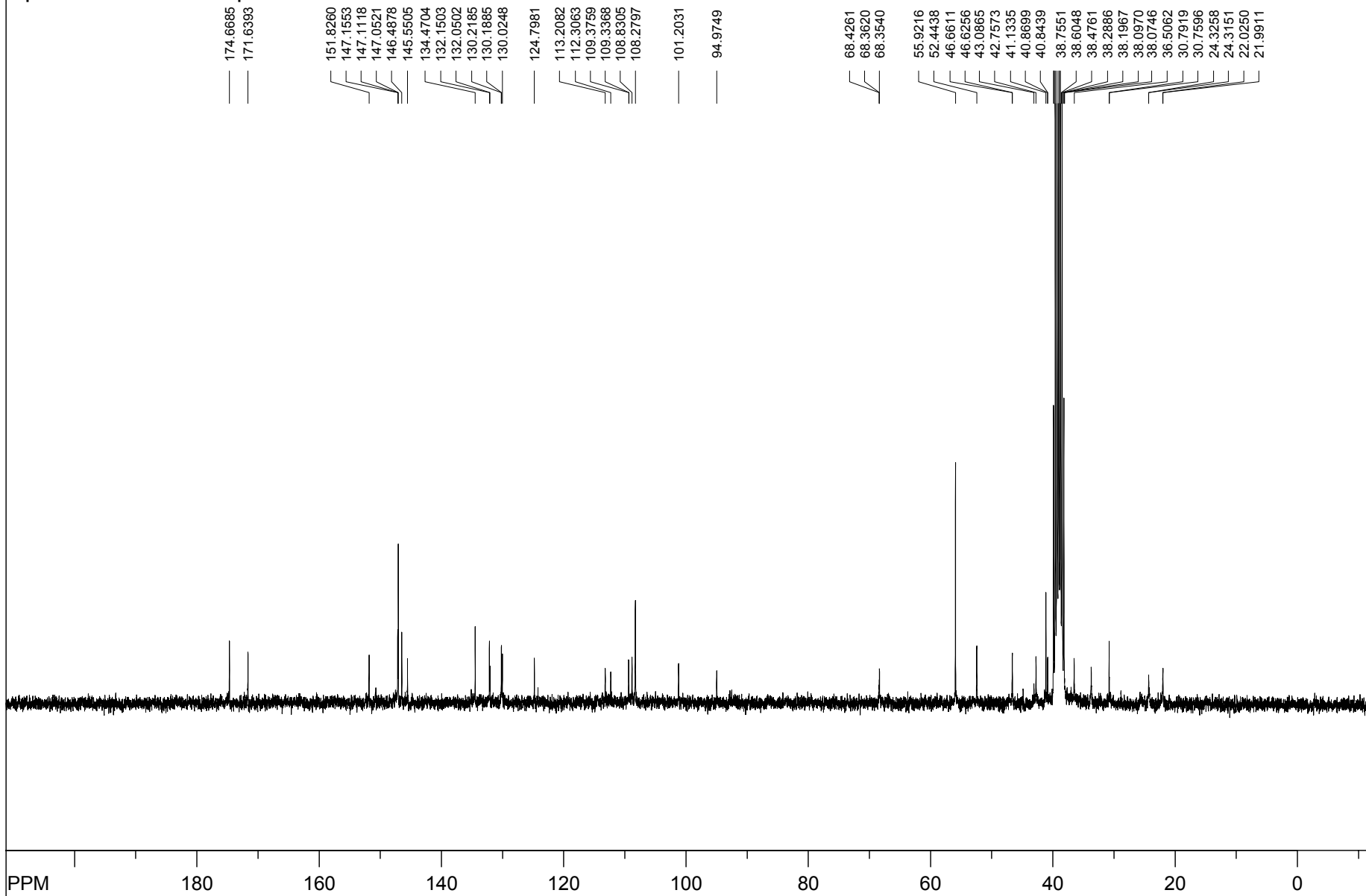
SpinWorks 2.5: Sample Ay-54 13-C in CDCl3



file: C:\Arun\NMR\bh-ay-54.zip 13c\bh-ay-54\1fid expt: <zpgg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.300 GB: 0.0000
Hz/cm: 719.353 ppm/cm: 9.53097

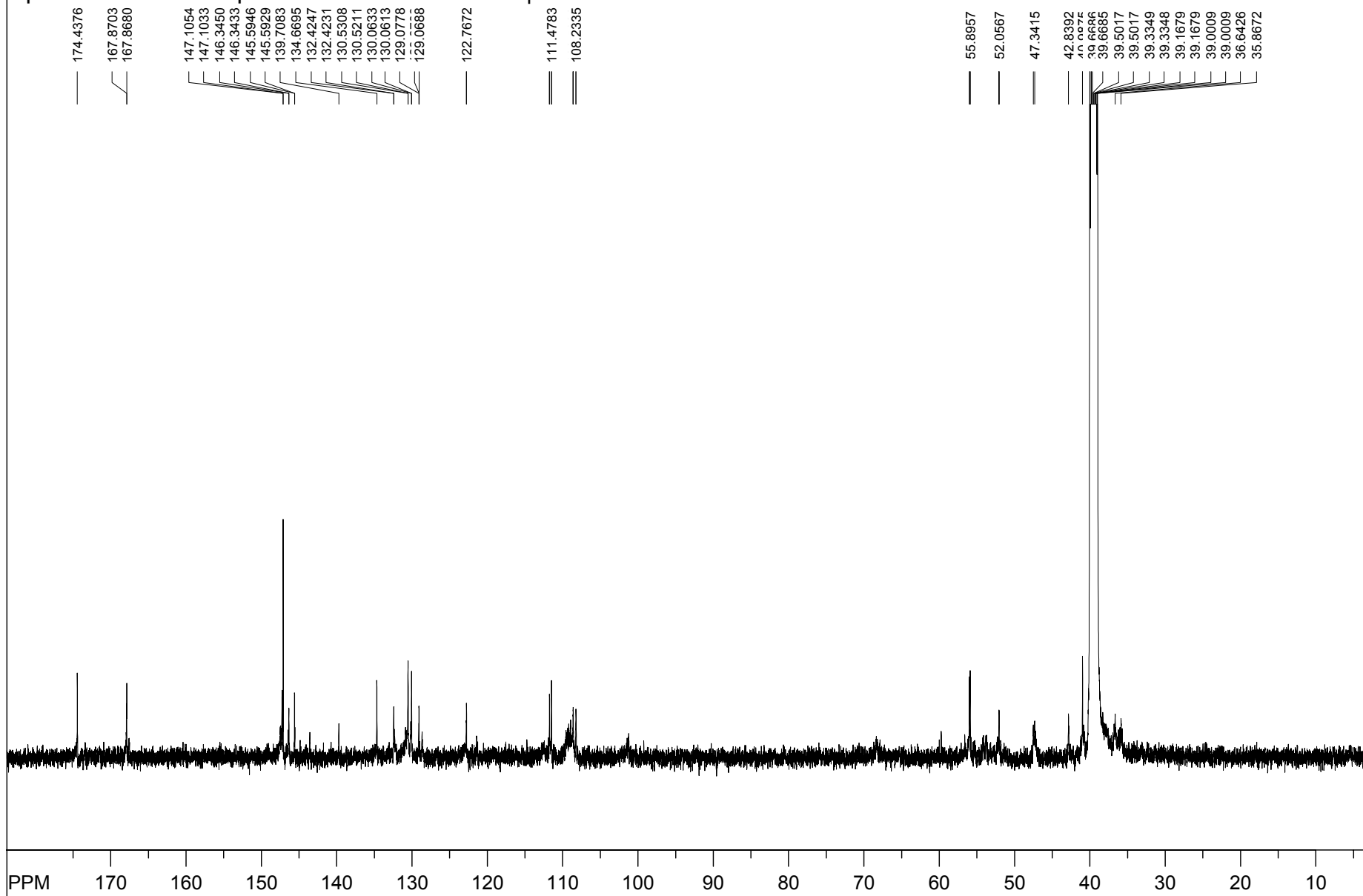
SpinWorks 2.5: Sample AY-68A 13-C in dmso-d6



file: C:\Arun\NMR\lh-ay-68a\lh-ay-68a\1\fid expt: <zpgp30>
 transmitter freq.: 75.475295 MHz
 time domain size: 65536 points
 width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
 number of scans: 1024

freq. of 0 ppm: 75.467787 MHz
 processed size: 32768 complex points
 LB: 0.300 GB: 0.0000
 Hz/cm: 674.393 ppm/cm: 8.93529

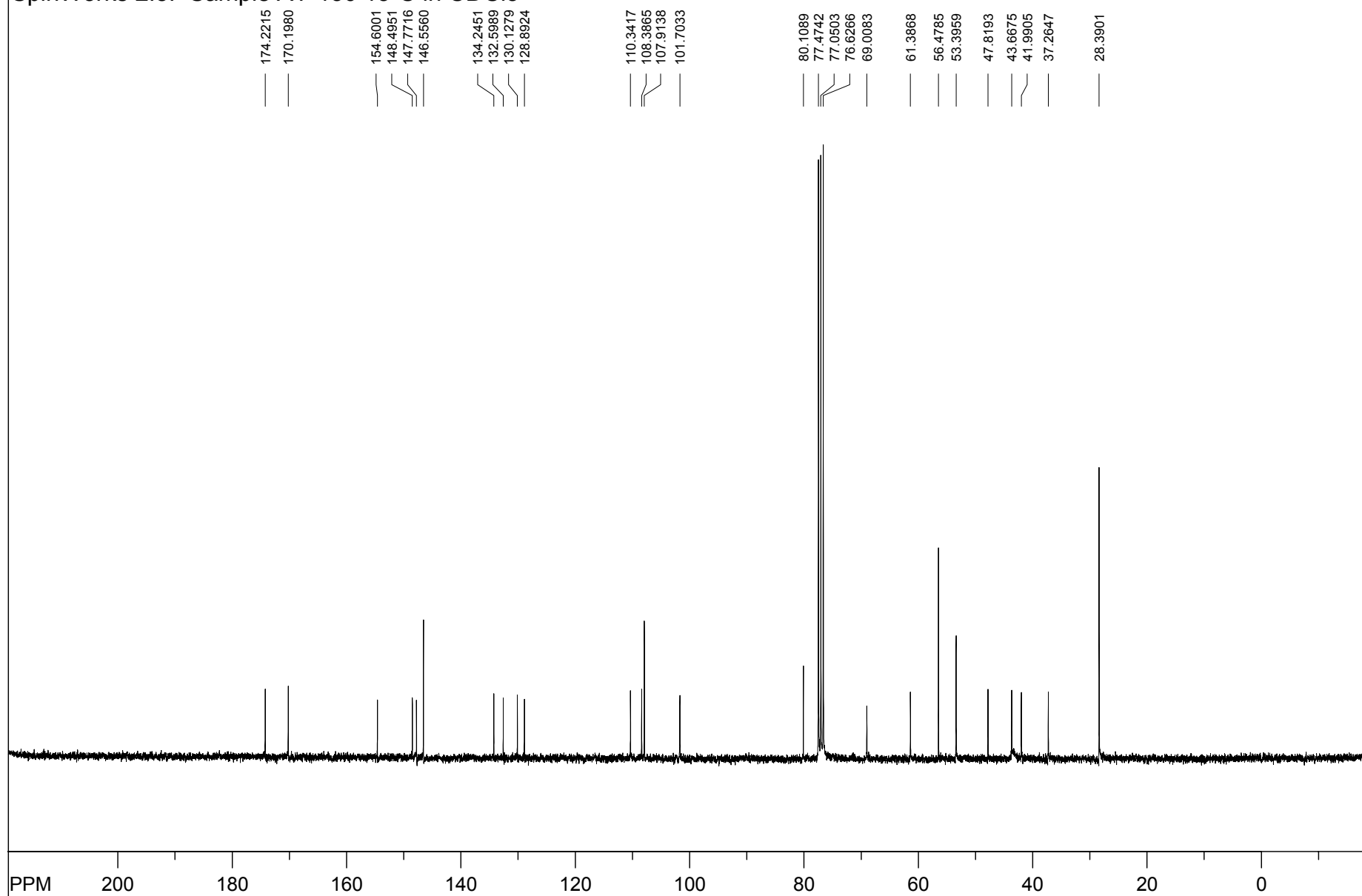
SpinWorks 2.5: Sample AY-70C in dms0-d6 on |Avance 500



file: C:\Arun\NMR\ay-70c\ay-70c\2\fid expt: <zgpg30>
transmitter freq.: 125.770364 MHz
time domain size: 65536 points
width: 29761.90 Hz = 236.636866 ppm = 0.454131 Hz/pt
number of scans: 4096

freq. of 0 ppm: 125.757852 MHz
processed size: 32768 complex points
LB: 1.000 GB: 0.0000
Hz/cm: 910.589 ppm/cm: 7.24009

SpinWorks 2.5: Sample AY-130 13-C in CDCl3



file: C:\Arun\NMR\bh-ay-130.zip 13C\bh-ay-130\1\fid expt: <zgpg30>

transmitter freq.: 75.475295 MHz

time domain size: 65536 points

width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt

number of scans: 1024

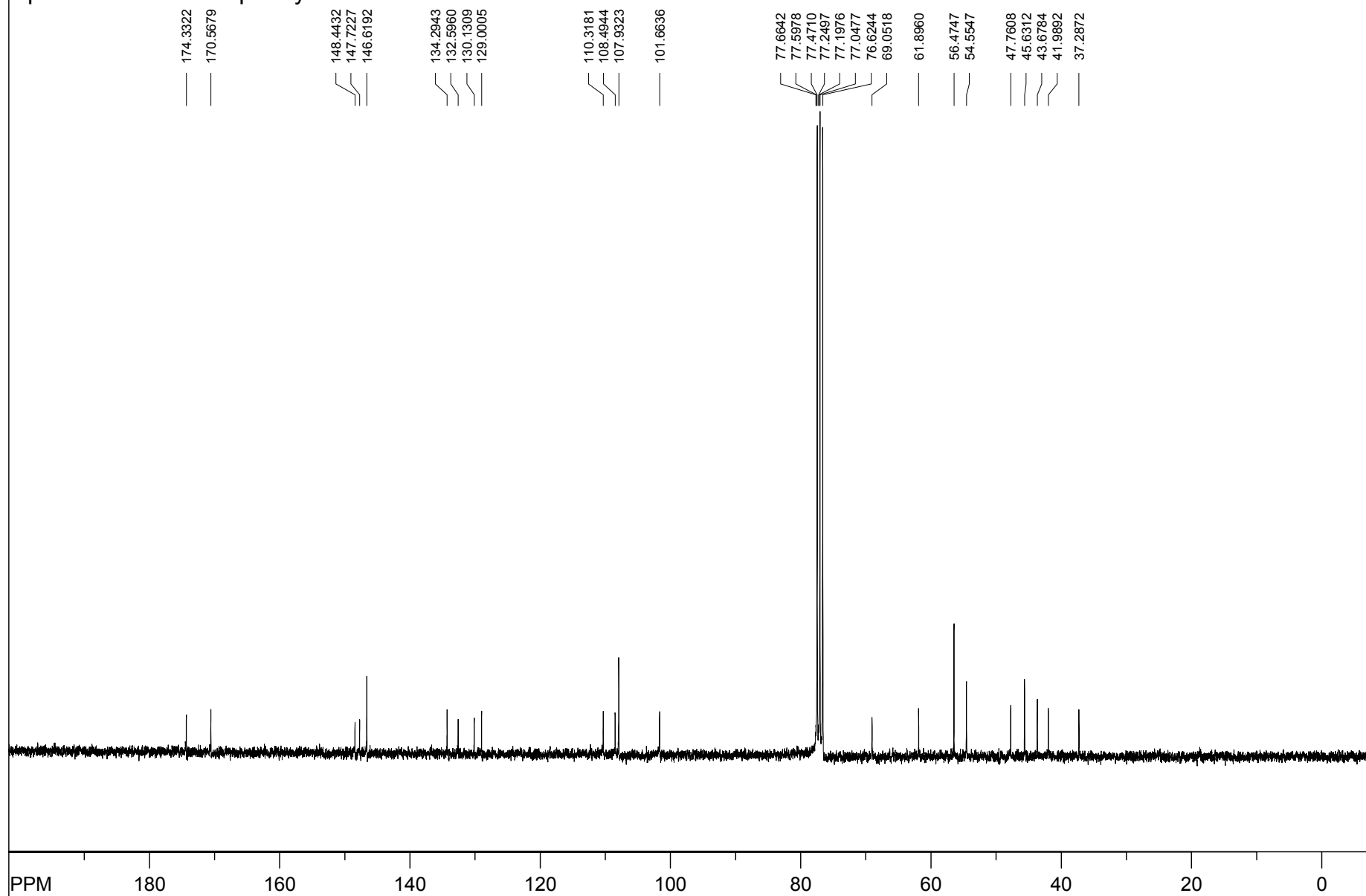
freq. of 0 ppm: 75.467749 MHz

processed size: 32768 complex points

LB: 0.300 GB: 0.0000

Hz/cm: 719.353 ppm/cm: 9.53097

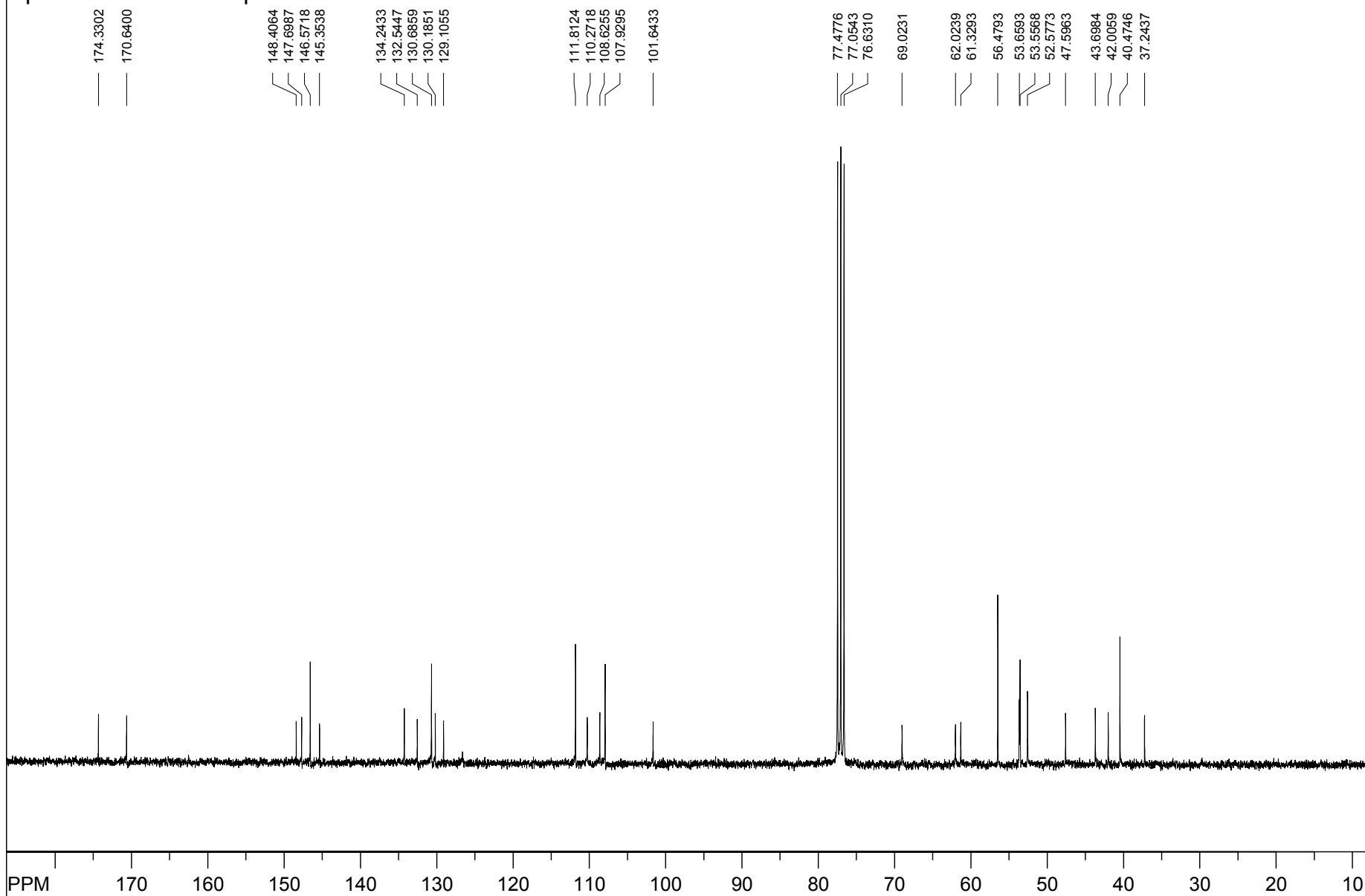
SpinWorks 2.5: Sample Ay-132 13-C in CDCl3



file: C:\Arun\NMR\bh-ay-132.zip 13C\bh-ay-132\1\fid exp: <zpgg30>
 transmitter freq.: 75.475295 MHz
 time domain size: 65536 points
 width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
 number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
 processed size: 32768 complex points
 LB: 0.300 GB: 0.0000
 Hz/cm: 632.243 ppm/cm: 8.37683

SpinWorks 2.5: Sample AY-134 13-C nmr in CDCl3



file: C:\Arun\NMR\bh-ay-134.zip 13C\bh-ay-134\1\fid exp: <zgpg30>

transmitter freq.: 75.475295 MHz

time domain size: 65536 points

width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt

number of scans: 1024

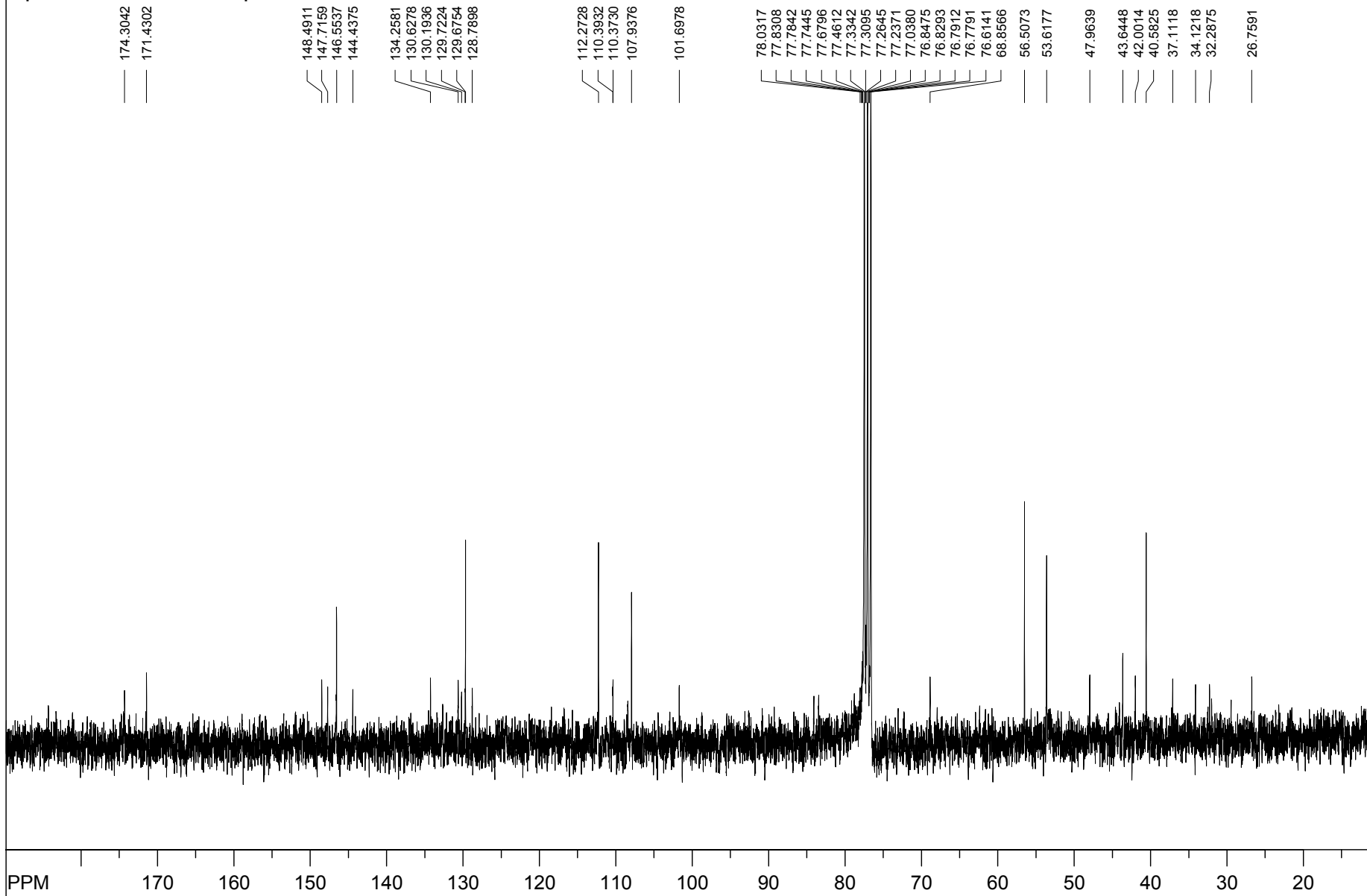
freq. of 0 ppm: 75.467749 MHz

processed size: 32768 complex points

LB: 0.000 GB: 0.0000

Hz/cm: 539.514 ppm/cm: 7.14823

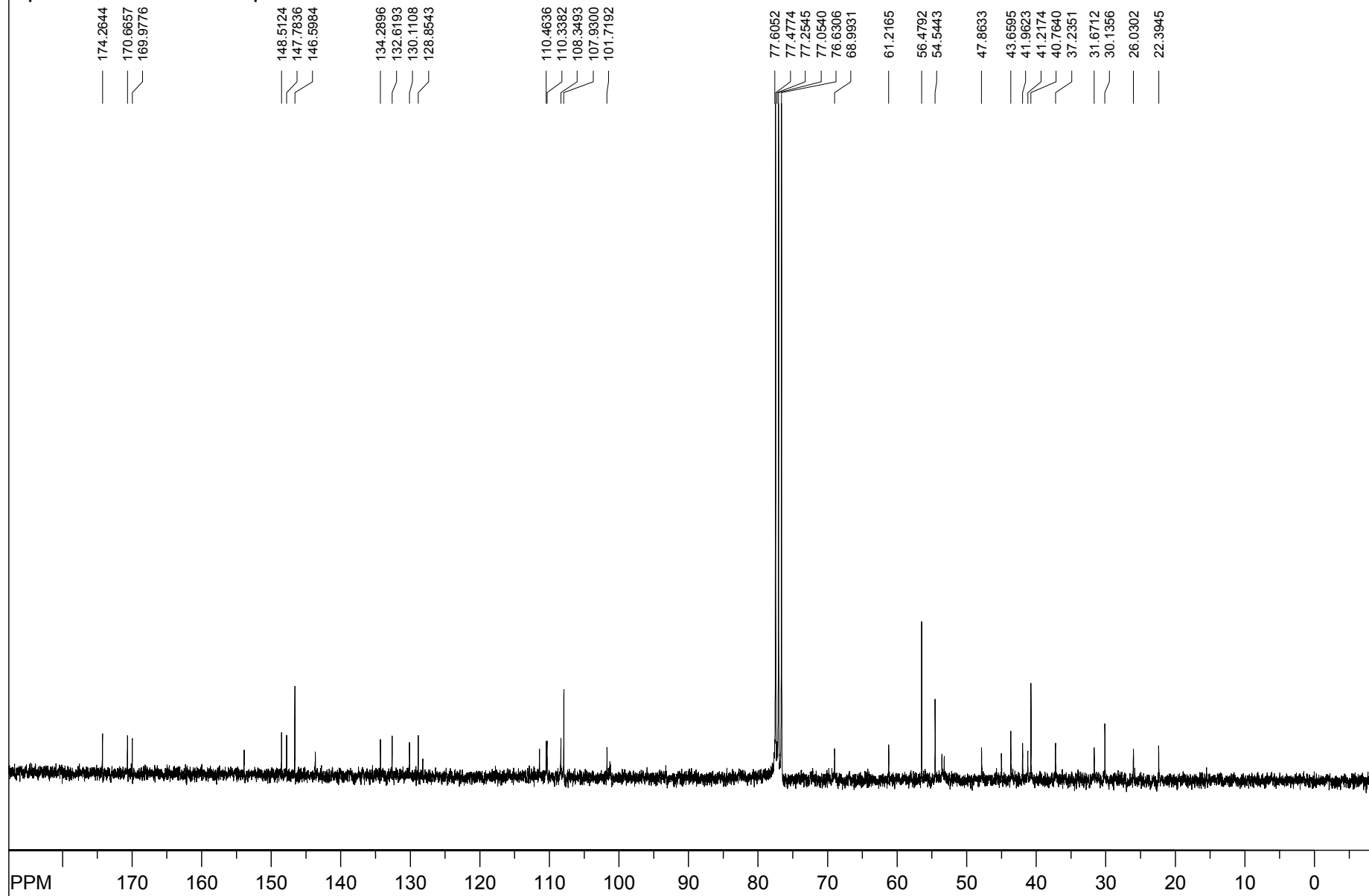
SpinWorks 2.5: Sample AY-136A 13-C nmr in CDCl3



file: C:\Arun\NMR\bh-ay-136a\bh-ay-136a\1\fid exp: <zpgg30>
transmitter freq.: 75.475295 MHz
time domain size: 65536 points
width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000
Hz/cm: 539.514 ppm/cm: 7.14823

SpinWorks 2.5: Sample AY-138 13-C nmr in CDCl3



file: C:\Arun\NMR\bh-ay-138-13c\bh-ay-138-13c\1\fid expt: <zpgg30>
 transmitter freq.: 75.475295 MHz
 time domain size: 65536 points
 width: 17985.61 Hz = 238.297995 ppm = 0.274439 Hz/pt
 number of scans: 1024

freq. of 0 ppm: 75.467749 MHz
 processed size: 32768 complex points
 LB: 1.000 GB: 0.0000
 Hz/cm: 592.728 ppm/cm: 7.85327