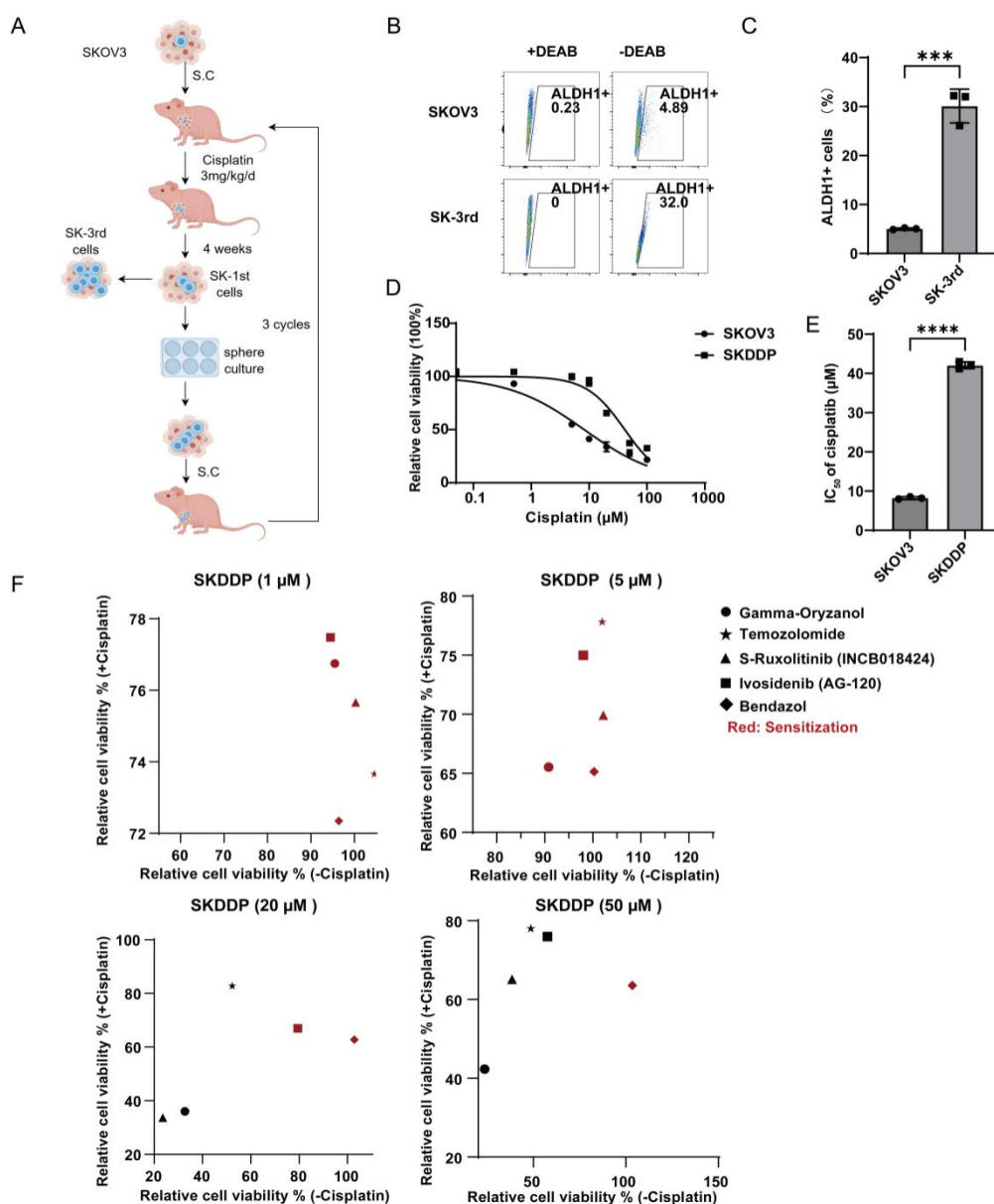




Supplementary Figure 1. Screening of a small molecule compound library shows that Ivosidenib enhances the sensitivity of ovarian cancer cells to cisplatin

(A) Schematic showing the method of SK-3rd model construction, as described in Materials and Methods.

(B) Representative FACS analysis showing the ALDH1+ cell populations in SK-3rd and SKOV3 cells.

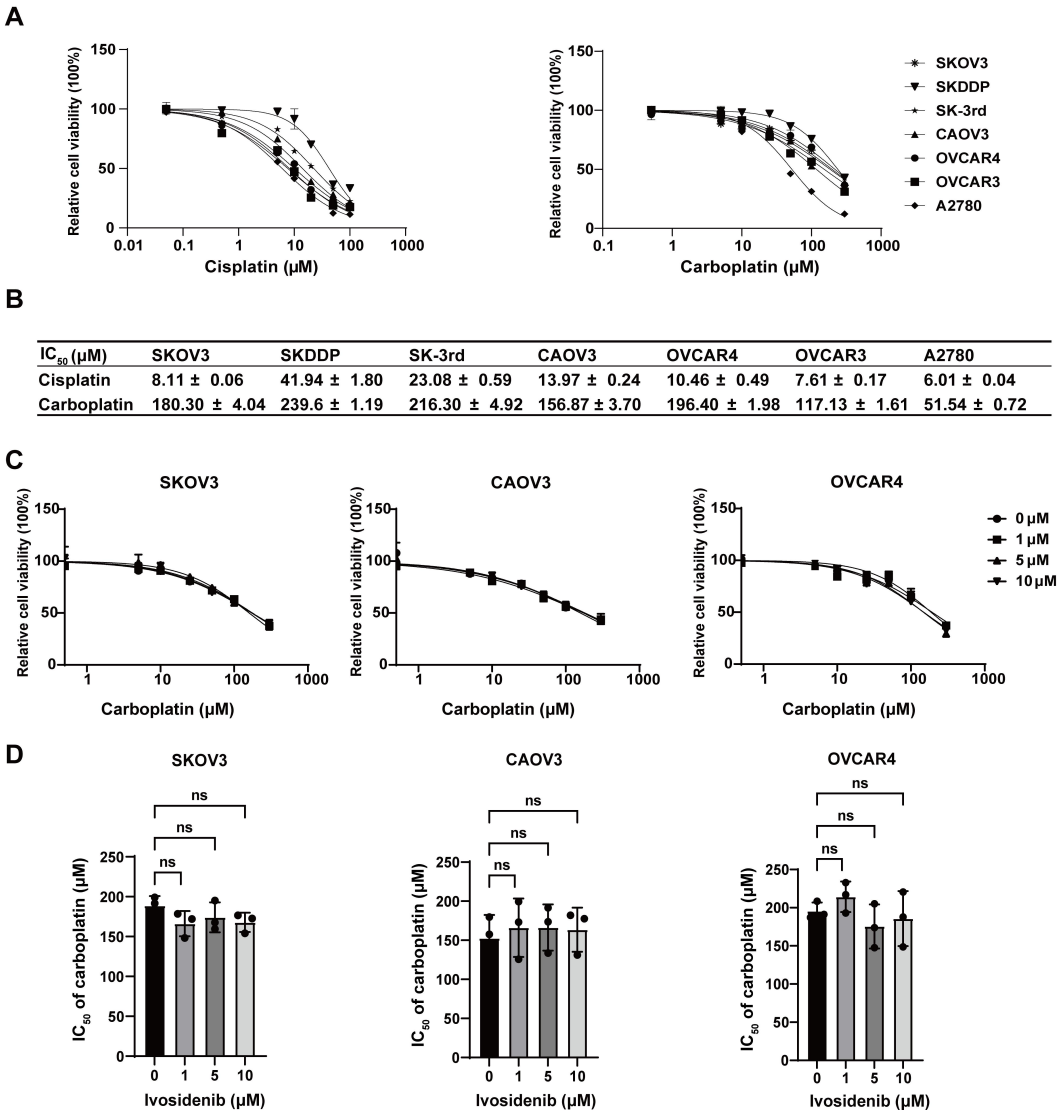
(C) The proportion of ALDH1+ cells was analyzed statistically in SKOV3 and SK-3rd. Data is represented as mean $\pm$ SD of three biologically independent experiments. *** P < 0.001 using an unpaired Student's t test.

(D) Dose-response curves of SKOV3 and SKDDP after cisplatin treatment for 72 hours detected by MTT assay. Data represent mean $\pm$ SD of three biologically independent experiments.

(E) The IC₅₀ of the curves statistically in (D) were calculated by Graph Pad Prism 9.5.0. Data represent mean $\pm$ SD of three biologically independent experiments. **** P < 0.0001 using an unpaired Student's t test.

(F) Scatter plot showing cell viability in SKDDP cells treated with the five selected compounds alone or

with the compounds plus cisplatin at a concentration of 1 μ M, 5 μ M, 20 μ M, and 50 μ M (n=4). The red dots represent drugs that have a sensitizing effect at that concentration.



Supplementary Figure 2. Ivosidenib increases the sensitivity of ovarian cancer cells to cisplatin

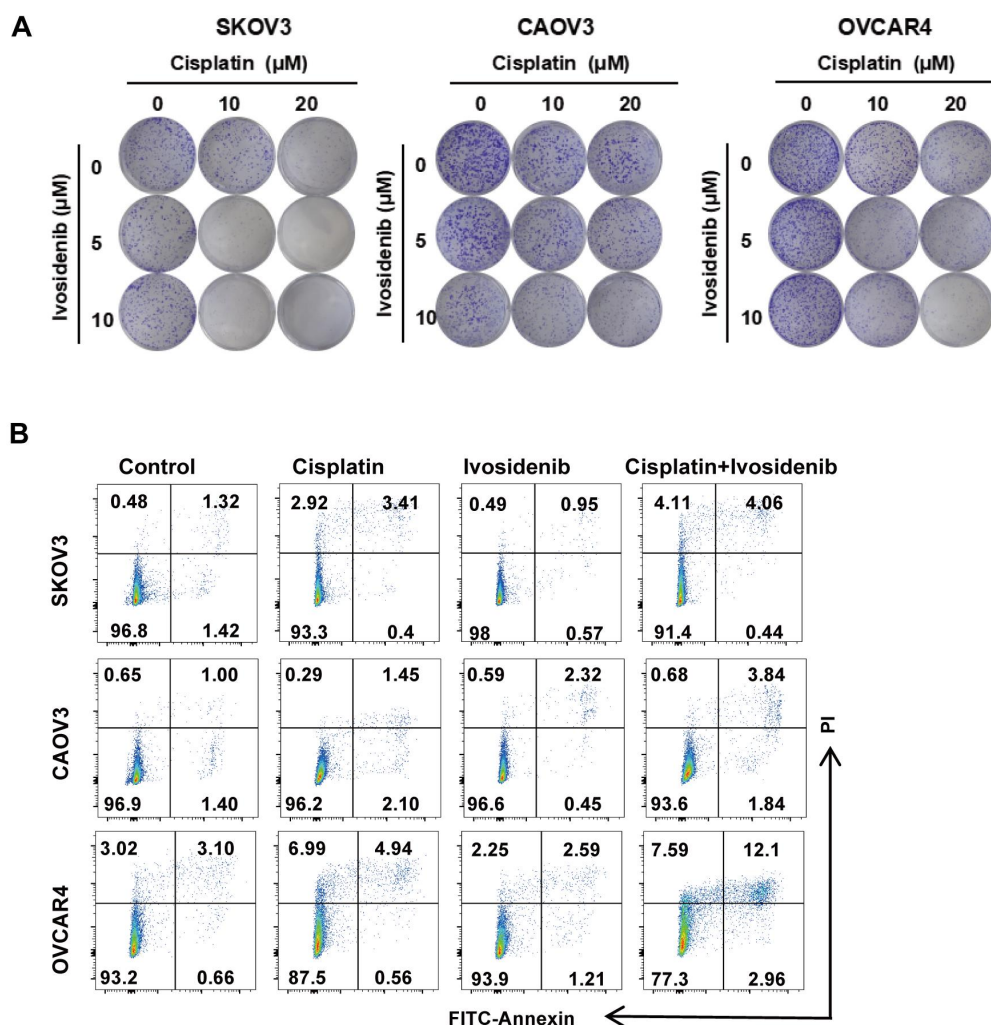
(A) Dose-response curves of SKOV3, SKDDP, SK-3rd, CAOV3, OVCAR4, OVCAR3, and A2780 detected by MTT assay treated with cisplatin or carboplatin for 72 h.

(B) The IC₅₀ of SKOV3, SKDDP, SK-3rd, CAOV3, OVCAR4, OVCAR3, and A2780 to cisplatin and carboplatin in (A) calculated by Graph Pad Prism 9.5.0. Data represent mean $\pm$ SD of three biologically independent experiments.

(C) Dose-response curves of SKOV3, CAOV3, and OVCAR4 detected by MTT assay treated with carboplatin and 0 μ M, 1 μ M, 5 μ M, and 10 μ M Ivosidenib for 72 h. Data represent mean $\pm$ SD of three biologically independent experiments.

(D) The IC₅₀ of SKOV3, CAOV3, and OVCAR4 to carboplatin in (C) calculated by Graph Pad Prism 9.5.0. Data represent mean $\pm$ SD of three biologically independent experiments. ns, not significant using a

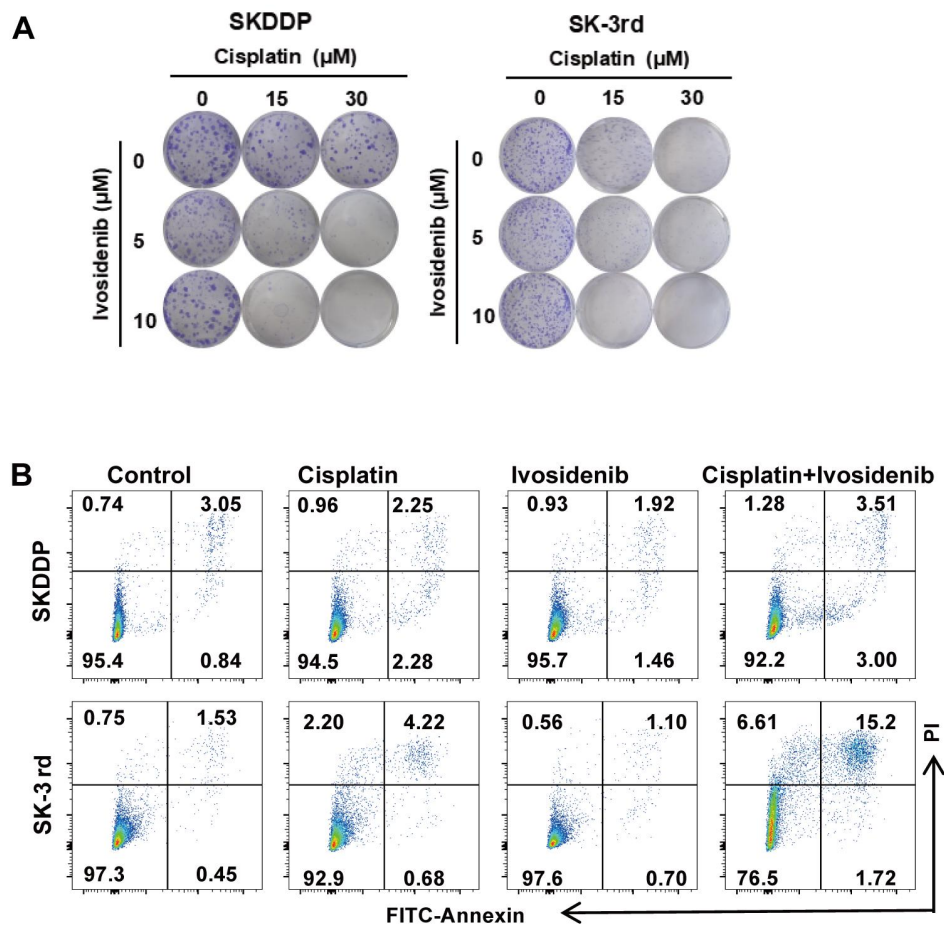
one-way ANOVA followed by Tukey's post hoc test for multiple comparisons.



Supplementary Figure 3. Ivosidenib combined with cisplatin reduces colony formation and enhances apoptosis in ovarian cancer cells

(A) Representative images of colony formation assay for SKOV3, CAOV3, and OVCAR4 cells treated with Ivosidenib, cisplatin, or their combination as indicated.

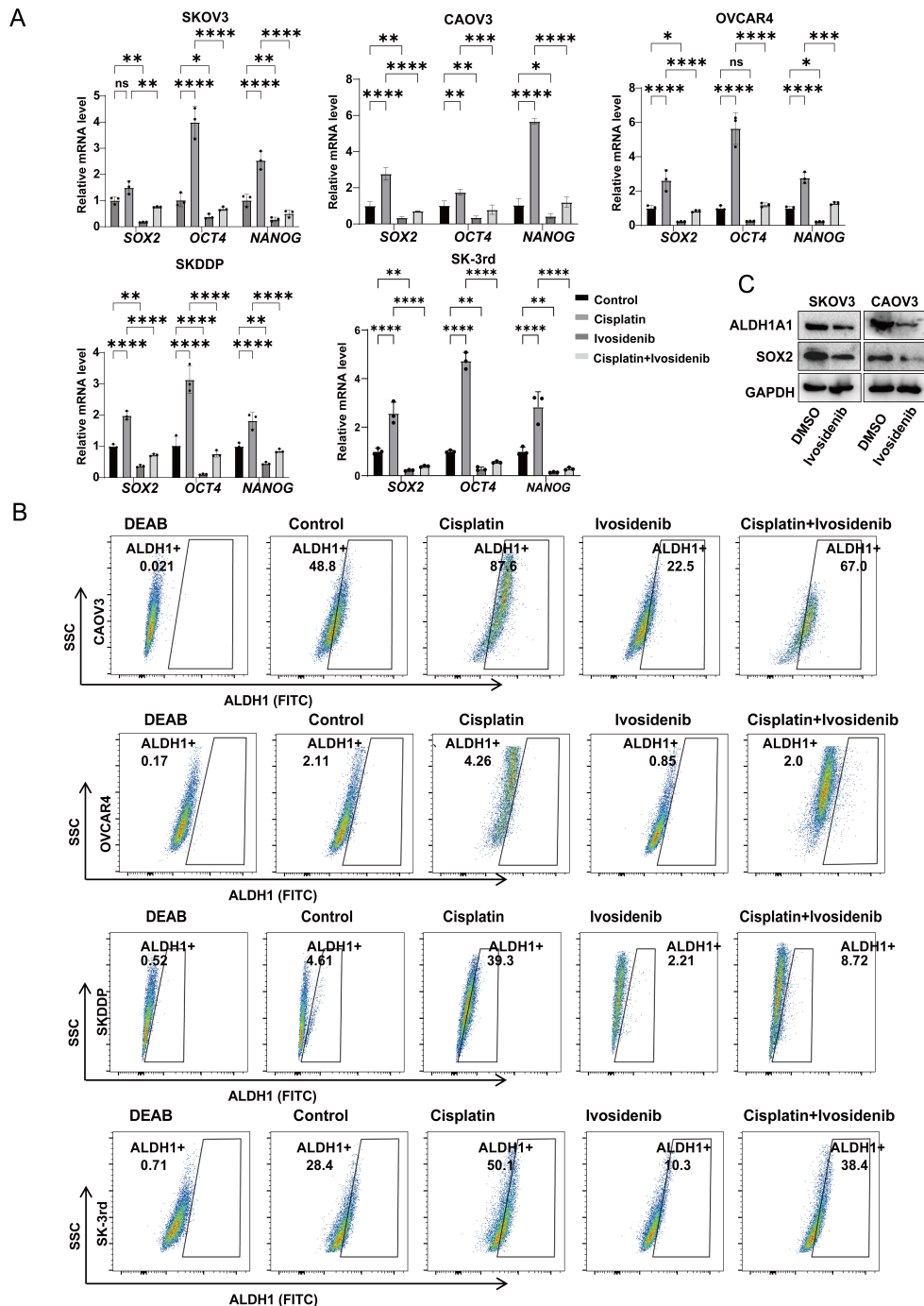
(B) Representative images of cell apoptosis analysis in SKOV3, CAOV3, and OVCAR4 cells treated with 10 μ M Ivosidenib, 10 μ M cisplatin, or their combination for 72 h. Annexin V-positive cells were analyzed by flow cytometry after treatment.



Supplementary Figure 4. Ivosidenib increases the sensitivity of SKDDP and SK-3rd to cisplatin

(A) Representative images of colony formation assay for SKDDP and SK-3rd cells treated with Ivosidenib, cisplatin, or their combination as indicated.

(B) Representative images of cell apoptosis analysis in SKDDP and SK-3rd cells treated with DMSO, 10 μM Ivosidenib, 10 μM cisplatin, or their combination for 72 h. Annexin V-positive cells were analyzed by flow cytometry after treatment.



Supplementary Figure 5. Ivosidenib reduces the stemness of ovarian cancer cells

(A) Quantitative analysis of the mRNA levels of stemness-related genes, including *SOX2*, *OCT4*, and *NANOG* in SKOV3, CAOV3, OVCAR4, SKDDP, and SK-3rd treated with DMSO, 10 μ M Ivosidenib, 10 μ M cisplatin, or their combination for 72 h by qRT-PCR. Data is represented as mean $\pm$ SD of three biologically independent experiments. ns, not significant; * P < 0.05; ** P < 0.01; *** P < 0.001; **** P < 0.0001 using a one-way ANOVA followed by Tukey's post hoc test for multiple comparisons.

(B) Representative images of ALDH1+ cells were analyzed using flow cytometry in CAOV3, OVCAR4, SKDDP, and SK-3rd cells treated with DMSO, 10 μ M Ivosidenib, 10 μ M cisplatin, or their combination for 72 h. DEAB was used as the negative control for ALDH1 activity.

(C) Western blot analysis of stemness markers ALDH1A1 and SOX2 in SKOV3 and CAOV3 cells treated with DMSO or 10 μ M Ivosidenib.

Table S1. A collection of 105 compounds

Cat	Name	Rack Num	Formula	Working	Target	Pathway	Informa	M.w.	CAS Num	DMSO (m	DMSO (m	Water (m	Water (m	URL	Formula	Form	Synonym	SMILES	ALogP	HBA	Cou	HBD	Cou Rotatable
S1007	Roxadust	L2000-01	in 10mM	10 µM	HIF	Angiogeni	Roxadust	352.34	808118-4	70.00	198.67	<1		http://sel	C19H16N	free base	ASP1517	CC1=NC(=	2.306	4	2	5	
S1030	Panobino	L2000-01	in 10mM	10 µM	HDAC	Epigeneti	Panobino	349.43	404950-8	69.00	197.46	<1		http://sel	C21H23N	Free Base	NVP-LBH	CC1=C(CC	3.194	1	3	7	
S1033	Nilotinib (	L2000-01	in 10mM	10 µM	Bcr-Abl	Angiogeni	Nilotinib (	529.52	641571-1	27.00	50.99	<1		http://sel	C28H22F3	free base	N/A	CC1=C[N]	5.084	5	2	7	
S1047	Vorinosta	L2000-01	in 10mM	10 µM	Autophag	Epigeneti	Vorinosta	264.30	149647-7	52.00	196.75	<1		http://sel	C14H20N	free base	SAHA, M	ONC(=O)	2.005	2	2	8	
S1053	Entinosta	L2000-01	in 10mM	10 µM	HDAC	Epigeneti	Entinosta	376.41	209783-8	75.00	199.25	<1		http://sel	C21H20N	free base	SNDX-275	NC1=CC=	4.071	4	3	7	
S1055	Enzastaur	L2000-01	in 10mM	10 µM	PKC	TGF-beta	Enzastaur	515.61	170364-5	30.00	58.18	<1		http://sel	C32H29N	free base	N/A	C[N]1C=C	2.320	3	1	5	
S1085	Belinostat	L2000-01	in 10mM	10 µM	HDAC	Epigeneti	Belinostat	318.35	414864-0	64.00	201.04	<1		http://sel	C15H14N	free base	NSC7266	ONC(=O)	1.875	3	2	5	
S1168	Valproic a	L2000-01	in 10mM	10 µM	GABA Rec	Neuronal	Valproic a	166.19	1069-66-7	33.00	198.57	33.00	198.57	http://sel	C8H15Na	Sodium s	N/A	CCCC(CCC	1.200	0	0	5	
S1200	Decitabin	L2000-01	in 10mM	10 µM	DNA Met	Epigeneti	Decitabin	228.21	2353-33-7	45.00	197.19	10.00	43.82	http://sel	C8H12N4	free base	Deoxycyt	NC1=NC(=	-1.093	4	3	2	
S1209	Fluoroura	L2000-01	in 10mM	10 µM	DNA/RNA	DNA Dam	Fluoroura	130.08	51-21-8	26.00	199.88	<1		http://sel	C4H3FN2	free base	NSC 1989	FC1=CN(=	-1.102	2	2	0	
S1233	2-Methox	L2000-01	in 10mM	10 µM	HIF	Angiogen	2-Methox	302.41	362-07-2	60.00	198.41	<1		http://sel	C19H26O	free base	NSC 6598	COC1=C(C	3.821	1	2	1	
S1237	Temozolc	L2000-01	in 10mM	10 µM	DNA/RNA	DNA Dam	Temozolc	194.15	85622-93	38.00	195.72	<1		http://sel	C6H6N6O	free base	CRG810	CN1=N=NC	0.052	5	1	1	
S1373	Daptomyi	L2000-01	in 10mM	10 µM	Anti-infec	DNA Dam	Daptomyi	1620.67	103060-5	100.00	61.70	100.00	61.70	http://sel	C72H1011	free base	LY146032	CCCCCCCC	-7.895	21	18	35	
S1378	Ruxolitin	L2000-01	in 10mM	10 µM	JAK	JAK/STAT	Ruxolitin	306.37	941678-4	61.00	199.11	<1		http://sel	C17H18N	free base	N/A	N#CC(C(C	2.880	3	1	4	
S1396	Resveratr	L2000-01	in 10mM	10 µM	Autophag	Autophag	Resveratr	228.24	501-36-0	45.00	197.16	<1		http://sel	C14H12O	free base	N/A	OC1=CC=	3.090	0	3	2	
S1421	Staurospc	L2000-02	in 10mM	10 µM	PKC,ADC	TGF-beta	Staurospc	466.53	62996-74	93.00	199.34	<1		https://w	C28H26N	Free Base	CGP 4125	CNC1CC2	3.819	3	2	2	
S1573	Fasudil (H	L2000-01	in 10mM	10 µM	Autophag	Cell Cycle	Fasudil(H	327.83	105628-0	5.00	15.25	65.00	198.27	http://sel	C14H18Cl	Hydrochl	N/A	Cl.O=][S]	0.570	3	1	2	
S1703	Divalproe	L2000-01	in 10mM	10 µM	HDAC	Epigeneti	Divalproe	310.41	76584-70	62.00	199.74	62.00	199.74	http://sel	C16H31N	Sodium S	N/A	[Na+][C	4.025	1	0	10	
S1756	Enoxacin	L2000-01	in 10mM	10 µM	Toiposom	DNA Dam	Enoxacin	320.32	74011-58	32.00	99.90	<1		http://sel	C15H17F7	free base	AT-2266,	CNC1=C	-1.483	3	1	3	
S1782	Azacitidin	L2000-01	in 10mM	10 µM	DNA Met	DNA Dam	Azacitidin	244.20	320-67-2	48.00	196.56	<1		http://sel	C8H12N4	free base	NSC 1028	NC1=NC(=	-2.505	4	4	2	
S1831	Carvedilo	L2000-01	in 10mM	10 µM	Adrenerg	Neuronal	Carvedilo	406.47	72956-09	81.00	199.28	<1		http://sel	C24H26N	free base	BM-1419	CNC1=CC	0.414	3	3	10	
S1899	Nicotinan	L2000-01	in 10mM	10 µM	Sirtuin	DNA Dam	Nicotinan	122.12	98-92-0	24.00	196.53	24.00	196.53	http://sel	C6H6N2O	free base	Niacinan	NC(=O)C	-0.319	2	1	1	
S2105	Pantopra:	L2000-01	in 10mM	10 µM	Proton P:	Transmer	Pantopra:	383.37	102625-7	76.00	198.24	<1		http://sel	C16H15F5	free base	N/A	OC1=C(C	2.737	6	1	7	
S2250	(-)-Epigall	L2000-01	in 10mM	10 µM	DNA Met	DNA Dam	(-)-Epigall	458.37	989-51-5	72.00	157.08	23.00	50.18	http://sel	C22H18O	free base	EGCG	OC1=CC3	3.093	3	8	4	
S2271	Berberine	L2000-01	in 10mM	10 µM	Anti-infec	Microbiol	Berberine	371.81	633-65-8	40.00	107.58	<1		http://sel	C20H18Cl	chloride	N/A	[C-].COC	-1.289	4	0	2	
S2280	Chlorogre	L2000-01	in 10mM	10 µM	Others	Others	Chlorogre	354.31	327-97-9	71.00	200.39	18.00	50.80	http://sel	C16H18O	free base	NSC 4072	OC1=CC(=	0.440	3	4	5	
S2341	(-)-Parthe	L2000-01	in 10mM	10 µM	HDAC,NF	NF-kB	(-)-Parthe	248.32	20554-84	49.00	197.33	<1		http://sel	C15H20O	free base	N/A	CC1=C(C	2.923	3	0	0	
S2347	Quercetin	L2000-01	in 10mM	10 µM	Others	Others	Quercetin	338.27	6151-25-7	67.00	198.07	<1		http://sel	C15H14O	Dihydrate	Sophoret	O.O.O=C1	1.216	2	5	1	
S2391	Quercetin	L2000-01	in 10mM	10 µM	Src,Sirtui	Epigeneti	Quercetin	302.24	117-39-5	61.00	201.83	<1		http://sel	C15H10O	Free Base	Sophoret	OC1=CC(=	1.230	2	5	1	
S2410	Paeoniflo	L2000-01	in 10mM	10 µM	Others	Others	Paeoniflo	480.46	23180-57	96.00	199.81	96.00	199.81	http://sel	C23H28O	free base	N/A	CC1=CC3	-1.683	6	4	7	
S2468	Fenbenda	L2000-01	in 10mM	10 µM	Anti-infec	Microbiol	Fenbenda	299.35	43210-67	4.00	13.36	<1		http://sel	C15H13N	free base	N/A	OC(=O)N	3.769	3	2	4	
S2485	Mitoxant	L2000-01	in 10mM	10 µM	Toiposom	DNA Dam	Mitoxant	517.40	70476-82	89.00	172.01	89.00	172.01	http://sel	C22H30Cl	Dihydrocl	NSC-3017	Cl.Cl.OCC	0.832	2	8	12	
S2542	Phenform	L2000-01	in 10mM	10 µM	AMPK	PI3K/Akt	Phenform	241.72	834-28-6	48.00	198.58	48.00	198.58	http://sel	C10H16Cl	Hydrochl	N/A	Cl.NC(=N)	1.339	0	3	6	
S2554	Daphneti	L2000-01	in 10mM	10 µM	PKA,EGFR	Angiogen	Daphneti	178.14	486-35-1	35.00	196.47	<1		http://sel	C9H6O4	free base	N/A	OC1=CC(=	1.415	2	2	0	
S2680	Ibrutinib (	L2000-01	in 10mM	10 µM	BTK	Angiogen	Ibrutinib (	440.50	936563-9	88.00	199.77	<1		http://sel	C25H24N	free base	N/A	NC1=C2C	3.985	5	1	5	
S2736	Ledratinit	L2000-01	in 10mM	10 µM	JAK	JAK/STAT	Ledratinit	524.68	936091-2	100.00	190.59	<1		http://sel	C27H36N	free base	N/A	CC1=C(NC	5.132	5	3	11	
S2789	Tofacitinil	L2000-01	in 10mM	10 µM	JAK	JAK/STAT	Tofacitinil	312.37	477600-7	62.00	198.48	<1		http://sel	C16H20N	free base	N/A	CC1CN(C)	1.512	3	1	3	
S2851	Baricitini	L2000-01	in 10mM	10 µM	JAK	JAK/STAT	Baricitini	371.42	118759-4	74.00	199.24	<1		http://sel	C16H17N	free base	N/A	CC1=CC(=	0.360	5	1	5	
S2902	S-Ruxoliti	L2000-01	in 10mM	10 µM	JAK	JAK/STAT	S-Ruxoliti	306.37	941685-3	61.00	199.11	5.00	16.32	http://sel	C17H18N	free base	N/A	N#CC(C(C	2.880	3	1	4	
S3001	Clevudine	L2000-01	in 10mM	10 µM	DNA/RNA	DNA Dam	Clevudine	260.22	163252-3	52.00	199.83	52.00	199.83	http://sel	C10H13F7	free base	N/A	CC1=CC(=	-1.065	3	3	2	
S3023	Bufexama	L2000-01	in 10mM	10 µM	COX	Neuronal	Bufexama	223.27	2438-72-7	45.00	201.55	<1		http://sel	C12H17N	free base	N/A	CCCCC1C	1.291	2	1	6	
S3147	Entacapone	L2000-01	in 10mM	10 µM	Histone N	Epigeneti	Entacapone	305.29	130929-5	61.00	199.81	<1		http://sel	C14H15N	free base	OR-611	CN(C)C(C	1.658	1	2	5	
S3273	Hypericin	L2000-02	in 10mM	10 µM	MAO	Metabolis	Hypericin	504.44	548-04-9	100.00	198.24	-1.00		http://wv	C30H16O	free base	Hyp, HY	CC1=C2C	5.040	2	6	0	
S3341	Palmitole	L2000-02	in 10mM	10 µM	AMPK	PI3K/Akt	Palmitole	254.41	373-49-9	liquid, which can be dissolved in any pro				https://w	C16H30O	Free Base	POA, Palm	CCCCC(C	5.948	1	0	13	
S3589	Bendazol	L2000-02	in 10mM	10 µM	NOS	Immunok	Bendazol	208.26	621-72-7	42.00	201.67	<1		http://wv	C14H12N	Free Base	2-Benzylc	Cl(C1=NC	3.305	1	1	2	
S3592	Benzenet	L2000-02	in 10mM	10 µM	HDAC	DNA Dam	4-Phenyl	164.20	1821-12-1	33.00	200.97	<1		http://wv	C10H12O	Free Base	Benzenet	OC(=O)CC	2.407	1	0	4	
S3609	Berberine	L2000-01	in 10mM	10 µM	Bcr-Abl	Angiogen	Berberine	681.65	6078-17-7	100.00	146.70	100.00	146.70	http://sel	C37H42Cl	dihydrocl	N/A	Cl.Cl.COC	7.756	5	1	3	
S3639	Tacrine h	L2000-01	in 10mM	10 µM	ACHR	Neuronal	Tacrine h	198.26	206658-9	50.00	252.19	50.00	252.19	http://sel	C13H14N	hydrochl	Tacrine,	T.NC1=C2C	4.258	1	1	0	
S3694	Glucosam	L2000-01	in 10mM	10 µM	Others	Others	Glucosam	215.63	66-84-2	4.00	18.55	43.00	199.42	http://sel	C6H14ClN	hydrochl	2-Amino-	Cl.NC1(C	-1.422	1	4	1	
S3781	Ginkgolid	L2000-01	in 10mM	10 µM	Others	Others	Ginkgolid	440.40	15291-76	88.00	199.82	<1		http://sel	C20H24O	free base	BN-5202	CC1(=O)	-2.753	7	3	1	
S3850	Glucosam	L2000-01	in 10mM	10 µM	Others	Others	Glucosam	277.25	29031-19	4.00	14.43	55.00	198.38	http://sel	C6H15NO	sulfate	D-Glucos	NC(=O)C	-3.688	1	5	5	
S3944	Valproic a	L2000-01	in 10mM	10 µM	HDAC	Epigeneti	Valproic a	144.21	99-66-1	liquid, which can be dissolved in any pro				http://sel	C8H16O2	free base	2-Propyl	CCCC(CCC	2.749	1	0	5	
S3957	Gamma-C	L2000-01	in 10mM	10 µM	Others	Others	Gamma-C	602.89	11042-64	100.00	165.87	<1		http://sel	C40H58O	free base	N/A	OC1=CC	9.808	3	1	9	
S3984	Nordihydr	L2000-01	in 10mM	10 µM	Lipoxyer	Metabolis	Nordihyd	302.36	500-38-9	60.00	198.44	<1		http://sel	C18H22O	free base	N/A	CC(C1=C	4.706	0	4	5	
S4021	Tolcapone	L2000-01	in 10mM	10 µM	Transfere	Metabolis	Tolcapone	273.24	134308-1	55.00	201.29	<1		http://sel	C14H11N	free base	Ro 40-75	CC1=CC(=	3.130	1	2	3	
S4023	Procaine	L2000-01	in 10mM	10 µM	NMDAR,S	Transmer	Procaine	272.77	51-05-8	55.00	201.64	55.00	201.64	http://sel	C13H21Cl	HCl	Novocain	Cl.CN(C	2.157	2	1	7	
S4125	Sodium P	L2000-01	in 10mM	10 µM	HDAC	DNA Dam	Sodium P	186.18	1716-12-7	8.00	42.97	30.00	161.13	http://sel	C10H11N	Sodium S	N/A	[Na]O(C(=	2.497	2	0	5	
S4246	Tranylcyp	L2000-01	in 10mM	10 µM	MAO	Metabolis	Tranylcyp	169.65	1986-47-7	33.00	194.52	33.00	194.52	http://sel	C9H12ClN	Hydrochl	SKF-385	1-N.C1=CC	2.309	0	1	1	
S4268																							