Table S1. Predicted physicochemical and ADME properties of the test compounds.

Compounds		Compound-X	Compound-Y	Compound-Z	E4031
Physicochemical properties	MW	441.488	442.472	442.476	415.559
	ClogP	1.7415	1.8649	1.2208	3.28902
	Rotatable Bonds	10	10	10	8
	Acceptors	7	7	8	5
	Donors	5	5	6	1
	TPSA	184.604	184.058	183.789	172.949
Absorption	Water solubility (log mol/L)	-2.907	-2.911	-2.903	-4.414
	Caco2 permeability (log Papp)	-0.822	-0.758	-0.797	1.093
	Intestinal absorption (%)	28.627	25.758	22.436	92.885
	Skin Permeability (log Kp)	-2.735	-2.735	-2.735	-3.35
	P-gp substrate	Yes	Yes	Yes	Yes
	P-gp I inhibitor	No	No	No	No
	P-gp II inhibitor	No	No	No	Yes
Distribution	VDss (human) (log L/kg)	-0.62	-0.25	-0.224	0.677
	Fraction unbound	0.282	0.204	0.369	0.286
	BBB permeability (log BB)	-1.544	-1.67	-1.649	-0.448
	CNS permeability (log PS)	-3.528	-3.545	-3.654	-2.916
Metabolism	CYP2D6 substrate	No	No	Yes	No
	CYP3A4 substrate	No	No	No	Yes
	CYP1A2 inhibitior	No	No	No	No
	CYP2C19 inhibitior	No	No	No	No
	CYP2C9 inhibitior	No	No	No	No
	CYP2D6 inhibitior	No	No	No	No
	CYP3A4 inhibitior	No	No	No	Yes
Excretion	Total Clearance (log ml/min/kg)	0.689	0.722	0.481	0.744
	Renal OCT2 substrate	No	No	No	No

BBB: blood–brain barrier; CLogP o/w: lipophilicity (recommended value: LogP <5); CYP1A2: cytochrome P450 family 1 subfamily A member 2; CYP3A4: cytochrome P450 family 3 subfamily A member 4; CYP2C9: cytochrome P450 family 2 subfamily C member 9; CYP2C19: cytochrome P450 family 2 subfamily C member 19; CYP2D6: cytochrome P450 family 2 subfamily D member 6; Lipinski (criteria: MW≤500, LogP≤5, N or O ≤ 10, NH or OH≤5); MW: Molecular weight of the compounds; OCT2: organic cation transporter 2; P-gp: P-glycoprotein substrate; TPSA: topological polar surface area. Conclusions