

**Supplemental Table 1. Selectivity of VU0152099 and VU0152100 were evaluated in radioligand binding assays in the LeadProfilingScreen® by MDS Pharma ([www.mdsp.com](http://www.mdsp.com)). VU0152099 and VU0152100 were tested at 10µM for orthosteric radioligand displacement against a large panel of 68 discrete GPCRs, ion channels, transporters and enzymes to ensure a clean ancillary pharmacology profile.**

Target	Species	% Inhibition		Target	Species	% Inhibition	
		VU0152099	VU0152100			VU0152099	VU0152100
Adenosine A1	human	28	-1	Histamine H <sub>3</sub>	human	10	9
Adenosine A2	human	46	43	Imidazoline I <sub>2</sub> , Central	rat	7	8
Adenosine A3	human	28	40	Interleukin IL-1	mouse	-19	-4
Adrenergic α <sub>1A</sub>	rat	10	9	Leukotriene, Cysteinyl CysLT <sub>1</sub>	human	-4	-6
Adrenergic α <sub>1B</sub>	rat	-7	-7	Melatonin MT <sub>1</sub>	human	15	20
Adrenergic α <sub>1D</sub>	human	1	1	Muscarinic M <sub>1</sub>	human	-3	0
Adrenergic α <sub>2A</sub>	human	7	17	Muscarinic M <sub>2</sub>	human	-1	-4
Adrenergic β <sub>1</sub>	human	17	17	Muscarinic M <sub>3</sub>	human	-1	-2
Adrenergic β <sub>2</sub>	human	30	35	Neuropeptide Y Y <sub>1</sub>	human	2	9
Androgen (testosterone)AR	rat	6	6	Neuropeptide Y Y <sub>2</sub>	human	-2	2
Bradykinin B <sub>1</sub>	human	13	1	Nicotinic Acetylcholine	human	6	-6
Bradykinin B <sub>2</sub>	human	-5	-9	Nicotinic Acetylcholine α1, Bungarotoxin	human	-10	-4
Calcium channel L-type, benzothiazepine	rat	13	7	Opiate δ (OP1, DOP)	human	2	-13
Calcium channel L-type, dihydropyridine	rat	21	17	Opiate κ (OP2, KOP)	human	5	2
Calcium channel N-type	rat	-8	-4	Opiate μ (OP3, MOP)	human	2	-2
Dopamine D <sub>1</sub>	human	6	7	Phorbol Ester	mouse	2	4
Dopamine D <sub>2S</sub>	human	2	0	Platelet Activating Factor (PAF)	human	13	22
Dopamine D <sub>3</sub>	human	-1	5	Potassium Channel [K <sub>A</sub> TP]	hamster	3	6
Dopamine D <sub>4.2</sub>	human	-13	-11	Potassium Channel hERG	human	5	5
Endothelin ET <sub>A</sub>	human	-8	-8	Prostanoid EP <sub>4</sub>	human	15	7
Endothelin ET <sub>B</sub>	human	2	-4	Purinergic P <sub>2X</sub>	rabbit	6	-4
Epidermal Growth Factor (EGF)	human	9	-5	Purinergic P <sub>2Y</sub>	rat	15	14
Estrogen ERα	human	-1	-1	Rolipram	rat	36	29
G protein-coupled receptor GPR103	human	-3	-4	Serotonin (5-Hydroxytryptamine) 5-HT <sub>1A</sub>	human	2	2
GABA <sub>A</sub> Flunitrazepam, central	rat	51	43	Serotonin (5-Hydroxytryptamine) 5-HT <sub>3</sub>	human	-2	14
GABA <sub>A</sub> Muscimol, central	rat	6	9	Sigma σ <sub>1</sub>	human	2	6
GABA <sub>B1A</sub>	human	-7	12	Sigma σ <sub>2</sub>	rat	-8	-3
Glucocorticoid	human	-3	8	Sodium Channel, Site 2	rat	11	20
Glutamate, Kainate	rat	3	-15	Tachykinin NK <sub>1</sub>	human	-15	-18
Glutamate, NMDA, Agonism	rat	17	22	Thyroid Hormone	rat	-1	0
Glutamate, NMDA, Glycine	rat	3	2	Transporter, Dopamine (DAT)	human	27	46
Glutamate, NMDA, Phencyclidine	rat	2	3	Transporter, GABA	rat	26	13
Histamine H <sub>1</sub>	human	14	7	Transporter, Norepinephrine (NET)	human	34	22
Histamine H <sub>2</sub>	human	7	10	Transporter, Serotonin (5-Hydroxytryptamine) (SERT)	human	0	4