Supplementary Table S1. In vitro Ki values and in vivo C_{50} values of various antipsychotics for dopamine D_2 receptor

Drugs	In vitro Ki (nM)			Protein binding ratio		In vivo C_{50} (ng/mL)	In vivo $C_{50,free}$[a] (nM)	Reference of C_{50}
	This study[b]	Asenapine IF[c]	Schotte et al.[d]		Mean			
Asenapine	0.344	1.26	-	0.973[e] 0.95[e]	0.962	0.528	0.0711	S1
Clozapine		135	190	0.909[f] 0.97[g]	0.940	105.3	19.5	S2
Haloperidol	0.517	1.45	2.2	0.92[h]		0.532 0.32	0.0878	S1 S2
Olanzapine	12.8	21.4	31	0.93[i,j]		5.29 7.1	1.37	S1 S2
Ziprasidone	1.25		4.6	0.99[k]		15.4 32.9	0.545	S1 S2
Blonanserin patch	0.0997					0.857	0.00700	Fig. 3
Blonanserin	0.0997		-	0.997[l]		0.112 0.0797[m]	0.000914 0.000650	Fig. 3 S3

[a]: Calculated with the equation of $C_{50,free}$ (nM) = C_{50} (ng/mL) × (1 - protein binding) / (molecular weight) × 1000. Shown as geometric mean, if two in vivo C_{50} values are available.

[b]: Measured in house with the procedure described separately below.

[c]: Interview form of asenapine (sycrest® sublingual tablets) [Japanese]. Oct 2021. https://www.info.pmda.go.jp/go/interview/1/780009_1179056F1021_1_1F.pdf

[d]: Schotte A, Janssen PFM, Gommeren W, et al. Risperidone compared with new and reference antipsychotic drugs: in vitro and in vivo receptor binding. *Psychopharmacology* 1996;124:57−73.

[e]: Label of asenapine. Feb 2017. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022117s022lbl.pdf

[f]: Interview form of clozapine (Clozaril® tablets) [Japanese]. Jun 2021. https://www.info.pmda.go.jp/go/interview/1/300242_1179049F1021_1_CLO_1F.pdf

[g]: Label of clozapine (Clozaril® tablets). Feb 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/019758s088lbl.pdf

[h]: Interview form of haloperidol (Serenace®) [Japanese]. May 2021. https://www.info.pmda.go.jp/go/interview/1/400093_1179020C1191_1_028_1F.pdf

[i]: Interview form of olanzapine (Zyprexa® tablets) [Japanese]. Sep 2020. https://www.info.pmda.go.jp/go/interview/1/530471_1179044F4028_1_18F_4F.pdf

[j]: Label of olanzapine (Zyprexa® tablets) Oct 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020592s074,021086s048,021253s061lbl.pdf

[k]: Label of ziprasidone (Geodon® capsules) May 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020825s062,020919s050lbl.pdf

[l]: Interview form of blonanserin (Lonasen® tablets) [Japanese]. Dec 2021. https://www.info.pmda.go.jp/go/interview/1/400093_1179048B1025_1_026_1F.pdf

[m]: Estimated with Emax model without fixing maximum binding based on the data from the reference S3.

Dopamine D_{2L} receptor binding assay procedure

D_{2L} receptor binding assay was performed in reference to a method described by Hirose et al.[S4] In the presence or absence of test compounds, human D_{2L} receptor-expressing CHO cell membrane samples were incubated with [^{3}H]-spiperone (final concentration 0.5 nM) for 60 minutes at room temperature, and then it was quickly filtered under reduced pressure. Nonspecific binding was measured in the presence of 10 μM of spiperone, and [^{3}H]-spiperone binding inhibition rate in the presence of test drug (in the range of 0.1-10000 nM, 30 to 333-fold concentration range for each test drug) was determined. Ki values were derived from IC_{50} values obtained by in vitro binding assays according to the relationship of $Ki = IC_{50}/(1 + L/Kd)$, where L is the concentration of radioligand and Kd is the dissociation constant.

Reference

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S3. Tateno A, Arakawa R, Okumura M, et al. Striatal and extrastriatal dopamine D_2 receptor occupancy by a novel antipsychotic, blonanserin: A PET study with [^{11}C]raclopride and [^{11}C]FLB 457 in schizophrenia. *J Clin Psychopharmacol*. 2013;33(2):162–169. https://doi.org/10.1097/JCP.0b013e3182825bce.

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