Supplementary Table 2. Parameters for the Fluvoxamine Model in Simcyp® version 25 (Certara).

Parameter	Value/Setting
Physiochemical properties	
Molecular weight (g/mol)	318.3
Log $P_{o:w}$	3
Compound type	Monoprotic Base
pKa	8.7
Polar surface area	56.84
Hydrogen bond donors	1
Hydrogen bond acceptors	4
B/P	1.5
fu_p	0.14
Absorption	
Absorption model	First-order
MDCK II permeability ($\times 10^{-6}$ cm/s)	31.7 (scalar: 1.3983)
$P_{eff,man}$ ($\times 10^{-4}$ cm/s)	5.6745
k_a (h^{-1})	0.7
f_a	1
f_{ugut}	0.14
Q_{gut} (l/h)	15.871
Distribution	
Distribution model	Minimal PBPK model
V_{ss} (l/kg)	21
Q (l/h)	0.5

V_{sac} (l/kg)	6
Elimination	
CYP2D6 Vmax (pmol/min/pmol of isoform)	70
CYP2D6 Km (μM)	38.6
Active hepatic scalar	3
Additional clearance HLM (μl/min/mg protein)	14
Interaction	
CYP1A2 Ki (μM)	0.002
CYP2C9 Ki (μM)	0.131
CYP2C19 Ki (μM)	0.0087
CYP2D6 Ki (μM)	0.403
CYP3A4 Ki (μM)	0.51
CYP3A5 Ki (μM)	0.51

B/P, blood-to-plasma ratio; fa, fraction available from dosage form; fugut, fraction unbound in enterocytes; fup, fraction unbound in plasma; ka, absorption rate constant; Ki, concentration of inhibitor that supports half maximal inhibition; Km, Michaelis constant; Log Po:w, logarithmic partition coefficient octonal:water; Peff,man, effective permeability in humans; pKa, logarithm of acid dissociation constant; Q, inter-compartment clearance; Qgut, flow rate for overall delivery of drug to the gut; Vmax, maximum metabolic rate; Vsac, single adjusted compartment volume; Vss, volume of distribution at steady state.