Supporting Information

The Identification of Multiple 5HT4 Partial Agonist Clinical Candidates for the Treatment of Alzheimer's Disease

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(Supplemental Table 1-3: measured and predicted brain concentrations for compounds **2d**, **3**, and **4**; Supplemental Table 4: Summary of Target Systems in Toxicology Test Species; Supplemental Table 5: Bioprint Data for Compounds **2d**, **3**, and **4**).

Supplemental Table 1: Measured and predicted brain concentrations for Compound **3**

Time (min)	C_{bt} (ng/mL)	C_{bu} (nM)	%RO	FCOB
-68	0	0	0	1.01
-51	0	0	0	1.07
-34	0	0	0	1.03
-17	0	0	0	0.92
0	0	0	0	1.19
17	93.74	32.44	92.32	1.64
34	79.09	27.37	91.02	1.27
51	66.72	23.09	89.53	0.90
68	56.29	19.48	87.83	1.34
85	47.49	16.43	85.89	1.58
102	40.07	13.86	83.70	1.37
119	33.80	11.70	81.25	1.21
136	28.52	9.87	78.52	0.99
153	24.06	8.33	75.51	1.06
170	20.30	7.02	72.23	0.87
187	17.12	5.93	68.70	0.93

Total brain concentration of compound **3** $C_{b,t}$ (ng/mL) observed in neuropharmacokinetic studies were fitted to a non-compartmental model; total brain concentrations $C_{b,t}$ (ng/mL) were simulated over 0-187 minutes as shown below. Free brain concentrations $C_{b,u}$ (nM) values for **3**, at 5 mg/kg, S.C., in male Sprague Dawley rats were calculated using the equation: $C_{b,u}$ (nM) = ($C_{b,t}$ * 1000* $f_{u,b}$)/MW where $f_{u,b}$ (free fraction in brain homogenates using equilibrium dialysis)

= 0.15 and MW (molecular weight) = 433.5. %RO was calculated using the equation: ($C_{b,u}$ *100)/($C_{b,u}$ + K_i) where K_i = 2.7 nM; FCOB (fold change over baseline) was calculated using ACh release for each time point in microdialysis studies using the following equation: ACh release in animals treated with **3**/ACh release in vehicle treated animals.

Supplemental Table 2: Measured and predicted brain concentrations for Compound **2d**

Time (min)	C_{bt} (ng/mL)	C_{bu} (nM)	%RO	FCOB
-68	0	0	0	0.86
-51	0	0	0	0.94
-34	0	0	0	1.03
-17	0	0	0	1.11
0	0	0	0	1.03
17	3.19	1.25	79.16	1.23
34	2.55	1.00	75.23	1.57
51	2.04	0.80	70.84	1.97
68	1.69	0.66	66.81	1.41
85	1.31	0.51	60.94	1.25
102	1.05	0.41	55.57	1.24
119	0.84	0.33	50.01	1.12
136	0.67	0.26	44.38	1.32
153	0.53	0.21	38.70	1.18
170	0.43	0.17	33.87	1.63
187	0.34	0.13	28.82	1.62

Total brain concentrations of compound **2d** $C_{b,t}$ (ng/mL) observed in neuropharmacokinetic studies were fitted to a non-compartmental model; total brain concentration $C_{b,t}$ (ng/mL) were simulated over 0-187 minutes as shown below. Free brain concentrations $C_{b,u}$ (nM) values for **2d**, at 5 mg/kg, S.C., in male Sprague Dawley rats were calculated using the equation: $C_{b,u}$ (nM) = ($C_{b,t}$ * 1000* $f_{u,b}$)/MW where $f_{u,b}$ (free fraction in brain homogenates using equilibrium dialysis) = 0.17 and MW (molecular weight) = 432.5; %RO was calculated using the equation: ($C_{b,u}$ *100)/($C_{b,u}$ + K_i) where K_i = 0.33 nM; FCOB (fold change over baseline) was calculated using ACh release for each time point in microdialysis studies using the following equation: ACh release in animals treated with **2d**/ACh release in vehicle treated animals.

Supplemental Table 3: Measured and predicted brain concentrations for Compound **4**

Time (min)	C_{bt} (ng/mL)	C_{bu} (nM)	%RO	FCOB
-68	0	0	0	1.02
-51	0	0	0	0.84
-34	0	0	0	1.02
-17	0	0	0	1.10
0	0	0	0	1.07
17	1256.69	193.34	99.44	1.72
34	1769.71	272.26	99.60	2.27
51	1923.72	295.96	99.63	2.71
68	1908.55	293.62	99.63	1.27
85	1817.52	279.62	99.61	1.22
102	1696.19	260.95	99.58	1.55

119	1566.50	241.00	99.55	1.94
136	1438.76	221.35	99.51	2.06
153	1317.53	202.70	99.47	1.88
170	1204.58	185.32	99.42	1.84
187	1100.37	169.29	99.36	1.48

Total brain concentrations of compound **4** $C_{b,t}$ (ng/mL) observed in neuropharmacokinetic studies were fitted to a non-compartmental model; total brain concentration $C_{b,t}$ (ng/mL) were simulated over 0-187 minutes as shown below. Free brain concentrations $C_{b,u}$ (nM) values for **4**, at 5 mg/kg, S.C., in male Sprague Dawley rats were calculated using the equation: $C_{b,u}$ (nM) = ($C_{b,t}$ * 1000* $f_{u,b}$)/MW where $f_{u,b}$ (free fraction in brain homogenates using equilibrium dialysis) = 0.069 and MW (molecular weight) = 448.5; %RO was calculated using the equation: ($C_{b,u}$ *100)/($C_{b,u}$ + K_i) where K_i = 1.09 nM; FCOB (fold change over baseline) was calculated using ACh release for each time point in microdialysis studies using the following equation: ACh release in animals treated with **4**/ACh release in vehicle treated animals.

Supplemental Table 4: Summary of Target Systems in Toxicology Test Species

Target Organ	Species	Threshold Dose (mg/kg)			X-Fold Projected Efficacious Free Concentration (EC_{50}) over C_{max} (nM)		
		Compound **2d**	Compound **3**	Compound **4**	Compound **2d**	Compound **3**	Compound **4**
<u>Nervous System:</u>							
Convulsions	Dog	30[a]	30	30	19158	3240	9606
	Rat	100 (F)	NA	NA	9314	NA	NA
NOEL for Convulsions	Dog	10	20	20	3167	1226	8083
	Rat	30 (F)	NA	NA	2267	NA	NA
<u>Cardiovascular System:</u>							
↑ Systolic Blood Pressure (BP)	Dog	10	0.05[d]	0.1[d]	1072	<1	8
NOEL for BP effect	Dog	3	0.005	NA	200	<1	NA
<u>Gastrointestinal System:</u>							

Emesis	Dog	30[b]	20	20	6192	1226	6336
NOEL for Emesis	Dog	10	10	10	3167	546	3493
↓ Body weight (BW)	Rat	100 (M)	30 (F), 100 (M)	30 (F), 100 (M)	911	1638	3902
NOEL for BW change	Rat	30 (F)	30 (M)	30 (M)	861	752	2044
GI toxicity[c]	Rat	NA	30 (F), 100 (M)	30 (F), 100 (M)	NA	1638	3902
NOEL for GI toxicity	Rat	NA	30 (M)	30 (M)	NA	752	2044

M = male, F = female, NA = not applicable. Studies up to 1-month in duration (dogs, rats) were conducted with compounds **2d** and **3** and up to 7-days (dogs) or 14-days with compound **4**. [a]Exposure at 30 mg/kg in 7-day study. [b]Exposure at 30 mg/kg in single-dose study. [c]Necrosis, degeneration, and regeneration of crypt epithelium from duodenum to colon; villous attenuation and vacuolation of villous epithelium. [d]After first dose only. [e]Multiples based on total exposure values. There were additional findings in the adrenal cortex (necrosis) with PF-03382792 in rats (≥30 mg/kg, F) and the lens (fiber swelling) in rats with PF-03382792 (≥30 mg/kg) and PF-01352968 (30 mg/kg, M; ≥3 mg/kg, F).

Methods section for supplemental section:

Safety Studies. Toxicology studies up to 1 month were completed in Sprague-Dawley rats and Beagle dogs. Drug formulations were prepared in 0.5% methylcellulose and administered at a dosage volume of 10 mL/kg in rats and 1 mL/kg in dogs. Monitored endpoints in these studies included clinical signs (daily), food intake (daily or weekly), body weight (daily or weekly), clinical pathology (hematology, serum chemistry, urinalysis; end of study), vital signs (heart rate, respiratory rate; dogs, predose and postdose at about Tmax at end of study), electrocardiogram (dogs, predose and postdose at about T_{max} at end of study), ophthalmology (predose and at end of study), plasma drug levels (day 1 and end of study; 4-5 time points on each sampling day), and gross/histopathology (end of dosing phase in repeat dose studies).

Safety Pharmacology Cardiovascular Studies: Cardiovascular parameters were assessed in up to four male dogs (unrestrained; telemetry) after single doses in a cross-over design with a one-week wash-out between doses. The following doses were evaluated for compounds **2d** (1, 3, 10 mg/kg), **3** (0.005, 0.05, 0.5, 1.5, 5 mg/kg) and **4** (0.1, 1 mg/kg).

All procedures performed on these animals were in accordance with regulations and established guidelines and were reviewed and approved by an Institutional Animal Care and Use Committee or through an ethical review process. Convulsions in dogs were either self-limiting or required intervention with a standard anticonvulsant. Exposure and estimated safety margins derived from toxicology studies in rats and in dogs are summarized in Table 1.

Supplemental Table 5: Bioprint Data for Compounds **2d**, **3**, and **4**

Screen Title	Dose	Data Type	Unit	Analog 2d	Analog 3	Analog 4
SERT / Cerep Cat ref.0439 (808-Uh)	10 µM	% INHB	PCT	3	-3	8
5-HT1a / Cerep Cat ref.0131 (808-1ah)	10 µM	% INHB	PCT	48	-9	-11
5-HT2a / Cerep Cat ref.0471 (808-2ah)	10 µM	% INHB	PCT	29	12	9
5-HT2b / Cerep Cat ref.1333 (808-2bah)	10 µM	% INHB	PCT	79	43	45
5-HT2b / Cerep Cat ref.1333 (808-2bah)		K_I	nM	1900		
5-HT2b / Cerep Cat ref.1333 (808-2bah)		IC_{50}	nM	1900		
5-HT2C HUMAN AGONIST SITE (_5HT2C_ag_site) CEREP BIOPRINT Cat. 808-8cha	10 µM	% INHB	PCT	19	12	7
5-HT3 / Cerep Cat ref.0411 (808-3h)	10 µM	%	PCT	71	92	80

		INHB				
5-HT3 / Cerep Cat ref.0411		K_I	nM	1900	290	1200
5-HT3 / Cerep Cat ref.0411		IC_{50}	nM	2800	410	1700
5-HT4E HUMAN (_5HT4E) CEREP BIOPRINT Cat. 808-4eh, % Inhibition	10 µM	% INHB	PCT	101	101	101
5-HT4E HUMAN (_5HT4E) CEREP BIOPRINT Cat. 808-4eh		IC_{50}	nM	0.39	4.64	6.08
5-HT4E HUMAN (_5HT4E) CEREP BIOPRINT Cat. 808-4eh		K_I	NM	0.126	1.55	2.02
5-HT7 / Cerep Cat ref.0144 (808-7h)	10 µM	% INHB	PCT	39	0	-12
ADENOSINE 1 HUMAN (A1) CEREP BIOPRINT Cat. 801-1h	10 µM	% INHB	PCT	-17	-9	-7
A2A / Cerep Cat ref.0004 (801-2ah)	10 µM	% INHB	PCT	45	-4	1
ACE / Cerep Cat ref.3441 (763-rh)	10 µM	% INHB	PCT	-6	-5	-18
AChase / Cerep Cat ref.0363 (761-h)	10 µM	% INHB	PCT	12	5	2
ADRENERGIC ALPHA 2A HUMAN (Alpha2A) CEREP BIOPRINT Cat. 802-1bAh	10 µM	% INHB	PCT	43	5	5
alpha2b / Cerep Cat ref.1344 (802-1bBc)	10 µM	% INHB	PCT	2	-4	-7
ANGIOTENSIN 1 HUMAN (AT1) CEREP BIOPRINT Cat. 821-1h	10 µM	% INHB	PCT	-5	-30	-32
Beta1 / Cerep Cat ref.0018 (802-2ah)	10 µM	% INHB	PCT	13	2	0
Beta2 / Cerep Cat ref.0020 (802-2bh)	10 µM	% INHB	PCT	79	19	8
ß2 / Cerep Cat ref.0020		K_I	NM	950		
ß2 / Cerep Cat ref.0020		IC_{50}	NM	2200		
ADRENERGIC BETA 3 HUMAN (Beta3) CEREP BIOPRINT Cat. 802-3h	10 µM	% INHB	PCT	2	-8	6
CB1 / Cerep Cat ref.0036 (835-ch)	10 µM	% INHB	PCT	-5	20	0
CB2 / Cerep Cat ref.0037 (835-ph)	10 µM	% INHB	PCT	-11	-2	-2

CCK1 / Cerep Cat ref.0039 (824-1h)	10 µM	% INHB	PCT	-3	-7	-6
CCK2 / Cerep Cat ref.0041 (824-2h)	10 µM	% INHB	PCT	0	3	0
CHT1 / Cerep Cat ref.1552 (806-Uh)	10 µM	% INHB	PCT	65	35	31
CHT1 / Cerep Cat ref.1552		K_i	NM	6300		
CHT1 / Cerep Cat ref.1552		IC_{50}	NM	11000		
COX2 / Cerep Cat ref.0727 (777-2hr)	10 µM	% INHB	PCT	17	-12	-4
D1 / Cerep Cat ref.0044 (803-1h)	10 µM	% INHB	PCT	21	-3	-9
DOPAMINE D2 HUMAN (D2S (h)) CEREP BIOPRINT Cat. 803-2h	10 µM	% INHB	PCT	17	1	0
DOPAMINE D3 HUMAN (D3) CEREP BIOPRINT Cat. 803-3h	10 µM	% INHB	nM	79	38	8
DOPAMINE D3 HUMAN (D3) CEREP BIOPRINT Cat. 803-3h		K_i	nM	540		
DOPAMINE D3 HUMAN (D3) CEREP BIOPRINT Cat. 803-3h		IC_{50}	nM	2400		
DAT / Cerep Cat ref.0052 (803-Uh)	10 µM	% INHB	PCT	21	20	24
delta-opioid / Cerep Cat ref.0114 (841-h)	10 µM	% INHB	PCT	2	6	11
ENDOTHELIN A HUMAN (ETA (h)) CEREP BIOPRINT Cat. 825-1h	10 µM	% INHB	PCT	-3	18	11
ENDOTHELIN B HUMAN (ETB) CEREP BIOPRINT Cat. 825-2h	10 µM	% INHB	PCT	-10	14	5
GR / Cerep Cat ref.0469 (812-h)	10 µM	% INHB	PCT	7	-7	-4
H1 / Cerep Cat ref.0870 (805-1h)	10 µM	% INHB	PCT	80	6	7
H1 / Cerep Cat ref.0870		K_i	NM	810		
H1 / Cerep Cat ref.0870		IC_{50}	NM	2200		
H2 (h) CEREP BIOPRINT Cat. 805-2hc	10 µM	% INHB	PCT	4	1	4

H3 / Cerep Cat ref.1332 (805-3h)	10 µM	% INHB	PCT	11	17	18
M1 / Cerep Cat ref.0091 (806-1h)	10 µM	% INHB	PCT	29	23	25
M2 HUMAN (M2) CEREP BIOPRINT Cat. 806-2h	10 µM	% INHB	PCT	37	36	42
M3 / Cerep Cat ref.0095 (806-3h)	10 µM	% INHB	PCT	14	12	10
mu-opioid / Cerep Cat ref.0118 (843-h)	10 µM	% INHB	PCT	18	14	22
nAChR (muscle) / Cerep Cat ref.0936 (807-mh)	10 µM	% INHB	PCT	6	-4	-10
NET / Cerep Cat ref.0355 (802-Uh)	10 µM	% INHB	PCT	17	5	0
NEUROKININ 1 HUMAN (NK1) CEREP BIOPRINT Cat. 826-1h	10 µM	% INHB	PCT	16	18	12
p38alpha kinase / Cerep Cat ref.2881 (789-p38a)	10 µM	% INHB	PCT	-36	15	8
PHOSPHODIESTERASE III HUMAN (PDE3) CEREP BIOPRINT Cat. 752-ch	10 µM	% INHB	PCT	12	13	3
PHOSPHODIESTERASE IV HUMAN (PDE4) CEREP BIOPRINT Cat. 752-d	10 µM	% INHB	PCT	29	0	49
VEGFR1-tyrosine kinase (h) (FLT-1) CEREP BIOPRINT Cat. 709-v1	10 µM	% INHB	PCT	0	-14	-12
5-HT2A HUMAN (_5HT2A) CEREP BIOPRINT Cat. 808-2h	10 µM	% INHB	PCT	21	5	7
5-HT2C HUMAN (_5HT2C) CEREP BIOPRINT Cat. 808-1ch	10 µM	% INHB	PCT	20	16	8
5-HT6 HUMAN (_5HT6) CEREP BIOPRINT Cat. 808-6h	10 µM	% INHB	PCT	15	4	-1
ADENOSINE 3 HUMAN (A3) CEREP BIOPRINT Cat. 801-3h	10 µM	% INHB	PCT	-6	11	-3
Abl kinase / Cerep Cat ref. 781-Abl	10 µM	% INHB	PCT	5	-2	2
ADRENERGIC ALPHA 2C HUMAN (Alpha2C) CEREP BIOPRINT Cat. 802-1bCh	10 µM	% INHB	PCT	26	18	12
CALCIUM MODULATED KINASE II HUMAN (CaMK2alpha (h)) CEREP BIOPRINT Cat. 781-CM	10 µM	% INHB	PCT	7	1	-3
Caspase-3 (h) CEREP BIOPRINT Cat. 724-3, %	10 µM	%	PCT	-8	0	-1

Inhibition		INHB				
CXCR4 (CXCR4) CEREP BIOPRINT Cat. 877-4h, % Inhibition	10 µM	% INHB	PCT	7	10	6
CYP2C19 HUMAN (CYP2C19) CEREP BIOPRINT Cat. 900-2, % Inhibition	10 µM	% INHB	PCT	54	17	19
CYP2C19 HUMAN (CYP2C19) CEREP BIOPRINT Cat. 900-2		IC_{50}	NM	14000		
CYP2C9 HUMAN (CYP2C9) CEREP BIOPRINT Cat. 900-4, % Inhibition	10 µM	% INHB	PCT	54	14	21
CYP2C9 HUMAN (CYP2C9) CEREP BIOPRINT Cat. 900-4		IC50	NM	12000		
CYP3A4 HUMAN (CYP3A4) CEREP BIOPRINT Cat. 900-3, % Inhibition	10 µM	% INHB	PCT	30	15	30
CYP3A4 HUMAN, BENZOXYRESORUFIN (CYP3A4bzr) CEREP BIOPRINT Cat. 900-3r, % Inhibition	10 µM	% INHB	PCT	37	36	-6
D2s / Cerep Cat ref.1322 (803-2ha)	10 µM	% INHB	PCT	20	6	0
DOPAMINE D4.4 HUMAN (D4_4) CEREP BIOPRINT Cat. 803-44h, % Inhibition	10 µM	% INHB	PCT	75	25	-4
DOPAMINE D4.4 HUMAN (D4_4) CEREP BIOPRINT Cat. 803-44h		K_I	NM	2000		
DOPAMINE D4.4 HUMAN (D4_4) CEREP BIOPRINT Cat. 803-44h		IC_{50}	NM	5000		
H4 (h) CEREP BIOPRINT Cat. 805-4h	10 µM	% INHB	PCT	7	-2	-1
LEUKOTRIENE D4 (LTD4) CEREP BIOPRINT Cat. 887-h	10 µM	% INHB	PCT	-10	-4	0
M4 HUMAN (M4) CEREP BIOPRINT Cat. 806-4h	10 µM	% INHB	PCT	18	31	42
M5 HUMAN (M5) CEREP BIOPRINT Cat. 806-5h	10 µM	% INHB	PCT	7	19	8
MELANOCORTIN 3 HUMAN (MC3) CEREP BIOPRINT Cat. 889-3h	10 µM	% INHB	PCT	1	1	-1
MC4 HUMAN (MC4) CEREP BIOPRINT Cat. 889-4h	10 µM	% INHB	PCT	-4	5	-11
MELANIN CONCENTRATING HORMONE 1 HUMAN (MCH1) CEREP BIOPRINT Cat. 849-1hc	10 µM	% INHB	PCT	0	-11	-15
MOTILIN HUMAN (Motilin) CEREP BIOPRINT Cat. 846-h	10 µM	% INHB	PCT	-3	1	12

NK2 / Cerep Cat ref.0102 (826-2h)	10 µM	% INHB	PCT	3	15	26
PHOSPHODIESTERASE XI HUMAN (PDE11) CEREP BIOPRINT Cat. 752-kp	10 µM	% INHB	PCT	-3	4	-2
PHOSPHODIESTERASE II HUMAN (PDE2) CEREP BIOPRINT Cat. 752-b	10 µM	% INHB	PCT	40	8	18
PHOSPHODIESTERASE V HUMAN (PDE5) CEREP BIOPRINT Cat. 752-e	10uM	% INHB	PCT	12	-23	-4
SOMATOSTATIN 4 HUMAN (Sst4) CEREP BIOPRINT Cat. 816-4h	10 µM	% INHB	PCT	-3	-1	2
TNF-alpha (h) CEREP BIOPRINT Cat. 871-h	10 µM	% INHB	PCT	-25	-3	4
VASOPRESSIN 2 HUMAN (V2) CEREP BIOPRINT Cat. 831-2h	10 µM	% INHB	PCT	-5	-2	-5
VIP1 HUMAN (VIP1) CEREP BIOPRINT Cat. 832-1h	10 µM	% INHB	PCT	-11	6	0
ZETA-ASSOCIATED P70 KINASE HUMAN (ZAP70 kinase (h)) CEREP BIOPRINT Cat. 781-zp	10 µM	% INHB	PCT	-2	5	-1
AR / Cerep Cat ref.0933 (815-h)	10 µM	% INHB	PCT	-2	-3	1
COX1 / Cerep Cat ref.0726	10 µM	% INHB	PCT	-29	-13	-14
METALLOPROTEINASE 9 HUMAN (MMP_9) CEREP BIOPRINT Cat. 753-9	10 µM	% INHB	PCT	7	-1	6
p56lyn KINASE HUMAN (Lyn kinase (h)) CEREP BIOPRINT Cat. 781	10 µM	% INHB	PCT	0	14	-17
NEUROPEPTIDE Y1 HUMAN (Y1) CEREP BIOPRINT Cat. 827-1h	10 µM	% INHB	PCT	-7	-2	-8
GLYCINE STRYCHNINE-INSENSITIVE, rat cerebral cortex (Glycine) CEREP BIOPRINT Cat. 895-5	10 µM	% INHB	PCT	-6	45.5	-10
COPY OF N-TYPE CALCIUM CHANNEL, rat cerebral cortex (Ca_chan_NTYPE) CEREP BIOPRINT Cat. 861-N	10 µM	% INHB	PCT	-25	-6	0
L-type Ca2+ (verapamil) / Cerep Cat ref.0163	10 µM	% INHB	PCT	19	13	14
L-type Ca2+ (DHP) / Cerep Cat ref.0161	10 µM	% INHB	PCT	-2	0	13
L-type Ca2+ (diltiazem) / Cerep Cat ref.0162	10 µM	% INHB	PCT	36	41	62

L-type Ca2+ (diltiazem) / Cerep Cat ref.0162		IC_{50}	NM			11000
L-type Ca2+ (diltiazem) / Cerep Cat ref.0162		K_I	NM			9600
GABAa-BZD / Cerep Cat ref.0028	10 µM	% INHB	PCT	9	2	2
GABAa / Cerep Cat ref.0058	10 µM	% INHB	PCT	2	7	3
AMPA / Cerep Cat ref.0064 (895-1)	10 µM	% INHB	PCT	-22	-4	-20
alpha1 / Cerep Cat ref.0008 (802-1a)	10 µM	% INHB	PCT	20	-2	0
GABA transporter / Cerep Cat ref.0060	10 µM	% INHB	PCT	8	9	12
GLUTAMATE RECEPTOR KAINATE SITE, rat cerebral cortex (Kainate) CEREP BIOPRINT Cat. 895-2	10 µM	% INHB	PCT	6	-5	4
Na+ channel (site 2) / Cerep Cat ref.0169 (862-a)	10 µM	% INHB	PCT	53	35	42
Na+ channel (site 2) / Cerep Cat ref.0169		IC_{50}	NM	5800		
Na+ channel (site 2) / Cerep Cat ref.0169		K_I	NM	5200		
NICOTINIC ACHR NEURONAL ALPHA-BGTX-INSENSITIVE, rat (alpha -BGTX-insensitive) (alpha 4beta 2)Cat. 807-n1	10 µM	% INHB	PCT	0	3	-3
GLUTAMATE RECEPTOR NMDA SITE, rat (NMDA) CEREP BIOPRINT Cat. 895-3	10 µM	% INHB	PCT	-10	14	2
THYROID HORMONE RECEPTOR, rat (TH) CEREP BIOPRINT Cat. 855	10 µM	% INHB	PCT	-14	-7	-11
MAO-A / Cerep Cat ref.0443 (838-a)	10 µM	% INHB	PCT	17	14	2
5-HT1b / Cerep Cat ref.0132 (808-1b)	10 µM	% INHB	PCT	-2	-16	-14
IMIDAZOLINE 1, bovine (I1) CEREP BIOPRINT Cat. 809-1p	10 µM	% INHB	PCT	20	0	4
PHOSPHODIESTERASE 6, bovine (PDE6) CEREP BIOPRINT Cat. 752-f	10 µM	% INHB	PCT	-5	-4	-13
ROLIPRAM, mouse (Rolipram) CEREP BIOPRINT Cat. 833	10 µM	% INHB	PCT	12	2	20
K CHANNEL CALCIUM DEPENDENT, rat (SK+Ca channel) CEREP BIOPRINT Cat. 863-3	10 µM	% INHB	PCT	-1	10	5

GABAa Cl- channel / Cerep Cat ref.0170 (864)	10 µM	% INHB	PCT	-11	3	-1
MELANOCORTIN 1, mouse (MC1) CEREP BIOPRINT Cat. 889-1	10 µM	% INHB	PCT	-4	-5	-9
SIGMA NON-SELECTIVE, rat CEREP BIOPRINT Cat. 891	10 µM	% INHB	PCT	100	58	74
SIGMA NON-SELECTIVE, rat CEREP BIOPRINT Cat. 891		IC_{50}	NM	150	110	9.4
SIGMA NON-SELECTIVE, rat CEREP BIOPRINT Cat. 891		K_I	NM	120	89	7.4
CYP2D6 inhibition (MFC substrate) human CEREP BIOPRINT Cat. 900-51	10 µM	% INHB	PCT	4	-6	-7
UT-1 / Cerep Cat ref.1386 (853-hc)	10 µM	% INHB	PCT	5	3	9
GABA-B 1B HUMAN (GABA-B(1b) (h)) CEREP BIOPRINT Cat. 804-1b	10 µM	% INHB	PCT	-13	4	-10
VASOPRESSIN 1A HUMAN (V1a (h)) CEREP BIOPRINT Cat. 831-1ah	10 µM	% INHB	PCT	3	-4	0
PCP / Cerep Cat ref.0124 (895-6)	10 µM	% INHB	PCT	0	26	-29
PPAR-y / Cerep Cat ref.0641 (854-gh)	10 µM	% INHB	PCT	5	-1	-4
LTB4 HUMAN (BLT1) (LTB4 (h) (BLT1)) CEREP BIOPRINT Cat. 885-hr	10 µM	% INHB	PCT	-3	-7	4
MELATONIN 2 (MT3) HAMSTER (ML2 (MT3)) CEREP BIOPRINT Cat. 892-2	10 µM	% INHB	PCT	42	4	32
5-HT1D, rat CEREP BIOPRINT Cat. 808-1dc	10 µM	% INHB	PCT	5	5	1
kappa-opioid / Cerep Cat ref.1971 (842-r)	10 µM	% INHB	PCT	7	17	24
CARBONIC ANHYDRASE II HUMAN (Carb_anhydr) CEREP BIOPRINT Cat. 762-hc	10 µM	% INHB	PCT	-5	-3	-3
MELATONIN 1, human (MT1/ML1a) CEREP BIOPRINT Cat. 892-1h	10 µM	% INHB	PCT	-7	1	-2
5-HT4 agonism / Cerep Cat ref.1044 (758-24a)		IC_{50}	NM			2.6
Alpha1a / Cerep Cat ref.2338 (802-1Ah)	10 µM	% INHB	PCT	0	-38	0
5-HT4e CEREP functional cAMP agonist EC50	10 µM	% INHB	PCT	34	47	89.8