

Supporting Information

WBQ5187, a Multitarget Directed Agent, Ameliorates Cognitive Impairment in a Transgenic Mouse Model of Alzheimer's Disease and Modulates Cerebral β -Amyloid, Gliosis, cAMP Levels, and Neurodegeneration

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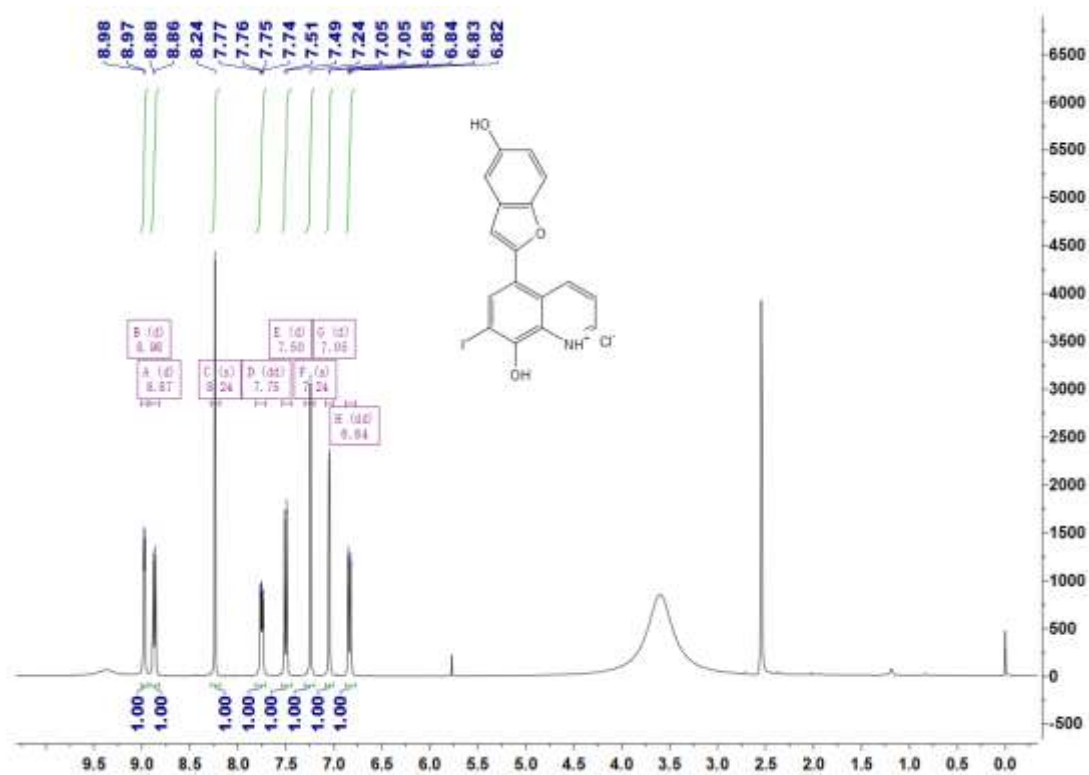
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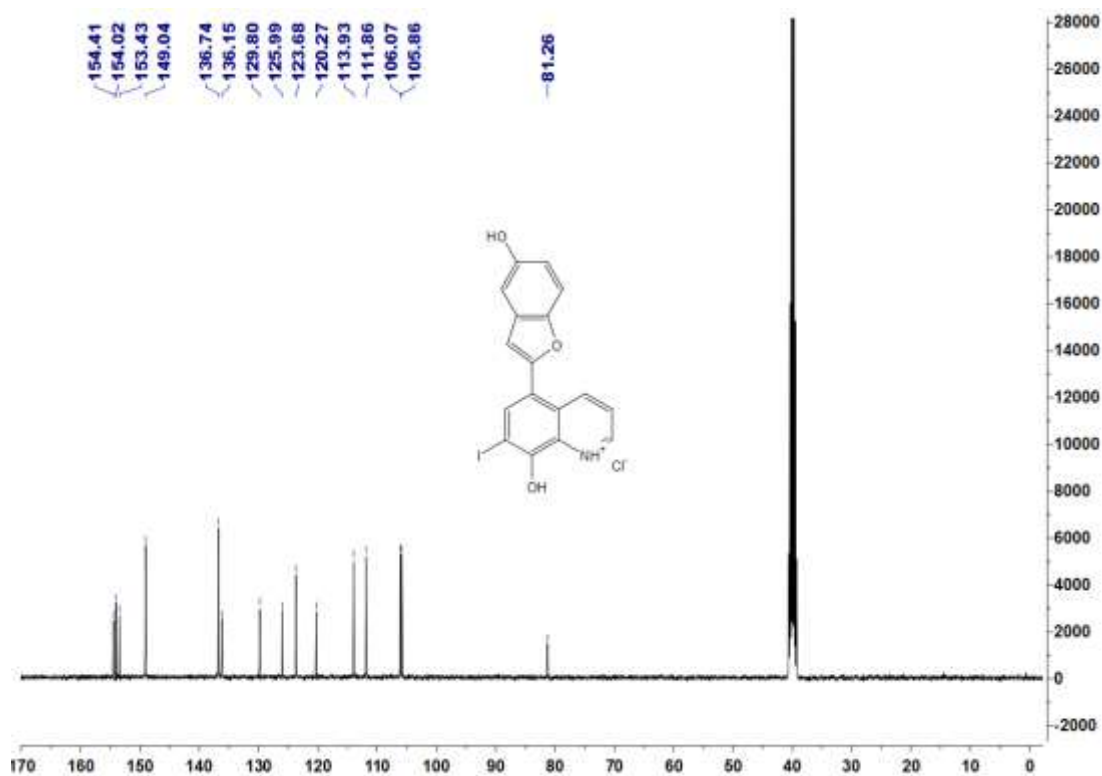
S2	NMR spectra of compound WBQ5187
S3-S4	Pharmacokinetic study of WBQ5187

1. NMR of the compound WBQ5187

$^1\text{H-NMR}$ of WBQ5187



$^{13}\text{C-NMR}$ of WBQ5187



2. Pharmacokinetic study of WBQ5187

Table 1. The concentration of WBQ5187 in the plasma of SD rats after intravenous administration (i.v. 5 mg/kg) or oral dosing (p.o. 30 mg/kg), data were expressed as mean \pm SD, n = 3.

Time of blood sampling (hr)	Concentration of QBQ5187 in plasma (ng/mL)				
	No. of rat				
	<u>IV (5 mg/kg)</u>				
	101	102	103	Mean	SD
0	BLQ	BLQ	BLQ	NA	NA
0.083*	10127.63	10982.45	12503.00	11204.36	1203.13
0.25*	6965.53	7177.26	7324.99	7155.93	180.68
0.5	3610.19	3425.56	3319.18	3451.64	147.24
1	2741.98	2907.79	2714.57	2788.11	104.54
2	2907.12	3022.43	2631.11	2853.55	201.09
4	2094.88	2457.53	2648.16	2400.19	281.06
8	1854.30	1787.95	1965.50	1869.25	89.72
24	1148.40	968.69	1038.17	1051.75	90.62

Time of blood sampling (hr)	Concentration of QBQ5187 in plasma (ng/mL)				
	No. of rat				
	<u>PO (30 mg/kg)</u>				
	201	202	203	Mean	SD
0	BLQ	BLQ	BLQ	NA	NA
0.083	1271.65	435.43	496.89	734.65	466.06
0.25	2744.18	2516.30	2569.61	2610.03	119.19
0.5	2808.60	2681.17	2693.51	2727.76	70.28
1	2699.14	2690.59	2546.44	2645.39	85.80
2	3038.39	2728.39	2535.63	2767.47	253.65
4	2417.64	2272.21	2525.15	2405.00	126.94
8	2100.98	1921.56	2200.20	2074.24	141.23
24	1046.14	1254.20	1086.12	1128.82	110.41

Table 2. The pharmacokinetic parameter of WBQ5187

No. of rat	$t_{1/2z}$	T_{max}	C_{max}	$AUC_{(0-t)}$	$AUC_{(0-\infty)}$	V_z	CL_z	$MRT_{(0-\infty)}$
	h	h	ng/mL	ng/mL*h	ng/mL*h	L/kg	L/hr/kg	h
IV (5 mg/kg)								
101	23.09	0.083	10127.63	45010.32	83258.66	2.00	0.06	31.20
102	14.14	0.083	10982.45	44433.02	64195.26	1.59	0.08	19.45
103	16.10	0.083	12503.00	46899.08	71014.34	1.64	0.07	21.66
mean	17.78	0.083	11204.36	45447.47	72822.75	1.74	0.07	24.10
SD	4.70	0.000	1203.13	1289.84	9659.51	0.22	0.01	6.24
No. of rat	$t_{1/2z}$	T_{max}	C_{max}	$AUC_{(0-t)}$	$AUC_{(0-\infty)}$	$MRT_{(0-\infty)}$	F^*	F^{**}
	h	h	ng/mL	ng/mL*h	ng/mL*h	h	%	%
PO (30 mg/kg)								
201	16.36	2.00	3038.39	44998.12	69689.27	22.75	16.50	15.95
202	24.03	2.00	2728.39	43760.87	87246.14	34.20	16.05	19.97
203	16.22	0.50	2693.51	45587.63	71001.22	22.95	16.72	16.25
mean	18.87	1.50	2820.10	44782.21	75978.88	26.63	16.42	17.39
SD	4.47	0.87	189.85	932.32	9779.76	6.55	0.34	2.24

$$* F = \frac{AUC_{(0-t)(PO)} \times Dose_{IV}}{AUC_{(0-t)(IV)} \times Dose_{(PO)}} \times 100\%$$

$$** F = \frac{AUC_{(0-\infty)(PO)} \times Dose_{IV}}{AUC_{(0-\infty)(IV)} \times Dose_{(PO)}} \times 100\%$$