

Supplementary Tables

Supplemental Table 1. TPI-287 pharmacokinetic parameters in mice after single intravenous dose.

Parameter:	Brain:	Plasma:	Ratio:
C _{max} (ng/ml)	3726.6	1550.2	2.40
AUC (0-96 h) (ng-hr/ml)	64,984.9	16,870.2	3.85
MRT (hr)	42.5	17.6	2.41
CL (ml/hr)	0.006	0.024	0.25

1. A single intravenous injection of 20 mg/kg TPI-287 was administered to mice and pharmacokinetic parameters calculated from plasma and brain homogenates.

2. C_{max}, maximal concentration; AUC, area under the curve; MRT, mean residence time; CL, clearance.

Supplemental Table 2. Brain/Plasma TPI 287 Concentration Ratios in Mice after a Single 20 mg/kg IV Dose

Brain/Plasma Concentration Ratio:						
Time (hr)	Mouse 1	Mouse 2	Mouse 3	Mouse 4	Mean	SD
0.083	1.586	1.233	0.984	1.044	1.212	0.271
0.25	2.968	2.176	1.584	2.537	2.316	0.586
2.0	2.032	3.869	3.624	3.511	3.259	0.831
8.0	13.707	3.857	3.893	3.000	6.114	5.079
24.0	16.163	10.743	6.445	7.107	10.115	4.453
32.0	11.754	13.095	15.169	7.181	11.800	3.384
48.0	90.601	32.147	35.674	12.142	42.641	33.611
72.0	71.597	109.392	17.686	25.426	56.025	42.805
96.0	48.579	105.511	22.377	78.702	63.792	36.099

Supplemental Table 3. TPI 287 Concentrations in the normal rat.

A. TPI 287 Concentrations in Rat Plasma, Brain, and CSF After a Single 20 mg/kg IV Dose

Plasma Concentration (nM)

Time (hr)	Rats #1, 6, 11	Rats #2, 7, 12	Rats #3, 8, 13	Rats #4, 9, 14	Rats #5, 10, 15	Mean	SD
0.2	8613.490	12699.817	8993.649	455.084	11530.596	10459.388	1976.759
2	910.649	1587.47	1093.502	937.552	1521.184	1210.072	322.773
6	273.369	313.026	422.079	389.657	253.679	330.362	73.070
Rat #4, shown in red, was excluded as an outlier.							

B. Brain TPI 287 Concentrations in Rats After a Single 20 mg/kg IV Dose

Brain Concentration (nM)

Time (hr)	Rats #1, 6, 11	Rats #2, 7, 12	Rats #3, 8, 13	Rats #4, 9, 14	Rats #5, 10, 15	Mean	SD
0.25	4100.318	6637.070	6332.098	86.182	4143.134	5303.155	1369.978
2	3800.679	4161.607	4730.760	4229.314	4692.949	4323.062	390.760
6	4131.079	5014.374	4177.129	4181.375	4710.513	4442.894	398.265
Rat #4, shown in red, was excluded as an outlier.							

C. CSF TPI 287 Concentrations in Rats After a Single 20 mg/kg IV Dose

CSF Concentration (nM)

Time (hr)	Rats #1, 6, 11	Rats #2, 7, 12	Rats #3, 8, 13	Rats #4, 9, 14	Rats #5, 10, 15	Mean	SD
0.25	17.885	190.955	BQL	NC	12.050	9.978	9.121
2	BQL	BQL	BQL	BQL	BQL	BQL	NC
6	BQL	BQL	BQL	BQL	BQL	BQL	NC

BQL<5.000 ng/mL; Some values may be listed as 0.000 for averaging.

NC = not calculated

Rat #4, shown in red, was excluded as an outlier.

Rat #2, shown in red, was excluded because CSF indicated the presence of blood.

D. Brain/Plasma TPI 287 Concentration Ratios in Rats After a Single 20 mg/kg IV Dose

Brain/Plasma Concentration Ratio

Time (hr)	Rats #1, 6, 11	Rats #2, 7, 12	Rats #3, 8, 13	Rats #4, 9, 14	Rats #5, 10, 15	Mean	SD
0.25	0.476	0.523	0.704	NC	0.359	0.516	0.143
2	4.174	2.622	4.326	4.511	3.085	3.743	0.838
6	15.112	16.019	0.897	10.731	18.569	14.065	3.664