

Table 8

Organ Weight - Summary

B131138

Day(s) Relative to Start Date

Sex: Male		Organ Weight (Rat)		
		Testes Ratio (%)	Prostate (g)	Prostate Ratio (%)
		29	29	29
0 mg/kg	Mean	0.774 <sup>1</sup>	0.620 <sup>1</sup>	0.150 <sup>1</sup>
	SD	0.075	0.082	0.023
	N	6	6	6
1 mg/kg	Mean	0.809	0.735	0.178
	SD	0.056	0.209	0.041
	N	6	6	6
10 mg/kg	Mean	0.780	0.477	0.121
	SD	0.170	0.105	0.014
	N	3	3	3
25 mg/kg	Mean	0.774	0.585	0.151
	SD	0.009	0.078	0.016
	N	2	2	2

1 [I - Automatic Transformation: Identity]

Table 8 Organ Weight - Summary

B131138

Day(s) Relative to Start Date

Sex: Female		Organ Weight (Rat)												
		Final Body Weight (g)	Brain (g)	Brain Ratio (%)	Pituitary (mg)	Pituitary Ratio ( $\times 10^{-3}\%$ )	Thyroids (mg)	Thyroids Ratio ( $\times 10^{-3}\%$ )	Thymus (mg)	Thymus Ratio ( $\times 10^{-3}\%$ )	Submand GLs (g)	Submand GLs Ratio (%)	Lungs (g)	Lungs Ratio (%)
		29	29	29	29	29	29	29	29	29	29	29	29	29
0 mg/kg	Mean	252.03 I <sup>1</sup>	1.878 I <sup>1</sup>	0.747 I <sup>1</sup>	20.38 I <sup>1</sup>	8.12 I <sup>1</sup>	23.33 I <sup>1</sup>	9.27 I <sup>1</sup>	388.3 I <sup>1</sup>	153.53 I <sup>1</sup>	0.478 I <sup>1</sup>	0.190 I <sup>1</sup>	1.202 I <sup>1</sup>	0.477 I <sup>1</sup>
	SD	16.30	0.066	0.035	1.78	0.95	3.01	1.13	69.6	20.81	0.039	0.017	0.106	0.024
	N	6	6	6	6	6	6	6	6	6	6	6	6	6
1 mg/kg	Mean	243.97	1.905	0.783	22.02	9.02	23.70	9.70	282.0 d <sup>2</sup>	115.61 d <sup>2</sup>	0.463	0.190	1.173	0.481
	SD	9.90	0.079	0.062	2.06	0.77	4.21	1.54	67.0	27.11	0.049	0.020	0.080	0.028
	N	6	6	6	6	6	6	6	6	6	6	6	6	6
10 mg/kg	Mean	245.07	1.910	0.783	22.62	9.27	23.15	9.46	317.3	128.25	0.438	0.179	1.248	0.511
	SD	17.93	0.067	0.066	2.02	1.09	3.16	1.25	82.8	25.09	0.061	0.027	0.048	0.036
	N	6	6	6	6	6	6	6	6	6	6	6	6	6

1 [I - Automatic Transformation: Identity]

2 [d - Test: Dunnett 2 Sided p &lt; 0.05]

Table 8 Organ Weight - Summary

B131138

Day(s) Relative to Start Date

Sex: Female		Organ Weight (Rat)											
		Heart (g)	Heart Ratio (%)	Liver (g)	Liver Ratio (%)	Spleen (g)	Spleen Ratio (%)	Kidneys (g)	Kidneys Ratio (%)	Adrenals (mg)	Adrenals Ratio ( $\times 10^{-3}\%$ )	Ovaries (mg)	Ovaries Ratio ( $\times 10^{-3}\%$ )
		29	29	29	29	29	29	29	29	29	29	29	29
0 mg/kg	Mean	0.842 <sup>1</sup>	0.335 <sup>1</sup>	6.670 <sup>1</sup>	2.649 <sup>1</sup>	0.553 <sup>R2</sup>	0.220 <sup>R2</sup>	1.653 <sup>1</sup>	0.656 <sup>1</sup>	73.05 <sup>1</sup>	28.98 <sup>1</sup>	92.38 <sup>1</sup>	36.65 <sup>1</sup>
	SD	0.058	0.025	0.431	0.138	0.031	0.020	0.139	0.023	8.94	2.86	12.62	4.55
	N	6	6	6	6	6	6	6	6	6	6	6	6
1 mg/kg	Mean	0.820	0.336	6.282	2.574	0.592	0.243	1.670	0.685	69.18	28.33	86.20	35.28
	SD	0.028	0.010	0.469	0.152	0.068	0.026	0.114	0.041	8.02	2.74	8.92	2.69
	N	6	6	6	6	6	6	6	6	6	6	6	6
10 mg/kg	Mean	0.908	0.372	6.672	2.726	0.822	0.343	1.797	0.735 <sup>d3</sup>	75.18	30.79	88.05	35.96
	SD	0.092	0.039	0.601	0.221	0.596	0.269	0.150	0.074	16.72	7.36	9.54	3.40
	N	6	6	6	6	6	6	6	6	6	6	6	6

1 [I - Automatic Transformation: Identity]  
3 [d - Test: Dunnett 2 Sided p < 0.05]

2 [R - Automatic Transformation: Rank]

Table 9 Necropsy - Summary

B131138

Removal Reason: Scheduled sacrifice	Male				Female		
	0 mg/kg	1 mg/kg	10 mg/kg	25 mg/kg	0 mg/kg	1 mg/kg	10 mg/kg
Number of Animals:	6	6	3	2	6	6	6
<b>Necropsy Findings</b>							
Present	0	1	3	2	0	3	5
Absent	6	5	0	0	6	3	1
<b>Spleen</b>							
Enlargement	.	.	.	.	.	.	1
<b>Administered Site</b>							
Nodule	.	0	1	2	.	3	4
Whitish patch	.	1	0	0	.	0	0
Hematoma	.	0	2	0	.	0	1
<b>Abdominal Cavity</b>							
Adhesion; multiple organs, nodule	.	.	.	1	.	.	.
<b>Whole Body</b>							
Anemia	.	.	1	.	.	.	.

Table 9 Necropsy - Summary

B131138

Removal Reason: Death	Male			Female	
	10 mg/kg	25 mg/kg	10 mg/kg	25 mg/kg	25 mg/kg
Number of Animals:	3	4	1	6	1
<b>Necropsy Findings</b>					
Present	3	4	1	6	1
<b>Stomach</b>					
Abnormal contents; dark red	.	.	.	1	.
<b>Duodenum</b>					
Abnormal contents; dark red	.	.	.	1	.
<b>Jejunum</b>					
Abnormal contents; dark red	.	1	.	1	.
<b>Ileum</b>					
Abnormal contents; dark red	.	1	.	1	.
<b>Lungs (And Bronchus)</b>					
Edema	1	1	.	2	.
<b>Kidney</b>					
Dilatation; pelvis, unilateral	.	0	.	1	.
Enlargement; unilateral	.	1	.	0	.
<b>Urinary Bladder</b>					
Abnormal urine; dark red	.	.	.	1	.
<b>Prostate</b>					
Dark reddish change	.	1	.	.	.
<b>Adrenal</b>					
Enlargement; bilateral	.	.	.	2	.
<b>Skin</b>					
Edema; subcutis	1	.	.	.	.

Table 9 Necropsy - Summary

B131138

Removal Reason: Death	Male			Female	
	10 mg/kg	25 mg/kg	10 mg/kg	25 mg/kg	25 mg/kg
Number of Animals:	3	4	1	6	1
<b>Administered Site</b>					
Nodule	0	1	0	1	1
Hematoma	3	3	1	5	0
<b>Thoracic Cavity</b>					
Increase; pleural fluid	1	2	.	.	.
<b>Abdominal Cavity</b>					
Increase; abdominal fluid	3	3	1	3	1
Adhesion; multiple organs, nodule	0	1	0	1	1
Adhesion; multiple organs, hematoma	2	1	1	2	0

Table 10-1 Drug Concentration in Plasma and Cerebral Spinal Fluid

B131138

&lt;First dosing, Male&gt;

Dose (mg/kg)	Animal No.	Plasma concentration of P092 after completion of dosing (ng/mL)					
		0.083 h	2 h	4 h	8 h	24 h	48 h
1	20101	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	20102	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	20103	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC
10	20201	8.47	6.86	BLQ	BLQ	BLQ	BLQ
	20203	15.4	8.32	7.22	5.41	5.88	5.80
	20204	17.5	9.57	6.11	5.44	BLQ	6.91
	Mean	13.8	8.25	BLQ	BLQ	BLQ	BLQ
	SD	4.7	1.36	NC	NC	NC	NC
25	20301	20.5	11.6	8.18	7.37	5.72	6.69
	20303	22.8	16.1	7.68	7.65	8.26	7.28
	20305	26.5	10.9	7.56	8.38	6.30	6.01
	Mean	23.3	12.9	7.81	7.80	6.76	6.66
	SD	3.0	2.8	0.33	0.52	1.33	0.64

BLQ: Below the lower limit of quantification (&lt;5 ng/mL)

NC: Not calculated

Table 10-2 Drug Concentration in Plasma and Cerebral Spinal Fluid

B131138

&lt;First dosing, Female&gt;

Dose (mg/kg)	Animal No.	Plasma concentration of P092 after completion of dosing (ng/mL)					
		0.083 h	2 h	4 h	8 h	24 h	48 h
1	60101	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60102	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60103	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC
10	60202	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60203	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60204	5.50	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC
25	60302	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60303	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60304	8.93	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC

BLQ: Below the lower limit of quantification (&lt;5 ng/mL)

NC: Not calculated



Table 10-3 Drug Concentration in Plasma and Cerebral Spinal Fluid

B131138

&lt;First dosing, Female&gt;

Dose (mg/kg)	Animal No.	Plasma concentration of P092 after completion of dosing (ng/mL)					
		0.083 h	2 h	4 h	8 h	24 h	48 h
1	60101	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60102	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60103	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC
10	60202	7.61	6.83	5.28	5.20	BLQ	5.23
	60203	7.24	BLQ	5.65	BLQ	BLQ	BLQ
	60204	11.5	7.08	5.52	5.20	5.29	BLQ
	Mean	8.78	BLQ	5.48	BLQ	BLQ	BLQ
	SD	2.36	NC	0.19	NC	NC	NC
25	60302	14.0	8.03	6.42	6.13	5.63	BLQ
	60303	10.4	7.36	6.41	BLQ	5.37	5.15
	60304	13.3	8.68	7.58	6.28	BLQ	5.38
	Mean	12.6	8.02	6.80	BLQ	BLQ	BLQ
	SD	1.9	0.66	0.67	NC	NC	NC

BLQ: Below the lower limit of quantification (&lt;5 ng/mL)

NC: Not calculated

These values were reference data because the QC samples did not meet the acceptable criteria.

Table 10-4 Drug Concentration in Plasma and Cerebral Spinal Fluid

B131138

&lt;4th dosing, Male&gt;

Dose (mg/kg)	Animal No.	Plasma concentration of P092 after completion of dosing (ng/mL)						
		Pre	0.083 h	2 h	4 h	8 h	24 h	48 h
1	20101	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	20102	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	20103	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC	NC
10	20201	BLQ	7.17	BLQ	BLQ	BLQ	BLQ	BLQ
	20202	BLQ	13.6	7.43	BLQ	BLQ	BLQ	BLQ
	20204	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	6.92	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	6.80	NC	NC	NC	NC	NC
25	20301	6.12	10.2	5.99	BLQ	5.04	BLQ	BLQ
	20303	BLQ	6.82	6.36	BLQ	BLQ	BLQ	BLQ
	20305	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	5.67	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	5.20	NC	NC	NC	NC	NC

BLQ: Below the lower limit of quantification (&lt;5 ng/mL)

NC: Not calculated

Table 10-5 Drug Concentration in Plasma and Cerebral Spinal Fluid

B131138

&lt;4th dosing, Female&gt;

Dose (mg/kg)	Animal No.	Plasma concentration of P092 after completion of dosing (ng/mL)						
		Pre	0.083 h	2 h	4 h	8 h	24 h	48 h
1	60101	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60102	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60103	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC	NC
10	60202	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60203	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60204	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC	NC
25	60301	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60302	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	60303	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	Mean	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
	SD	NC	NC	NC	NC	NC	NC	NC

BLQ: Below the lower limit of quantification (&lt;5 ng/mL)

NC: Not calculated

Table 10-6 Drug Concentration in Plasma and Cerebral Spinal Fluid

B131138

Sex	Dose (mg/kg)	Animal No.	CSF concentration of P092 (ng/mL)
Male	1	20101	BLQ
		20102	BLQ
		20103	BLQ
		20104	BLQ
		20105	BLQ
	10	20201	BLQ
		20202	BLQ
		20204	BLQ
	25	20301	146
		20303	BLQ
20305		6.54	
Female	1	60101	BLQ
		60102	BLQ
		60103	BLQ
		60104	BLQ
		60105	BLQ
	10	60201	BLQ
		60202	37.2
		60203	BLQ
		60204	BLQ
		60205	BLQ
	25	60301	7.91
		60302	BLQ
		60303	BLQ
		60305	BLQ

BLQ: Below the lower limit of quantification (&lt; 5 ng/mL)

Key Page

Code	Description
BD	Before dosing
T10	2-4 hours after dosing

## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	1	2	3	4	5	6	7	8	8	9	10	11	12	13	14	
					BD	T10	am	am	am	am	am	BD	T10	am	am	am	am	am	am	am	am
1	m	10101	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10102	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10103	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10104	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10105	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10106	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg

## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	15 BD	15 T10	16 am	17 am	18 am	19 am	20 am	21 am	22 BD	22 T10	23 am	24 am	25 am	26 am	27 am	28 am
1	m	10101	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10102	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10103	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10104	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10105	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10106	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg

## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	29 am	29 pm
1	m	10101	No Abnormalities Detected		X	.
		10102	No Abnormalities Detected		X	.
		10103	No Abnormalities Detected		X	.
		10104	No Abnormalities Detected		X	.
		10105	No Abnormalities Detected		X	.
		10106	No Abnormalities Detected		X	.

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg



## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	1	2	3	4	5	6	7	8	8	9	10	11	12	13	14		
					BD	T10	am	am	am	am	am	am	BD	T10	am	am	am	am	am	am	am	am
2	m	10201	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		10202	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10203	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10204	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10205	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10206	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg

## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	Day numbers relative to Start Date																
					15 BD	15 T10	16 am	17 am	18 am	19 am	20 am	21 am	22 BD	22 T10	23 am	24 am	25 am	26 am	27 am	28 am	
2	m	10201	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
		10202	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10203	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10204	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10205	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10206	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg

## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	29 am	29 pm
2	m	10201	No Abnormalities Detected		X	.
		10202	No Abnormalities Detected		X	.
		10203	No Abnormalities Detected		X	.
		10204	No Abnormalities Detected		X	.
		10205	No Abnormalities Detected		X	.
		10206	No Abnormalities Detected		X	.

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg

## Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	Day numbers relative to Start Date																	
					1 BD	1 T10	2 am	3 am	4 am	5 am	6 am	7 am	8 BD	8 T10	9 am	10 am	11 am	12 am	13 am	14 am		
3	m	10301	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
			Death		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
		10302	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
			Abnormal gait		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
			Anemic		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
		10303	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		10304	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Death		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.		
	10305	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
		Death		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.		
		10306	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		

Severity Codes: X = Present

Group 1 - 0 mg/kg    Group 2 - 1 mg/kg    Group 3 - 10 mg/kg    Group 4 - 25 mg/kg