

Table 5

Necropsy - Summary

B120716

Removal Reason: Scheduled sacrifice	Male				Female			
	0 mg/kg	50 mg/kg	150 mg/kg	500 mg/kg	0 mg/kg	50 mg/kg	150 mg/kg	500 mg/kg
Number of Animals:	5	5	5	5	5	5	5	5
Necropsy Findings								
Absent	5	5	5	5	5	5	5	5

Table 6 Plasma Concentrations and Toxicokinetic Parameters

B120716

<Male>

Dose (mg/kg)	Animal No.	Plasma concentration of P092 (ng/mL)						C _{max} (ng/mL)	T _{max} (h)	AUC _{0-24h} (ng·h/mL)
		0.5 h	1 h	2 h	4 h	8 h	24 h			
0	20101	BLQ	--	BLQ	--	--	--	--	--	--
	20102	BLQ	--	BLQ	--	--	--	--	--	--
	20103	BLQ	--	BLQ	--	--	--	--	--	--
	Mean	BLQ	--	BLQ	--	--	--	--	--	--
	SD	NC	--	NC	--	--	--	--	--	--
50	20201	BLQ	BLQ	9.84	12.6	BLQ	5.96	12.6	4	100
	20202	BLQ	10.3	11.3	13.6	5.87	5.03	13.6	4	164
	20203	6.63	49.0	8.73	8.18	6.10	10.1	49.0	1	220
	Mean	BLQ	19.8	9.96	11.5	BLQ	7.03	25.1	3.0	161
	SD	NC	25.8	1.29	2.9	NC	2.70	20.7	1.7	60
150	20301	6.52	30.6	20.2	38.0	7.63	14.0	38.0	4	359
	20302	12.9	37.8	13.5	18.5	15.1	10.2	37.8	1	343
	20303	18.8	34.1	12.9	22.9	11.0	13.9	34.1	1	344
	Mean	12.7	34.2	15.5	26.5	11.2	12.7	36.6	2.0	349
	SD	6.1	3.6	4.1	10.2	3.7	2.2	2.2	1.7	9
500	20401	126	73.0	21.7	9.40	14.2	7.08	126	0.5	377
	20402	14.1	50.0	58.3	29.6	14.7	8.03	58.3	2	432
	20403	8.92	23.3	18.3	20.8	14.3	36.0	36.0	24	543
	Mean	49.7	48.8	32.8	19.9	14.4	17.0	73.4	8.8	451
	SD	66.2	24.9	22.2	10.1	0.3	16.4	46.9	13.2	85

BLQ: Below the lower limit of quantification (<5 ng/mL)

NC: Not calculated

Table 6 Plasma Concentrations and Toxicokinetic Parameters

B120716

<Female>

Dose (mg/kg)	Animal No.	Plasma concentration of P092 (ng/mL)						C _{max} (ng/mL)	T _{max} (h)	AUC _{0-24h} (ng·h/mL)
		0.5 h	1 h	2 h	4 h	8 h	24 h			
0	60101	BLQ	--	BLQ	--	--	--	--	--	--
	60102	BLQ	--	BLQ	--	--	--	--	--	--
	60103	BLQ	--	BLQ	--	--	--	--	--	--
	Mean	BLQ	--	BLQ	--	--	--	--	--	--
	SD	NC	--	NC	--	--	--	--	--	--
50	60201	BLQ	20.4	13.8	11.9	5.78	BLQ	20.4	1	130
	60202	BLQ	BLQ	6.54	9.21	6.65	BLQ	9.21	4	104
	60203	5.46	39.0	21.1	8.75	5.56	BLQ	39.0	1	145
	Mean	BLQ	19.8	13.8	9.95	6.00	BLQ	22.9	2.0	126
	SD	NC	19.5	7.3	1.70	0.58	NC	15.0	1.7	21
150	60301	BLQ	20.8	6.90	8.57	7.26	5.01	20.8	1	164
	60302	8.19	30.4	14.7	18.3	10.3	BLQ	30.4	1	207
	60303	6.76	36.2	11.6	17.6	7.49	BLQ	36.2	1	176
	Mean	BLQ	29.1	11.1	14.8	8.35	BLQ	29.1	1.0	182
	SD	NC	7.8	3.9	5.4	1.69	NC	7.8	0.0	22
500	60401	12.3	46.7	45.4	11.7	9.92	10.9	46.7	1	331
	60402	24.5	31.2	22.4	18.6	7.47	14.0	31.2	1	312
	60403	BLQ	14.0	23.0	16.6	18.6	6.71	23.0	2	334
	Mean	12.3	30.6	30.3	15.6	12.0	10.5	33.6	1.3	326
	SD	12.3	16.4	13.1	3.6	5.8	3.7	12.0	0.6	12

BLQ: Below the lower limit of quantification (<5 ng/mL)

NC: Not calculated

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	1	1	1	1	1	2	3	4
					Before dosing	Time 10	Time 20	Time 30	Time 40	Time 50	a.m.	a.m.	a.m.
1	m	10101	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		10102	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		10103	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		10104	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		10105	No Abnormalities Detected		X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Group	Sex	Animal	Clinical Sign	Site	Day numbers relative to Start Date									
					5 a.m.	6 a.m.	7 a.m.	8 a.m.	9 a.m.	10 a.m.	11 a.m.	12 a.m.	13 a.m.	
1	m	10101	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		10102	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		10103	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		10104	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		10105	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	14	15
					a.m.	a.m.
1	m	10101	No Abnormalities Detected		X	X
		10102	No Abnormalities Detected		X	X
		10103	No Abnormalities Detected		X	X
		10104	No Abnormalities Detected		X	X
		10105	No Abnormalities Detected		X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	1	1	1	1	1	2	3	4	
					Before dosing	Time 10	Time 20	Time 30	Time 40	Time 50	a.m.	a.m.	a.m.	
2	m	10201	No Abnormalities Detected		X	X	X	X	X	.	X	X	X	
			Diarrhea		X
		10202	No Abnormalities Detected		X	X	X	X	X	X	.	X	X	X
			Diarrhea		X	.	.	.
		10203	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
10204	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X		
		10205	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	5	6	7	8	9	10	11	12	13
					a.m.								
2	m	10201	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
			Diarrhea	
		10202	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
			Diarrhea	
		10203	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		10204	No Abnormalities Detected		X	X	X	X	X	X	X	X	
		10205	No Abnormalities Detected		X	X	X	X	X	X	X	X	

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	14	15
					a.m.	a.m.
2	m	10201	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10202	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10203	No Abnormalities Detected		X	X
		10204	No Abnormalities Detected		X	X
		10205	No Abnormalities Detected		X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	Day numbers relative to Start Date									
					1 Before dosing	1 Time 10	1 Time 20	1 Time 30	1 Time 40	1 Time 50	2 a.m.	3 a.m.	4 a.m.	
3	m	10301	No Abnormalities Detected		X	X	X	X	.	.	X	X	X	
			Diarrhea	X	X	
		10302	No Abnormalities Detected		X	X	X	X	X	.	.	X	X	X
			Diarrhea	X	X
		10303	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		10304	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
			Diarrhea	X
		10305	No Abnormalities Detected		X	X	X	X	.	X	X	X	X	X
			Diarrhea	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

				Day numbers relative to Start Date									
				5	6	7	8	9	10	11	12	13	
				a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	
Group	Sex	Animal	Clinical Sign	Site									
3	m	10301	No Abnormalities Detected		X	X	X	X	X	X	X	X	
			Diarrhea	
		10302	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
			Diarrhea	
		10303	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		10304	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
			Diarrhea	
		10305	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
			Diarrhea	

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	14	15
					a.m.	a.m.
3	m	10301	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10302	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10303	No Abnormalities Detected		X	X
		10304	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10305	No Abnormalities Detected		X	X
			Diarrhea		.	.

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Group	Sex	Animal	Clinical Sign	Site	Day numbers relative to Start Date									
					1 Before dosing	1 Time 10	1 Time 20	1 Time 30	1 Time 40	1 Time 50	2 a.m.	3 a.m.	4 a.m.	
4	m	10401	No Abnormalities Detected		X	X	X	X	X	.	.	.	X	
			Diarrhea	X	X	X	.	.	
		10402	No Abnormalities Detected		X	X	X	.	.	.	X	X	X	X
			Diarrhea	.	.	.	X	X	X
		10403	No Abnormalities Detected		X	X	X	X	X	.	X	X	X	X
			Diarrhea	X
		10404	No Abnormalities Detected		X	X	X	X	X	.	X	X	X	X
			Diarrhea	X
		10405	No Abnormalities Detected		X	X	X	X	X	.	X	X	X	X
			Diarrhea	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	5	6	7	8	9	10	11	12	13	
					a.m.									
4	m	10401	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	
			Diarrhea	
		10402	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
			Diarrhea	
		10403	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
			Diarrhea	
		10404	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
			Diarrhea	
		10405	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
			Diarrhea	

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	14	15
					a.m.	a.m.
4	m	10401	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10402	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10403	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10404	No Abnormalities Detected		X	X
			Diarrhea		.	.
		10405	No Abnormalities Detected		X	X
			Diarrhea		.	.

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	Day numbers relative to Start Date									
					1 Before dosing	1 Time 10	1 Time 20	1 Time 30	1 Time 40	1 Time 50	2 a.m.	3 a.m.	4 a.m.	
1	f	50101	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		50102	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		50103	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		50104	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X
		50105	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

				Day numbers relative to Start Date									
				5	6	7	8	9	10	11	12	13	
				a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	a.m.	
Group	Sex	Animal	Clinical Sign	Site									
1	f	50101	No Abnormalities Detected		X	X	X	X	X	X	X	X	
		50102	No Abnormalities Detected		X	X	X	X	X	X	X	X	
		50103	No Abnormalities Detected		X	X	X	X	X	X	X	X	
		50104	No Abnormalities Detected		X	X	X	X	X	X	X	X	
		50105	No Abnormalities Detected		X	X	X	X	X	X	X	X	

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	14	15
					a.m.	a.m.
1	f	50101	No Abnormalities Detected		X	X
		50102	No Abnormalities Detected		X	X
		50103	No Abnormalities Detected		X	X
		50104	No Abnormalities Detected		X	X
		50105	No Abnormalities Detected		X	X

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	1	1	1	1	1	2	3	4
					Before dosing	Time 10	Time 20	Time 30	Time 40	Time 50	a.m.	a.m.	a.m.
2	f	50201	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50202	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50203	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50204	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50205	No Abnormalities Detected		X	X	X	X	X	.	X	X	X
			Diarrhea		X	.	.	.

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;

Day numbers relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	5	6	7	8	9	10	11	12	13
					a.m.								
2	f	50201	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50202	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50203	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50204	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
		50205	No Abnormalities Detected		X	X	X	X	X	X	X	X	X
			Diarrhea	

Severity Codes: X = Present

Group 1 - 0 mg/kg Group 2 - 50 mg/kg Group 3 - 150 mg/kg Group 4 - 500 mg/kg

Time 10 : About 0.5 hours after dosing; Time 20 : About 1 hours after dosing; Time 30 : 2 hours after dosing; Time 40 : About 4 hours after dosing; Time 50 : About 8 hours after dosing;