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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	PL (mg/dL)					IP (mg/dL)				
	-1	1	2	3	4	-1	1	2	3	4
	RP4F01	157	154	152	152	153	4.88	4.64	4.57	4.08
RP4F02	187	162	178	166	191	5.15	3.29	2.33	3.53	2.82
RP4F03	196	175	166	169	178	4.37	4.10	3.54	3.93	4.68
RP4F04	194	220	240	236	271	5.88	4.97	4.27	4.78	3.59
Mean	184	178	184	181	198	5.07	4.25	3.68	4.08	3.95
S.D.	18	29	39	38	51	0.63	0.73	1.00	0.52	0.92
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	CA (mg/dL)					NA (mEq/L)				
	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	9.89	9.70	9.54	9.36	9.46	149.9	146.0	144.2	146.1	144.7
RP4F02	10.79	9.27	9.82	9.06	9.72	163.6	150.9	148.2	149.6	152.5
RP4F03	9.90	9.79	9.73	9.48	9.64	150.7	150.7	147.9	150.5	149.6
RP4F04	9.79	9.19	9.44	9.20	10.71	152.7	148.9	147.5	150.3	148.9
Mean	10.09	9.49	9.63	9.28	9.88	154.2	149.1	147.0	149.1	148.9
S.D.	0.47	0.30	0.17	0.18	0.56	6.4	2.3	1.9	2.1	3.2
N	4	4	4	4	4	4	4	4	4	4

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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	K (mEq/L)					CL (mEq/L)				
	K (mEq/L)	K (mEq/L)	K (mEq/L)	K (mEq/L)	K (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)	CL (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	3.93	3.94	4.08	3.65	4.10	106.6	105.9	107.0	111.2	106.5
RP4F02	4.57	3.82	3.95	3.80	4.35	117.9	110.6	109.8	115.2	115.4
RP4F03	3.77	3.68	4.05	3.65	3.80	111.3	110.1	111.6	115.1	110.3
RP4F04	3.88	4.00	4.15	3.74	3.99	113.7	110.0	112.2	114.9	108.2
Mean	4.04	3.86	4.06	3.71	4.06	112.4	109.2	110.2	114.1	110.1
S.D.	0.36	0.14	0.08	0.07	0.23	4.7	2.2	2.3	1.9	3.9
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	TP (g/dL)					ALB (g/dL)				
	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	8.01	7.49	7.03	7.12	7.09	4.23	3.79	3.60	3.62	3.54
RP4F02	8.31	7.59	7.30	7.55	7.76	4.54	3.89	3.78	3.95	3.93
RP4F03	7.91	7.49	6.98	7.06	7.37	4.67	4.18	3.98	4.10	4.13
RP4F04	7.14	7.10	6.85	7.00	7.20	3.97	3.86	3.83	3.84	3.61
Mean	7.84	7.42	7.04	7.18	7.36	4.35	3.93	3.80	3.88	3.80
S.D.	0.50	0.22	0.19	0.25	0.29	0.31	0.17	0.16	0.20	0.28
N	4	4	4	4	4	4	4	4	4	4

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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	A/G					T-BA ( $\mu\text{mol/L}$ )				
	A/G	A/G	A/G	A/G	A/G	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	1.12	1.02	1.05	1.03	1.00	1.0	2.3	3.3	1.1	2.0
RP4F02	1.20	1.05	1.07	1.10	1.03	1.0	2.1	46.7	1.8	10.5
RP4F03	1.44	1.26	1.33	1.39	1.27	1.3	2.0	3.9	2.2	2.2
RP4F04	1.25	1.19	1.27	1.22	1.01	3.9	2.1	5.1	4.2	70.1
Mean	1.25	1.13	1.18	1.18	1.08	1.8	2.1	14.8	2.3	21.2
S.D.	0.14	0.11	0.14	0.15	0.13	1.4	0.1	21.3	1.3	32.8
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	CRP (mg/dL)				
	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)
	-1	1	2	3	4
RP4F01	0.19	0.23	0.28	0.30	0.27
RP4F02	0.14	0.07	0.16	0.13	0.16
RP4F03	0.04	0.04	0.06	0.06	0.06
RP4F04	0.14	0.09	0.21	0.16	3.11
Mean	0.13	0.11	0.18	0.16	0.90
S.D.	0.06	0.08	0.09	0.10	1.48
N	4	4	4	4	4

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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	AST (U/L)					ALT (U/L)				
	AST (U/L)	AST (U/L)	AST (U/L)	AST (U/L)	AST (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	20	21	21	18	21	27	34	37	43	51
RP5F02	20	20	18	21	22	12	20	16	12	16
RP5F03	20	21	17	21	18	21	24	22	22	22
RP5F04	29	22	23	25	24	42	46	50	56	54
Mean	22	21	20	21	21	26	31	31	33	36
S.D.	5	1	3	3	3	13	12	15	20	20
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	ALP (U/L)					LD (U/L)				
	ALP (U/L)	ALP (U/L)	ALP (U/L)	ALP (U/L)	ALP (U/L)	LD (U/L)	LD (U/L)	LD (U/L)	LD (U/L)	LD (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	686	746	750	787	933	252	243	212	189	232
RP5F02	1091	872	1073	1121	1252	214	211	208	196	194
RP5F03	402	465	445	393	423	175	196	166	159	145
RP5F04	567	571	645	613	661	382	237	218	215	217
Mean	687	664	728	729	817	256	222	201	190	197
S.D.	294	181	262	307	357	90	22	24	23	38
N	4	4	4	4	4	4	4	4	4	4



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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	CK (U/L)					GGT (U/L)				
	CK (U/L)	CK (U/L)	CK (U/L)	CK (U/L)	CK (U/L)	GGT (U/L)	GGT (U/L)	GGT (U/L)	GGT (U/L)	GGT (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	118	106	106	124	152	37.1	36.9	33.9	33.0	34.7
RP5F02	78	56	55	77	97	44.7	54.5	48.0	43.2	42.0
RP5F03	74	88	98	99	92	37.4	30.4	27.3	25.2	28.2
RP5F04	139	103	117	129	170	34.2	28.2	26.8	25.9	27.8
Mean	102	88	94	107	128	38.4	37.5	34.0	31.8	33.2
S.D.	32	23	27	24	39	4.5	11.9	9.9	8.4	6.7
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	GLDH (U/L)					LAP (U/L)				
	GLDH (U/L)	GLDH (U/L)	GLDH (U/L)	GLDH (U/L)	GLDH (U/L)	LAP (U/L)	LAP (U/L)	LAP (U/L)	LAP (U/L)	LAP (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	9	13	25	16	24	35	34	35	34	36
RP5F02	7	16	9	6	6	62	62	61	57	54
RP5F03	10	10	8	9	9	35	32	29	27	28
RP5F04	11	12	13	12	11	41	35	35	36	37
Mean	9	13	14	11	13	43	41	40	39	39
S.D.	2	3	8	4	8	13	14	14	13	11
N	4	4	4	4	4	4	4	4	4	4

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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	GLU (mg/dL)					BIL (mg/dL)				
	GLU (mg/dL)	GLU (mg/dL)	GLU (mg/dL)	GLU (mg/dL)	GLU (mg/dL)	BIL (mg/dL)	BIL (mg/dL)	BIL (mg/dL)	BIL (mg/dL)	BIL (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	94	87	87	77	75	0.11	0.31	0.11	0.12	0.08
RP5F02	92	79	79	93	86	0.12	0.15	0.06	0.10	0.14
RP5F03	88	92	100	92	86	0.11	0.10	0.08	0.08	0.08
RP5F04	86	73	87	76	114	0.27	0.37	0.21	0.28	0.19
Mean	90	83	88	85	90	0.15	0.23	0.12	0.15	0.12
S.D.	4	8	9	9	17	0.08	0.13	0.07	0.09	0.05
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	UN (mg/dL)					CRE (mg/dL)				
	UN (mg/dL)	UN (mg/dL)	UN (mg/dL)	UN (mg/dL)	UN (mg/dL)	CRE (mg/dL)	CRE (mg/dL)	CRE (mg/dL)	CRE (mg/dL)	CRE (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	17.7	20.6	18.1	16.3	17.9	0.85	0.99	0.90	0.97	0.91
RP5F02	15.5	17.7	20.7	14.1	15.6	0.79	0.92	0.76	0.85	0.90
RP5F03	18.1	14.4	18.5	15.2	15.1	0.68	0.79	0.74	0.75	0.74
RP5F04	18.8	18.7	17.4	15.3	16.7	0.83	0.85	0.79	0.87	0.96
Mean	17.5	17.9	18.7	15.2	16.3	0.79	0.89	0.80	0.86	0.88
S.D.	1.4	2.6	1.4	0.9	1.2	0.08	0.09	0.07	0.09	0.10
N	4	4	4	4	4	4	4	4	4	4

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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	CHO (mg/dL)					TG (mg/dL)				
	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	CHO (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)	TG (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	118	109	94	97	108	39	26	36	38	75
RP5F02	168	133	112	115	151	24	25	44	28	75
RP5F03	136	136	121	112	122	51	46	40	32	41
RP5F04	118	103	100	100	101	41	28	32	21	31
Mean	135	120	107	106	121	39	31	38	30	56
S.D.	24	17	12	9	22	11	10	5	7	23
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	PL (mg/dL)					IP (mg/dL)				
	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	PL (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)	IP (mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	165	158	154	155	198	3.13	4.20	3.73	3.06	4.46
RP5F02	181	154	171	151	204	3.35	2.71	1.43	2.80	4.54
RP5F03	148	164	155	138	143	3.14	3.86	3.22	3.16	3.55
RP5F04	153	146	147	143	146	3.86	3.21	3.29	3.92	4.07
Mean	162	156	157	147	173	3.37	3.50	2.92	3.24	4.16
S.D.	15	8	10	8	33	0.34	0.67	1.02	0.48	0.45
N	4	4	4	4	4	4	4	4	4	4

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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	CA (mg/dL)					NA (mEq/L)				
	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	CA (mg/dL)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)	NA (mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	9.66	9.55	9.54	9.36	9.61	154.6	150.5	148.1	152.6	154.3
RP5F02	9.44	9.56	9.76	9.09	9.23	152.5	149.9	149.1	146.8	147.3
RP5F03	9.38	9.44	9.36	8.98	9.35	147.1	147.7	146.7	146.3	147.3
RP5F04	10.29	9.47	9.55	9.43	10.46	156.0	149.4	149.6	152.0	157.1
Mean	9.69	9.51	9.55	9.22	9.66	152.6	149.4	148.4	149.4	151.5
S.D.	0.42	0.06	0.16	0.21	0.55	3.9	1.2	1.3	3.3	5.0
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	K (mEq/L)					CL (mEq/L)				
	K	K	K	K	K	CL	CL	CL	CL	CL
	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	4.10	4.10	4.31	4.01	4.50	116.9	111.7	111.3	117.2	112.1
RP5F02	3.76	3.96	3.84	3.51	3.51	111.7	108.0	109.7	110.7	107.9
RP5F03	3.72	3.54	3.76	3.36	3.83	113.5	109.9	111.3	114.2	112.6
RP5F04	4.81	4.25	5.00	4.64	5.77	113.2	110.5	115.6	116.1	112.7
Mean	4.10	3.96	4.23	3.88	4.40	113.8	110.0	112.0	114.6	111.3
S.D.	0.50	0.31	0.57	0.58	1.00	2.2	1.5	2.5	2.9	2.3
N	4	4	4	4	4	4	4	4	4	4



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## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	TP (g/dL)					ALB (g/dL)				
	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	TP (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)	ALB (g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	7.84	7.78	7.30	7.19	7.37	4.28	3.91	3.84	3.92	3.85
RP5F02	7.64	7.60	7.28	7.30	7.54	4.28	3.91	3.88	3.99	3.90
RP5F03	7.71	7.55	6.98	6.80	7.27	4.16	3.87	3.60	3.59	3.67
RP5F04	8.19	7.67	7.28	7.36	7.81	4.42	3.81	3.77	4.00	4.11
Mean	7.85	7.65	7.21	7.16	7.50	4.29	3.88	3.77	3.88	3.88
S.D.	0.24	0.10	0.15	0.25	0.24	0.11	0.05	0.12	0.19	0.18
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	A/G					T-BA ( $\mu\text{mol/L}$ )				
	A/G	A/G	A/G	A/G	A/G	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )	T-BA ( $\mu\text{mol/L}$ )
	-1	1	2	3	4	-1	1	2	3	4
RP5F01	1.20	1.01	1.11	1.20	1.09	1.5	1.9	3.6	2.3	24.1
RP5F02	1.27	1.06	1.14	1.21	1.07	0.5	2.0	7.4	1.3	2.8
RP5F03	1.17	1.05	1.07	1.12	1.02	0.5	0.5	1.1	0.5	0.5
RP5F04	1.17	0.99	1.07	1.19	1.11	0.5	2.2	4.7	0.5	6.1
Mean	1.21	1.03	1.10	1.18	1.07	0.8	1.7	4.2	1.2	8.4
S.D.	0.05	0.03	0.03	0.04	0.04	0.5	0.8	2.6	0.9	10.7
N	4	4	4	4	4	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	Week(s) Relative to Start Date				
	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)
	-1	1	2	3	4
RP5F01	0.20	0.17	0.17	0.19	0.43
RP5F02	0.02	0.06	0.03	0.02	0.05
RP5F03	0.03	0.04	0.07	0.03	0.03
RP5F04	0.09	0.08	0.11	0.11	0.12
Mean	0.09	0.09	0.10	0.09	0.16
S.D.	0.08	0.06	0.06	0.08	0.19
N	4	4	4	4	4

## A 4-Week Oral Dose Toxicity Study of TM5509 in Cynomolgus Monkeys

## Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	AST (U/L)					ALT (U/L)				
	AST (U/L)	AST (U/L)	AST (U/L)	AST (U/L)	AST (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)	ALT (U/L)
	-1	1	2	3	4	-1	1	2	3	4
RP6F01	19	24	26	207 E <sup>1</sup>	.	23	39	38	56 E <sup>1</sup>	.
RP6F02	31	32	32	33	31	24	25	20	26	28
RP6F03	24	33	49	622 E <sup>1</sup>	.	27	53	46	157 E <sup>1</sup>	.
RP6F04	15	18	19	105 E <sup>1</sup>	.	28	38	30	152 E <sup>1</sup>	.
Mean	22	27	32	33	31	26	39	34	26	28
S.D.	7	7	13	.	.	2	11	11	.	.
N	4	4	4	1	1	4	4	4	1	1

1 [E, Exclude]