

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low TM5509 2 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
RP2M01	0.05	0.07	0.04	0.05	0.04
RP2M02	0.07	0.05	0.06	0.06	0.06
RP2M03	0.07	0.12	0.09	0.09	0.11
RP2M04	0.01	0.01	0.03	0.01	0.01
Mean	0.05	0.06	0.06	0.05	0.06
S.D.	0.03	0.05	0.03	0.03	0.04
N	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3M01	27	27	25	26	30	23	25	23	26	30
RP3M02	28	28	28	31	31	23	25	24	26	27
RP3M03	28	26	24	30	27	26	23	19	24	25
RP3M04	28	23	22	24	27	34	24	21	21	19
Mean	28	26	25	28	29	27	24	22	24	25
S.D.	1	2	3	3	2	5	1	2	2	5
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	ALP (U/L)					LD (U/L)				
	-1	1	2	3	4	-1	1	2	3	4
	RP3M01	989	1319	1442	1268	1100	270	370	286	273
RP3M02	1735	2151	2369	1993	1860	243	303	246	237	219
RP3M03	1189	1514	1685	1748	1726	284	292	271	248	249
RP3M04	1738	1980	2368	2250	2218	252	327	280	289	334
Mean	1413	1741	1966	1815	1726	262	323	271	262	284
S.D.	383	389	475	418	466	18	35	18	24	58
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3M01	116	94	90	99	104	35.2	36.5	33.8	32.5	32.1
RP3M02	99	169	93	91	83	60.0	53.8	52.0	50.7	49.0
RP3M03	192	121	154	173	115	47.9	45.6	46.3	51.7	52.4
RP3M04	76	64	76	66	66	43.7	43.3	43.6	44.0	44.9
Mean	121	112	103	107	92	46.7	44.8	43.9	44.7	44.6
S.D.	50	45	35	46	22	10.3	7.1	7.6	8.8	8.9
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	GLDH (U/L)					LAP (U/L)				
	-1	1	2	3	4	-1	1	2	3	4
	RP3M01	10	10	9	11	13	69	64	61	62
RP3M02	9	9	9	8	13	66	59	61	60	59
RP3M03	13	9	10	10	13	53	47	46	47	48
RP3M04	20	11	12	10	8	54	50	51	51	49
Mean	13	10	10	10	12	61	55	55	55	54
S.D.	5	1	1	1	3	8	8	8	7	6
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3M01	63	90	78	94	81	0.19	0.17	0.14	0.10	0.11
RP3M02	76	88	99	89	85	0.07	0.07	0.07	0.04	0.04
RP3M03	85	73	85	77	70	0.43	0.88	0.39	0.45	0.50
RP3M04	83	70	81	77	82	0.09	0.14	0.09	0.08	0.10
Mean	77	80	86	84	80	0.20	0.32	0.17	0.17	0.19
S.D.	10	10	9	9	7	0.17	0.38	0.15	0.19	0.21
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	UN (mg/dL)					CRE (mg/dL)				
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP3M01	22.9	23.0	24.4	26.1	23.8	0.77	0.88	0.87	0.85	0.88
RP3M02	16.7	17.6	17.2	18.7	17.4	0.71	0.92	0.77	0.76	0.73
RP3M03	20.8	17.5	19.1	22.7	22.9	0.84	0.83	0.89	0.88	0.89
RP3M04	18.5	14.7	16.8	16.4	15.7	0.71	0.74	0.77	0.72	0.76
Mean	19.7	18.2	19.4	21.0	20.0	0.76	0.84	0.83	0.80	0.82
S.D.	2.7	3.5	3.5	4.3	4.0	0.06	0.08	0.06	0.07	0.08
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	CHO					TG				
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP3M01	150	130	130	127	129	21	40	58	57	46
RP3M02	138	155	139	141	133	47	43	44	45	41
RP3M03	164	165	137	155	157	16	18	17	8	14
RP3M04	103	119	108	114	112	29	20	23	13	18
Mean	139	142	129	134	133	28	30	36	31	30
S.D.	26	21	14	18	19	14	13	19	24	16
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	PL	PL	PL	PL	PL	IP	IP	IP	IP	IP
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP3M01	196	191	200	205	195	6.01	5.06	4.12	3.13	3.60
RP3M02	160	176	152	155	155	5.09	5.90	4.74	4.06	3.85
RP3M03	201	201	178	175	200	4.02	4.95	3.03	4.38	5.02
RP3M04	158	157	163	164	164	4.43	5.05	3.90	4.55	4.65
Mean	179	181	173	175	179	4.89	5.24	3.95	4.03	4.28
S.D.	23	19	21	22	22	0.87	0.44	0.71	0.63	0.67
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3M01	9.93	9.83	9.75	9.74	9.44	152.0	150.8	150.1	151.7	152.0
RP3M02	11.01	10.08	9.67	10.27	10.28	158.2	151.7	151.0	156.7	155.2
RP3M03	10.07	9.86	9.58	9.88	9.92	153.3	147.4	148.3	149.8	150.6
RP3M04	10.76	10.34	10.27	10.33	10.48	149.7	149.9	149.5	148.4	150.3
Mean	10.44	10.03	9.82	10.06	10.03	153.3	150.0	149.7	151.7	152.0
S.D.	0.52	0.24	0.31	0.29	0.46	3.6	1.9	1.1	3.6	2.2
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3M01	4.10	4.81	3.93	4.23	4.33	104.3	110.1	105.9	108.0	106.6
RP3M02	4.57	4.78	4.28	4.66	4.77	107.8	108.2	105.5	110.7	109.1
RP3M03	3.98	3.43	3.84	4.06	3.88	106.5	110.3	106.9	108.6	108.4
RP3M04	4.39	4.03	3.95	4.06	3.69	104.5	110.8	108.9	109.4	107.5
Mean	4.26	4.26	4.00	4.25	4.17	105.8	109.9	106.8	109.2	107.9
S.D.	0.27	0.66	0.19	0.28	0.48	1.7	1.1	1.5	1.2	1.1
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	TP	TP	TP	TP	TP	ALB	ALB	ALB	ALB	ALB
	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP3M01	7.82	7.74	7.63	7.60	7.66	4.12	4.11	4.00	4.07	4.07
RP3M02	8.63	8.01	8.23	8.24	8.09	4.78	4.36	4.54	4.50	4.51
RP3M03	8.16	8.04	7.78	7.86	7.92	4.26	4.14	4.00	4.13	4.15
RP3M04	8.32	8.12	8.15	8.07	8.35	4.75	4.55	4.58	4.58	4.71
Mean	8.23	7.98	7.95	7.94	8.01	4.48	4.29	4.28	4.32	4.36
S.D.	0.34	0.17	0.29	0.28	0.29	0.34	0.21	0.32	0.26	0.30
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	A/G					T-BA (µmol/L)				
	A/G	A/G	A/G	A/G	A/G	T-BA (µmol/L)	T-BA (µmol/L)	T-BA (µmol/L)	T-BA (µmol/L)	T-BA (µmol/L)
	-1	1	2	3	4	-1	1	2	3	4
RP3M01	1.11	1.13	1.10	1.15	1.13	0.5	1.5	4.2	17.6	13.1
RP3M02	1.24	1.19	1.23	1.20	1.26	1.5	1.4	2.4	2.4	5.1
RP3M03	1.09	1.06	1.06	1.11	1.10	0.5	0.5	0.5	0.5	0.5
RP3M04	1.33	1.27	1.28	1.31	1.29	11.7	2.8	4.6	3.5	2.8
Mean	1.19	1.17	1.17	1.19	1.20	3.6	1.6	2.9	6.0	5.4
S.D.	0.11	0.09	0.11	0.09	0.09	5.5	0.9	1.9	7.8	5.5
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3M01	0.12	0.12	0.16	0.11	0.08
RP3M02	0.17	0.22	0.12	0.16	0.16
RP3M03	0.06	0.08	0.10	0.07	0.08
RP3M04	0.28	0.29	0.29	0.25	0.26
Mean	0.16	0.18	0.17	0.15	0.15
S.D.	0.09	0.10	0.09	0.08	0.09
N	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	AST (U/L)					ALT (U/L)				
	-1	1	2	3	4	-1	1	2	3	4
	RP4M01	23	22	28	28	36	36	33	38	33
RP4M02	31	25	30	30	28	33	28	32	36	32
RP4M03	23	22	24	29	22	42	34	31	31	25
RP4M04	31	36	29	31	30	27	26	29	30	26
Mean	27	26	28	30	29	35	30	33	33	29
S.D.	5	7	3	1	6	6	4	4	3	4
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	ALP (U/L)					LD (U/L)				
	-1	1	2	3	4	-1	1	2	3	4
	RP4M01	2173	2676	3002	2521	2246	240	269	294	249
RP4M02	941	1017	1158	1086	1088	344	272	253	269	259
RP4M03	1220	1399	1598	1503	1543	280	307	305	371	311
RP4M04	2048	1893	2360	2260	2057	279	304	312	307	274
Mean	1596	1746	2030	1843	1734	286	288	291	299	286
S.D.	608	716	817	664	523	43	20	26	54	23
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	CK (U/L)					GGT (U/L)				
	-1	1	2	3	4	-1	1	2	3	4
	RP4M01	147	124	250	198	766	51.5	46.2	44.9	43.7
RP4M02	430	109	175	158	156	46.5	44.6	39.3	40.1	40.8
RP4M03	91	104	95	306	80	45.0	45.2	41.1	43.0	41.9
RP4M04	232	188	202	209	188	58.9	47.2	42.0	43.4	43.3
Mean	225	131	181	218	298	50.5	45.8	41.8	42.6	42.1
S.D.	148	39	65	63	316	6.3	1.1	2.3	1.7	1.0
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 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
RP4M01	10	10	12	9	10	61	49	53	53	50
RP4M02	10	11	14	13	12	41	39	36	37	37
RP4M03	11	9	7	8	8	46	39	38	39	38
RP4M04	11	13	10	11	10	55	43	43	44	45
Mean	11	11	11	10	10	51	43	43	43	43
S.D.	1	2	3	2	2	9	5	8	7	6
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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 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
RP4M01	81	75	85	88	121	0.11	0.10	0.08	0.08	0.08
RP4M02	74	72	92	79	80	0.14	0.13	0.09	0.08	0.08
RP4M03	87	81	78	89	83	0.13	0.10	0.13	0.12	0.08
RP4M04	99	70	96	105	100	0.17	0.12	0.10	0.08	0.09
Mean	85	75	88	90	96	0.14	0.11	0.10	0.09	0.08
S.D.	11	5	8	11	19	0.03	0.01	0.02	0.02	0.00
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	UN	UN	UN	UN	UN	CRE	CRE	CRE	CRE	CRE
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP4M01	20.0	17.9	18.7	19.4	21.1	1.17	1.17	1.21	1.11	1.20
RP4M02	15.4	16.3	16.6	16.8	17.2	0.75	0.80	0.77	0.75	0.76
RP4M03	17.7	17.7	15.4	15.3	17.1	0.80	0.72	0.75	0.77	0.79
RP4M04	17.8	16.7	18.0	17.9	17.1	1.03	1.00	0.99	0.97	0.96
Mean	17.7	17.2	17.2	17.4	18.1	0.94	0.92	0.93	0.90	0.93
S.D.	1.9	0.8	1.5	1.7	2.0	0.20	0.20	0.22	0.17	0.20
N	4	4	4	4	4	4	4	4	4	4