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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

Control 0.5%CMC-Na	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
RP1M01	19.0	18.5	16.9	21.6	19.0	1.01	0.97	0.89	0.95	0.90
RP1M02	19.0	20.3	19.2	21.0	21.7	0.92	0.94	0.90	0.88	0.92
RP1M03	24.5	21.0	22.6	20.3	22.5	0.77	0.77	0.79	0.75	0.75
RP1M04	21.8	19.4	20.0	22.0	20.6	0.91	0.99	0.94	0.95	0.96
Mean	21.1	19.8	19.7	21.2	21.0	0.90	0.92	0.88	0.88	0.88
S.D.	2.6	1.1	2.4	0.7	1.5	0.10	0.10	0.06	0.09	0.09
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

Control 0.5%CMC-Na	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
RP1M01	129	99	99	99	101	14	12	25	41	22
RP1M02	140	130	140	140	140	23	28	31	54	28
RP1M03	123	131	127	135	122	18	28	17	16	15
RP1M04	155	154	149	151	158	18	17	22	18	14
Mean	137	129	129	131	130	18	21	24	32	20
S.D.	14	23	22	23	24	4	8	6	18	7
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

Control 0.5%CMC-Na	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
RP1M01	173	129	138	154	137	4.39	3.57	3.93	2.22	3.55
RP1M02	154	149	160	190	162	5.03	4.35	4.62	3.08	4.57
RP1M03	153	155	145	157	145	4.93	5.20	5.53	4.70	3.91
RP1M04	218	204	215	219	221	5.41	5.48	6.03	5.73	5.94
Mean	175	159	165	180	166	4.94	4.65	5.03	3.93	4.49
S.D.	30	32	35	31	38	0.42	0.87	0.94	1.58	1.05
N	4	4	4	4	4	4	4	4	4	4

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

## Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1M01	9.66	9.64	9.50	9.68	9.81	147.6	146.8	144.4	143.6	144.7
RP1M02	9.95	9.92	9.74	10.12	9.94	155.4	152.0	148.7	153.9	149.6
RP1M03	10.42	10.11	9.63	9.97	9.84	156.6	155.0	151.2	153.9	152.0
RP1M04	10.36	10.05	9.60	9.62	9.94	158.2	156.9	152.7	153.2	155.8
Mean	10.10	9.93	9.62	9.85	9.88	154.5	152.7	149.3	151.2	150.5
S.D.	0.36	0.21	0.10	0.24	0.07	4.7	4.4	3.6	5.0	4.6
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

Control 0.5%CMC-Na	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
RP1M01	3.59	4.47	3.53	4.49	4.05	105.9	108.7	107.2	109.2	107.6
RP1M02	4.21	4.36	3.71	4.25	4.25	109.3	110.7	106.9	110.2	110.7
RP1M03	4.52	4.44	3.70	4.08	4.58	107.9	110.4	105.3	108.4	111.2
RP1M04	4.51	4.59	3.99	4.49	4.10	109.7	111.4	106.7	111.5	107.7
Mean	4.21	4.47	3.73	4.33	4.25	108.2	110.3	106.5	109.8	109.3
S.D.	0.44	0.10	0.19	0.20	0.24	1.7	1.1	0.8	1.3	1.9
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

Control 0.5%CMC-Na	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
RP1M01	8.16	7.72	7.82	7.85	7.91	4.22	4.07	4.04	4.11	4.12
RP1M02	8.14	7.63	7.63	7.68	7.79	4.03	3.92	3.79	3.89	3.86
RP1M03	8.32	8.21	8.06	8.15	7.87	4.78	4.68	4.63	4.61	4.58
RP1M04	8.16	8.20	7.77	7.80	8.08	4.44	4.48	4.34	4.30	4.43
Mean	8.20	7.94	7.82	7.87	7.91	4.37	4.29	4.20	4.23	4.25
S.D.	0.08	0.31	0.18	0.20	0.12	0.32	0.35	0.36	0.31	0.32
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

Control 0.5%CMC-Na	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
RP1M01	1.07	1.12	1.07	1.10	1.09	1.0	2.3	1.1	24.2	2.7
RP1M02	0.98	1.06	0.99	1.03	0.98	1.1	2.3	2.5	2.7	2.4
RP1M03	1.35	1.33	1.35	1.30	1.39	0.5	1.0	2.6	1.0	1.7
RP1M04	1.19	1.20	1.27	1.23	1.21	0.5	0.5	0.5	0.5	0.5
Mean	1.15	1.18	1.17	1.16	1.17	0.8	1.5	1.7	7.1	1.8
S.D.	0.16	0.12	0.17	0.12	0.18	0.3	0.9	1.0	11.4	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

Control 0.5%CMC-Na	CRP (mg/dL)				
	-1	1	2	3	4
	RP1M01	0.09	0.03	0.07	0.07
RP1M02	0.13	0.11	0.15	0.26	0.14
RP1M03	0.28	0.36	0.23	0.44	0.38
RP1M04	0.05	0.06	0.11	0.08	0.09
Mean	0.14	0.14	0.14	0.21	0.17
S.D.	0.10	0.15	0.07	0.18	0.14
N	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 TM5509 2 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
RP2M01	27	22	23	25	24	34	29	30	30	29
RP2M02	24	25	27	24	29	17	17	18	18	17
RP2M03	33	39	37	40	36	50	66	47	51	48
RP2M04	45	38	28	32	28	53	42	31	32	33
Mean	32	31	29	30	29	39	39	32	33	32
S.D.	9	9	6	7	5	17	21	12	14	13
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 TM5509 2 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
RP2M01	1684	2059	2131	1954	1797	263	263	223	259	249
RP2M02	986	971	1099	955	886	250	262	289	240	297
RP2M03	1568	2298	2622	2272	2120	409	629	533	527	451
RP2M04	499	392	471	468	433	313	428	353	383	300
Mean	1184	1430	1581	1412	1309	309	396	350	352	324
S.D.	550	901	975	843	784	72	174	133	133	88
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 TM5509 2 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
RP2M01	141	97	155	106	112	76.9	81.4	78.0	81.3	80.5
RP2M02	123	125	101	100	109	83.1	71.1	65.6	66.4	62.9
RP2M03	158	118	132	135	124	49.8	55.0	52.8	54.4	52.7
RP2M04	101	174	72	103	79	42.2	38.9	37.8	38.8	38.2
Mean	131	129	115	111	106	63.0	61.6	58.6	60.2	58.6
S.D.	24	33	36	16	19	20.0	18.6	17.2	18.0	17.8
N	4	4	4	4	4	4	4	4	4	4

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

## Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low TM5509 2 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
RP2M01	12	11	12	13	12	72	65	66	66	65
RP2M02	7	8	8	7	8	53	44	44	45	41
RP2M03	12	19	15	16	15	60	66	62	59	58
RP2M04	17	13	11	12	13	80	64	63	62	63
Mean	12	13	12	12	12	66	60	59	58	57
S.D.	4	5	3	4	3	12	11	10	9	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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low TM5509 2 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
RP2M01	76	72	74	72	72	0.14	0.21	0.16	0.16	0.16
RP2M02	90	72	80	82	65	0.13	0.11	0.14	0.10	0.09
RP2M03	69	66	73	85	95	0.13	0.14	0.12	0.10	0.10
RP2M04	100	82	99	81	109	0.34	0.31	0.17	0.18	0.12
Mean	84	73	82	80	85	0.19	0.19	0.15	0.14	0.12
S.D.	14	7	12	6	20	0.10	0.09	0.02	0.04	0.03
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 TM5509 2 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
RP2M01	19.5	17.7	20.5	19.5	20.4	0.79	0.80	0.81	0.80	0.81
RP2M02	19.6	14.1	14.1	14.9	16.5	0.65	0.71	0.68	0.70	0.69
RP2M03	19.2	15.6	16.8	16.8	19.8	0.83	0.90	0.95	0.89	0.93
RP2M04	19.9	19.2	19.9	19.2	20.8	0.85	0.77	0.84	0.80	0.87
Mean	19.6	16.7	17.8	17.6	19.4	0.78	0.80	0.82	0.80	0.83
S.D.	0.3	2.3	3.0	2.2	2.0	0.09	0.08	0.11	0.08	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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low TM5509 2 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
RP2M01	156	141	136	145	155	20	26	29	26	28
RP2M02	124	108	108	114	113	32	16	31	18	24
RP2M03	112	131	124	127	127	38	51	46	40	50
RP2M04	173	133	129	138	129	22	33	76	24	34
Mean	141	128	124	131	131	28	32	46	27	34
S.D.	28	14	12	14	18	8	15	22	9	11
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 TM5509 2 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
RP2M01	176	184	187	188	192	5.62	5.18	5.05	5.53	5.41
RP2M02	153	132	142	139	140	6.26	4.32	5.19	5.54	5.41
RP2M03	158	165	159	153	153	4.46	5.02	5.17	5.00	5.62
RP2M04	188	165	179	164	166	4.83	3.75	2.93	5.58	2.74
Mean	169	162	167	161	163	5.29	4.57	4.59	5.41	4.80
S.D.	16	22	20	21	22	0.81	0.66	1.11	0.28	1.37
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 TM5509 2 mg/kg/day	CA	CA	CA	CA	CA	NA	NA	NA	NA	NA
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)	(mEq/L)
	-1	1	2	3	4	-1	1	2	3	4
RP2M01	10.04	9.36	9.77	9.76	9.70	156.0	149.9	150.6	151.9	149.9
RP2M02	9.93	9.59	9.64	9.61	9.62	150.3	147.5	145.6	146.8	147.8
RP2M03	10.19	10.64	10.94	9.96	9.94	158.0	159.8	162.0	156.5	155.2
RP2M04	9.74	9.31	9.48	9.08	9.33	154.7	150.4	152.0	150.3	152.7
Mean	9.98	9.73	9.96	9.60	9.65	154.8	151.9	152.6	151.4	151.4
S.D.	0.19	0.62	0.67	0.38	0.25	3.3	5.4	6.9	4.0	3.2
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 TM5509 2 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
RP2M01	4.42	4.09	4.17	4.17	3.85	111.4	113.1	113.0	113.7	111.1
RP2M02	3.83	3.71	3.98	3.96	3.95	106.4	108.9	109.8	110.6	109.8
RP2M03	4.89	4.91	5.36	4.43	4.93	110.3	115.0	113.8	111.7	112.3
RP2M04	5.38	4.67	5.14	4.66	4.79	107.8	109.5	109.6	107.7	108.6
Mean	4.63	4.35	4.66	4.31	4.38	109.0	111.6	111.6	110.9	110.5
S.D.	0.66	0.55	0.69	0.30	0.56	2.3	2.9	2.2	2.5	1.6
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

Low TM5509 2 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
RP2M01	7.92	7.61	7.46	7.51	7.58	4.01	4.00	3.94	4.04	4.12
RP2M02	8.68	7.99	7.85	7.81	7.83	4.74	4.40	4.41	4.44	4.38
RP2M03	7.38	7.93	7.92	7.58	7.68	3.78	4.03	3.99	3.86	3.90
RP2M04	7.59	6.90	7.09	7.21	7.21	4.24	3.83	3.89	3.96	4.09
Mean	7.89	7.61	7.58	7.53	7.58	4.19	4.07	4.06	4.08	4.12
S.D.	0.57	0.50	0.38	0.25	0.26	0.41	0.24	0.24	0.25	0.20
N	4	4	4	4	4	4	4	4	4	4

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

## Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Low TM5509 2 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
RP2M01	1.03	1.11	1.12	1.16	1.19	1.3	1.2	1.0	0.5	0.5
RP2M02	1.20	1.23	1.28	1.32	1.27	1.2	1.2	1.8	1.1	1.4
RP2M03	1.05	1.03	1.02	1.04	1.03	1.0	0.5	0.5	0.5	0.5
RP2M04	1.27	1.25	1.22	1.22	1.31	1.7	2.7	2.4	2.2	3.4
Mean	1.14	1.15	1.16	1.18	1.20	1.3	1.4	1.4	1.1	1.5
S.D.	0.12	0.10	0.12	0.12	0.12	0.3	0.9	0.8	0.8	1.4
N	4	4	4	4	4	4	4	4	4	4