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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

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
RP6M01	35	52	52	54	59	34	48	48	54	53
RP6M02	27	48	348	.	.	33	47	108	.	.
RP6M03	30	49	42	43	36	49	69	50	66	79
RP6M04	42	52	48	52	54	48	42	38	40	47
Mean	34	50	123	50	50	41	52	61	53	60
S.D.	7	2	150	6	12	9	12	32	13	17
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 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
RP6M01	858	576	525	484	527	437	563	472	436	450
RP6M02	2171	1586	2256	.	.	288	460	550	.	.
RP6M03	951	1191	874	682	682	308	421	369	331	310
RP6M04	1564	1448	1233	1093	897	268	328	261	234	234
Mean	1386	1200	1222	753	702	325	443	413	334	331
S.D.	610	447	747	311	186	76	97	126	101	110
N	4	4	4	3	3	4	4	4	3	3

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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

High TM5509 300 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
RP6M01	85	161	227	293	239	41.4	35.0	31.5	29.7	29.3
RP6M02	170	145	98	.	.	78.2	69.2	192.8	.	.
RP6M03	129	158	132	178	157	39.5	46.6	41.7	36.6	76.0
RP6M04	127	360	121	128	148	49.2	42.7	37.8	36.8	35.8
Mean	128	206	145	200	181	52.1	48.4	76.0	34.4	47.0
S.D.	35	103	57	85	50	17.9	14.7	78.0	4.0	25.3
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 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
RP6M01	17	10	8	8	14	49	36	34	33	35
RP6M02	13	43	265	.	.	95	109	700	.	.
RP6M03	15	72	13	26	41	48	61	55	49	158
RP6M04	21	10	7	10	11	54	42	39	40	41
Mean	17	34	73	15	22	62	62	207	41	78
S.D.	3	30	128	10	17	22	33	329	8	69
N	4	4	4	3	3	4	4	4	3	3

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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

High TM5509 300 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
RP6M01	109	44	64	84	81	0.15	1.37	1.18	0.45	0.88
RP6M02	107	58	78	.	.	0.15	0.63	2.99	.	.
RP6M03	88	64	90	104	93	0.14	0.61	0.51	0.26	0.11
RP6M04	97	80	89	78	79	0.08	0.18	0.18	0.76	0.45
Mean	100	62	80	89	84	0.13	0.70	1.22	0.49	0.48
S.D.	10	15	12	14	8	0.03	0.49	1.25	0.25	0.39
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 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
RP6M01	18.6	22.3	17.7	19.5	25.7	0.61	0.86	0.74	0.72	0.67
RP6M02	22.5	34.6	52.7	.	.	1.02	1.59	1.34	.	.
RP6M03	22.4	22.5	21.4	17.7	16.3	0.72	1.10	1.08	0.89	0.84
RP6M04	20.7	16.4	17.0	23.6	20.4	0.73	0.85	0.88	0.93	0.94
Mean	21.1	24.0	27.2	20.3	20.8	0.77	1.10	1.01	0.85	0.82
S.D.	1.8	7.6	17.1	3.0	4.7	0.18	0.35	0.26	0.11	0.14
N	4	4	4	3	3	4	4	4	3	3

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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

High TM5509 300 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
RP6M01	140	118	116	120	114	27	48	43	53	32
RP6M02	113	90	100	.	.	40	81	116	.	.
RP6M03	132	141	102	104	118	23	43	66	53	59
RP6M04	130	125	103	95	95	29	34	65	50	67
Mean	129	119	105	106	109	30	52	73	52	53
S.D.	11	21	7	13	12	7	21	31	2	18
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 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
RP6M01	182	147	151	161	143	4.16	3.82	2.82	2.81	5.32
RP6M02	143	139	195	.	.	5.87	4.88	4.20	.	.
RP6M03	186	185	132	146	186	4.44	3.75	3.25	2.34	1.99
RP6M04	183	190	174	167	165	4.62	4.49	3.78	4.32	4.78
Mean	174	165	163	158	165	4.77	4.24	3.51	3.16	4.03
S.D.	20	26	27	11	22	0.76	0.54	0.60	1.03	1.79
N	4	4	4	3	3	4	4	4	3	3

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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

High TM5509 300 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
RP6M01	9.35	8.77	8.69	9.06	8.72	145.4	145.1	148.1	150.2	144.8
RP6M02	10.10	9.16	8.67	.	.	151.1	144.4	130.1	.	.
RP6M03	9.88	9.45	9.57	9.43	9.74	152.6	148.7	148.0	149.5	151.4
RP6M04	9.95	9.46	9.48	9.55	9.61	150.8	152.0	150.9	150.0	154.6
Mean	9.82	9.21	9.10	9.35	9.36	150.0	147.6	144.3	149.9	150.3
S.D.	0.33	0.32	0.49	0.26	0.56	3.1	3.5	9.5	0.4	5.0
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 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
RP6M01	4.55	3.85	4.56	4.58	4.46	105.7	107.3	111.2	113.0	104.6
RP6M02	4.67	3.56	3.36	.	.	110.4	98.9	79.0	.	.
RP6M03	4.01	3.27	3.59	4.18	4.28	110.2	104.9	101.9	109.7	108.1
RP6M04	3.86	3.97	3.56	4.07	4.16	108.6	110.8	106.0	111.6	109.7
Mean	4.27	3.66	3.77	4.28	4.30	108.7	105.5	99.5	111.4	107.5
S.D.	0.40	0.31	0.54	0.27	0.15	2.2	5.0	14.2	1.7	2.6
N	4	4	4	3	3	4	4	4	3	3

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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

High TM5509 300 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
RP6M01	7.44	7.03	6.76	6.83	6.74	4.18	3.60	3.48	3.56	3.51
RP6M02	7.67	7.69	6.71	.	.	4.32	3.62	2.38	.	.
RP6M03	7.76	8.03	7.80	7.50	7.84	4.37	4.03	3.79	3.64	3.49
RP6M04	7.87	7.85	7.69	7.43	7.78	4.62	4.02	3.99	3.76	4.05
Mean	7.69	7.65	7.24	7.25	7.45	4.37	3.82	3.41	3.65	3.68
S.D.	0.18	0.44	0.59	0.37	0.62	0.18	0.24	0.72	0.10	0.32
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 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
RP6M01	1.28	1.05	1.06	1.09	1.09	6.0	21.1	32.2	13.0	48.3
RP6M02	1.29	0.89	0.55	.	.	1.4	16.4	114.9	.	.
RP6M03	1.29	1.01	0.95	0.94	0.80	1.9	2.8	5.4	7.9	13.7
RP6M04	1.42	1.05	1.08	1.02	1.09	2.7	5.6	2.9	35.3	9.2
Mean	1.32	1.00	0.91	1.02	0.99	3.0	11.5	38.9	18.7	23.7
S.D.	0.07	0.08	0.25	0.07	0.16	2.1	8.7	52.4	14.6	21.4
N	4	4	4	3	3	4	4	4	3	3

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

High TM5509 300 mg/kg/day	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)	CRP (mg/dL)
	-1	1	2	3	4
RP6M01	0.07	0.08	0.14	0.09	0.13
RP6M02	0.04	0.13	1.36	.	.
RP6M03	0.16	0.35	0.14	0.15	0.25
RP6M04	0.09	0.15	0.10	0.09	0.12
Mean	0.09	0.18	0.44	0.11	0.17
S.D.	0.05	0.12	0.62	0.03	0.07
N	4	4	4	3	3

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

Appendix 7 Clinical chemistry (males)

General Footnote: The T-BA value of 0.5 $\mu\text{mol/L}$ was half of the lower limit of quantification (1 $\mu\text{mol/L}$).

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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

Control 0.5%CMC-Na	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
RP1F01	43	28	24	27	22	90	63	44	41	35
RP1F02	26	30	35	25	29	27	30	40	35	47
RP1F03	24	30	22	25	23	32	43	33	35	34
RP1F04	19	23	17	18	21	42	58	41	53	51
Mean	28	28	25	24	24	48	49	40	41	42
S.D.	10	3	8	4	4	29	15	5	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 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1F01	878	1025	988	974	999	388	214	211	221	176
RP1F02	1208	1387	1356	1152	1170	220	251	192	169	188
RP1F03	1169	1360	1450	1374	1356	105	149	117	113	108
RP1F04	905	1130	1127	962	955	176	210	171	153	162
Mean	1040	1226	1230	1116	1120	222	206	173	164	159
S.D.	173	177	211	193	183	120	42	41	45	35
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

Control 0.5%CMC-Na	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
RP1F01	1843	149	163	182	173	51.7	49.8	47.3	45.0	43.4
RP1F02	88	94	162	107	121	39.8	38.4	35.5	33.9	42.6
RP1F03	130	121	133	159	149	53.2	47.4	46.8	46.1	44.6
RP1F04	82	95	93	87	107	57.6	53.5	49.8	47.3	46.9
Mean	536	115	138	134	138	50.6	47.3	44.9	43.1	44.4
S.D.	872	26	33	44	29	7.6	6.4	6.4	6.2	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 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1F01	76	38	20	16	11	56	51	50	49	45
RP1F02	10	13	35	20	35	61	58	62	55	70
RP1F03	8	10	9	7	8	40	36	36	35	33
RP1F04	21	43	23	43	27	125	162	142	171	124
Mean	29	26	22	22	20	71	77	73	78	68
S.D.	32	17	11	15	13	37	58	48	63	40
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

Control 0.5%CMC-Na	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
RP1F01	92	66	124	74	111	0.11	0.12	0.11	0.15	0.14
RP1F02	90	85	96	81	92	0.18	0.11	0.08	0.07	0.07
RP1F03	96	83	107	89	106	0.13	0.12	0.10	0.08	0.08
RP1F04	98	88	95	98	95	0.14	0.16	0.17	0.15	0.12
Mean	94	81	106	86	101	0.14	0.13	0.12	0.11	0.10
S.D.	4	10	13	10	9	0.03	0.02	0.04	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 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1F01	19.9	18.6	21.2	16.8	16.8	0.65	0.61	0.55	0.62	0.58
RP1F02	18.1	16.8	20.7	16.9	20.8	0.81	0.80	0.71	0.73	0.72
RP1F03	21.9	19.1	21.8	16.9	20.1	0.96	0.96	0.91	0.92	0.90
RP1F04	17.9	18.4	16.7	14.8	16.9	0.76	0.77	0.72	0.75	0.75
Mean	19.5	18.2	20.1	16.4	18.7	0.80	0.79	0.72	0.76	0.74
S.D.	1.9	1.0	2.3	1.0	2.1	0.13	0.14	0.15	0.12	0.13
N	4	4	4	4	4	4	4	4	4	4