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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

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
RP3F01	20	19	24	22	18	34	55	60	76	58
RP3F02	27	24	21	24	21	36	27	24	28	26
RP3F03	22	20	21	20	20	26	23	22	23	26
RP3F04	24	25	19	20	20	23	34	25	26	21
Mean	23	22	21	22	20	30	35	33	38	33
S.D.	3	3	2	2	1	6	14	18	25	17
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

Low-Mid TM5509 6 mg/kg/day	ALP (U/L)					LD (U/L)				
	-1	1	2	3	4	-1	1	2	3	4
	RP3F01	588	584	534	514	547	305	338	259	244
RP3F02	1420	1724	1514	1386	1395	291	240	257	230	193
RP3F03	825	623	609	591	623	322	376	310	282	255
RP3F04	1481	1677	1719	1599	1616	267	261	224	206	178
Mean	1079	1152	1094	1023	1045	296	304	263	241	224
S.D.	441	634	610	551	540	23	64	36	32	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

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
RP3F01	132	140	93	109	129	33.4	30.8	31.1	30.3	31.5
RP3F02	136	88	162	131	107	50.1	44.5	42.0	40.0	41.6
RP3F03	131	55	61	67	87	57.4	48.9	50.3	47.9	48.0
RP3F04	159	103	90	98	105	39.0	37.9	34.3	34.4	32.9
Mean	140	97	102	101	107	45.0	40.5	39.4	38.2	38.5
S.D.	13	35	43	27	17	10.8	7.9	8.6	7.6	7.8
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

Low-Mid TM5509 6 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
RP3F01	16	34	47	63	31	42	44	44	43	41
RP3F02	9	9	8	10	10	69	58	56	53	52
RP3F03	7	9	8	7	9	42	35	37	36	36
RP3F04	9	15	10	11	9	47	44	41	41	40
Mean	10	17	18	23	15	50	45	45	43	42
S.D.	4	12	19	27	11	13	10	8	7	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 8 Clinical chemistry (females)

Sex: Female 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
RP3F01	79	66	66	79	69	0.26	0.36	0.15	0.18	0.20
RP3F02	101	88	120	114	118	0.09	0.09	0.06	0.06	0.07
RP3F03	84	71	67	70	70	0.20	0.20	0.11	0.12	0.09
RP3F04	98	93	79	82	113	0.11	0.12	0.09	0.08	0.09
Mean	91	80	83	86	93	0.17	0.19	0.10	0.11	0.11
S.D.	11	13	25	19	27	0.08	0.12	0.04	0.05	0.06
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

Low-Mid TM5509 6 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
RP3F01	13.2	14.1	17.7	13.6	16.1	0.65	0.75	0.69	0.67	0.67
RP3F02	16.5	19.0	22.0	18.6	19.4	0.74	0.76	0.71	0.72	0.77
RP3F03	17.5	19.9	20.8	17.3	16.6	0.80	0.85	0.79	0.76	0.70
RP3F04	19.3	18.7	20.5	18.5	21.0	0.88	0.92	0.80	0.85	0.73
Mean	16.6	17.9	20.3	17.0	18.3	0.77	0.82	0.75	0.75	0.72
S.D.	2.6	2.6	1.8	2.3	2.3	0.10	0.08	0.06	0.08	0.04
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

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
RP3F01	154	169	126	131	151	33	12	21	19	22
RP3F02	141	127	141	139	122	44	43	31	32	31
RP3F03	97	93	77	82	95	29	15	28	23	46
RP3F04	176	146	134	144	153	20	22	16	16	18
Mean	142	134	120	124	130	32	23	24	23	29
S.D.	33	32	29	29	27	10	14	7	7	12
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

Low-Mid TM5509 6 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
RP3F01	196	182	188	171	192	4.88	4.54	3.54	4.43	4.83
RP3F02	167	185	196	178	171	5.54	4.44	3.45	3.58	4.00
RP3F03	154	142	143	138	162	3.68	4.20	1.41	2.90	3.83
RP3F04	213	205	184	194	205	4.63	3.20	2.98	3.32	3.91
Mean	183	179	178	170	183	4.68	4.10	2.85	3.56	4.14
S.D.	27	26	24	24	20	0.77	0.61	0.99	0.65	0.46
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

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
RP3F01	9.70	9.68	9.79	9.39	9.40	150.9	147.6	150.1	148.6	147.0
RP3F02	10.03	9.56	9.73	9.34	9.47	159.6	148.2	148.2	147.3	146.5
RP3F03	9.68	9.16	9.30	9.23	9.47	152.1	147.6	149.3	149.1	148.0
RP3F04	10.48	10.46	10.18	10.19	10.08	154.4	151.3	148.4	152.1	147.4
Mean	9.97	9.72	9.75	9.54	9.61	154.3	148.7	149.0	149.3	147.2
S.D.	0.37	0.54	0.36	0.44	0.32	3.9	1.8	0.9	2.0	0.6
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	K (mEq/L)					CL (mEq/L)				
	K	K	K	K	K	CL	CL	CL	CL	CL
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	4.10	3.89	5.08	4.11	3.97	113.3	107.0	114.5	117.2	110.3
RP3F02	4.42	3.79	3.92	3.80	3.58	117.0	107.1	109.7	111.6	110.2
RP3F03	3.51	3.88	4.41	3.78	4.10	116.0	111.7	114.0	115.3	112.3
RP3F04	3.99	4.49	4.70	4.17	4.73	110.9	107.4	111.5	112.3	108.2
Mean	4.01	4.01	4.53	3.97	4.10	114.3	108.3	112.4	114.1	110.3
S.D.	0.38	0.32	0.49	0.20	0.48	2.8	2.3	2.2	2.6	1.7
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 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 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
RP3F01	7.74	7.51	6.94	6.86	7.06	4.16	4.01	3.78	3.80	3.77
RP3F02	8.16	7.64	7.27	7.13	7.15	4.45	4.10	3.98	3.99	3.89
RP3F03	7.79	7.22	7.16	7.01	7.21	4.07	3.84	3.87	3.81	3.76
RP3F04	8.02	7.98	7.37	7.49	7.47	4.46	4.34	4.11	4.25	4.12
Mean	7.93	7.59	7.19	7.12	7.22	4.29	4.07	3.94	3.96	3.89
S.D.	0.20	0.32	0.18	0.27	0.18	0.20	0.21	0.14	0.21	0.17
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

Low-Mid TM5509 6 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
RP3F01	1.16	1.15	1.20	1.24	1.15	4.0	5.8	8.1	3.8	1.4
RP3F02	1.20	1.16	1.21	1.27	1.19	1.2	1.3	14.0	2.0	3.8
RP3F03	1.09	1.14	1.18	1.19	1.09	1.7	1.9	25.1	9.1	10.2
RP3F04	1.25	1.19	1.26	1.31	1.23	2.8	1.3	1.8	9.3	9.7
Mean	1.18	1.16	1.21	1.25	1.16	2.4	2.6	12.3	6.1	6.3
S.D.	0.07	0.02	0.04	0.05	0.06	1.2	2.2	9.9	3.7	4.4
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 8 Clinical chemistry (females)

Sex: Female 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
RP3F01	0.20	0.13	0.15	0.16	0.17
RP3F02	0.11	0.16	0.18	0.20	0.12
RP3F03	0.15	0.03	0.05	0.07	0.13
RP3F04	0.07	0.05	0.05	0.06	0.08
Mean	0.13	0.09	0.11	0.12	0.13
S.D.	0.06	0.06	0.07	0.07	0.04
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

Mid TM5509 20 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
RP4F01	29	24	24	24	26	47	35	26	30	32
RP4F02	18	13	12	14	15	13	17	20	25	36
RP4F03	19	23	22	20	20	35	78	60	44	43
RP4F04	25	21	28	27	22	40	40	39	39	31
Mean	23	20	22	21	21	34	43	36	35	36
S.D.	5	5	7	6	5	15	26	18	9	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 8 Clinical chemistry (females)

Sex: Female 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
	RP4F01	851	1074	973	872	945	313	241	208	198
RP4F02	891	1113	1192	997	964	311	184	212	215	252
RP4F03	990	1399	1383	1235	1317	256	236	263	182	187
RP4F04	1636	1917	1798	1734	1788	234	237	276	258	227
Mean	1092	1376	1337	1210	1254	279	225	240	213	218
S.D.	367	389	350	381	395	40	27	35	33	28
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	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
RP4F01	104	88	113	134	141	49.8	41.2	37.2	35.3	34.9
RP4F02	105	91	97	136	166	31.5	27.4	25.9	24.7	27.2
RP4F03	102	78	82	86	107	47.9	41.7	40.7	37.1	39.2
RP4F04	240	113	221	191	122	58.6	52.6	49.6	47.6	46.8
Mean	138	93	128	137	134	47.0	40.7	38.4	36.2	37.0
S.D.	68	15	63	43	25	11.3	10.3	9.8	9.4	8.2
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	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
RP4F01	13	12	9	10	11	75	50	42	40	38
RP4F02	6	11	16	17	29	28	24	24	23	23
RP4F03	17	38	32	21	23	75	65	59	59	60
RP4F04	11	10	7	7	8	65	63	59	57	53
Mean	12	18	16	14	18	61	51	46	45	44
S.D.	5	14	11	6	10	22	19	17	17	16
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	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
RP4F01	87	80	94	102	123	0.14	0.10	0.08	0.10	0.07
RP4F02	103	76	67	74	75	0.29	0.22	0.11	0.15	0.10
RP4F03	100	82	86	77	83	0.19	0.15	0.09	0.09	0.11
RP4F04	90	62	75	67	80	0.16	0.18	0.11	0.11	0.11
Mean	95	75	81	80	90	0.20	0.16	0.10	0.11	0.10
S.D.	8	9	12	15	22	0.07	0.05	0.01	0.03	0.02
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	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
RP4F01	15.0	14.1	14.7	13.5	13.4	0.73	0.73	0.65	0.73	0.66
RP4F02	13.1	12.5	18.4	12.2	14.6	0.68	0.65	0.58	0.64	0.64
RP4F03	23.4	21.8	25.7	21.5	22.1	0.76	0.84	0.79	0.81	0.79
RP4F04	16.2	16.7	17.0	14.4	16.8	0.71	0.98	0.79	0.85	0.82
Mean	16.9	16.3	19.0	15.4	16.7	0.72	0.80	0.70	0.76	0.73
S.D.	4.5	4.1	4.8	4.2	3.9	0.03	0.14	0.11	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 8 Clinical chemistry (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 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
RP4F01	122	100	93	106	102	27	21	15	20	19
RP4F02	129	109	106	122	121	26	30	67	23	38
RP4F03	145	122	112	116	124	22	33	26	21	24
RP4F04	129	135	134	148	145	22	24	67	30	96
Mean	131	117	111	123	123	24	27	44	24	44
S.D.	10	15	17	18	18	3	5	27	5	35
N	4	4	4	4	4	4	4	4	4	4