

TK13152

Page: 46

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	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
RP4M01	134	112	112	105	106	40	49	80	71	55
RP4M02	133	127	115	124	123	14	18	18	16	15
RP4M03	160	148	145	162	156	22	45	50	22	31
RP4M04	129	102	104	103	104	26	38	51	40	35
Mean	139	122	119	124	122	26	38	50	37	34
S.D.	14	20	18	27	24	11	14	25	25	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 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 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
RP4M01	206	179	194	177	175	6.42	4.90	5.13	5.31	5.66
RP4M02	179	175	168	180	172	4.27	3.71	3.02	3.72	3.48
RP4M03	165	189	187	190	198	5.03	3.64	4.28	4.24	3.39
RP4M04	171	148	151	157	151	4.92	3.25	3.23	3.28	3.47
Mean	180	173	175	176	174	5.16	3.88	3.92	4.14	4.00
S.D.	18	18	19	14	19	0.90	0.71	0.98	0.87	1.11
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 48

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	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
RP4M01	10.75	9.64	10.09	9.66	9.38	159.1	152.3	157.7	152.6	149.2
RP4M02	9.41	9.43	9.38	9.60	9.38	149.6	148.6	149.2	149.5	149.0
RP4M03	9.57	9.72	9.22	9.54	9.97	152.8	150.3	150.4	149.7	150.5
RP4M04	10.31	9.43	9.60	9.70	9.69	155.8	149.8	150.1	150.7	150.0
Mean	10.01	9.56	9.57	9.63	9.61	154.3	150.3	151.9	150.6	149.7
S.D.	0.63	0.15	0.38	0.07	0.28	4.1	1.5	3.9	1.4	0.7
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male Week(s) Relative to Start Date

Mid TM5509 20 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
RP4M01	4.80	4.17	4.82	4.56	3.76	107.0	110.5	107.9	111.5	106.2
RP4M02	3.98	4.09	3.90	3.79	3.86	109.3	115.6	113.6	111.3	112.3
RP4M03	4.43	4.20	3.70	4.69	4.31	106.6	110.4	107.3	112.6	110.9
RP4M04	4.26	3.75	3.47	3.55	3.48	107.3	113.1	109.3	110.3	107.5
Mean	4.37	4.05	3.97	4.15	3.85	107.6	112.4	109.5	111.4	109.2
S.D.	0.34	0.21	0.59	0.56	0.34	1.2	2.5	2.8	0.9	2.9
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 50

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	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
RP4M01	8.61	8.29	8.58	8.11	8.15	4.73	4.30	4.46	4.31	4.25
RP4M02	7.66	7.39	7.39	7.36	7.48	4.44	4.13	3.99	4.07	4.17
RP4M03	7.94	7.89	7.95	8.01	8.15	4.27	4.22	4.13	4.15	4.25
RP4M04	8.01	7.55	7.67	7.61	7.71	4.41	4.05	3.96	3.96	4.04
Mean	8.06	7.78	7.90	7.77	7.87	4.46	4.18	4.14	4.12	4.18
S.D.	0.40	0.40	0.51	0.35	0.33	0.19	0.11	0.23	0.15	0.10
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	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
RP4M01	1.22	1.08	1.08	1.13	1.09	0.5	1.0	2.4	1.6	3.2
RP4M02	1.38	1.27	1.17	1.24	1.26	1.3	1.9	1.3	1.3	1.7
RP4M03	1.16	1.15	1.08	1.08	1.09	0.5	0.5	1.8	0.5	0.5
RP4M04	1.23	1.16	1.07	1.08	1.10	1.5	0.5	0.5	2.3	2.3
Mean	1.25	1.16	1.10	1.13	1.14	1.0	1.0	1.5	1.4	1.9
S.D.	0.09	0.08	0.05	0.07	0.08	0.5	0.7	0.8	0.7	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

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
RP4M01	0.04	0.04	0.03	0.05	0.04
RP4M02	0.29	0.29	0.34	0.40	0.34
RP4M03	0.03	0.11	0.10	0.07	0.07
RP4M04	0.14	0.15	0.16	0.18	0.17
Mean	0.13	0.15	0.16	0.18	0.16
S.D.	0.12	0.11	0.13	0.16	0.14
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-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
RP5M01	44	30	30	31	31	68	39	33	39	38
RP5M02	29	32	39	39	36	42	49	52	61	64
RP5M03	22	26	22	22	24	32	28	30	33	38
RP5M04	43	32	37	34	39	17	20	25	24	23
Mean	35	30	32	32	33	40	34	35	39	41
S.D.	11	3	8	7	7	21	13	12	16	17
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 54

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-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
RP5M01	1331	1627	1469	1414	1380	245	283	313	341	243
RP5M02	1474	1507	1432	1430	1215	327	367	415	404	270
RP5M03	1100	1244	1458	1212	1119	326	341	269	253	230
RP5M04	1773	1760	1930	1967	1952	564	290	324	294	317
Mean	1420	1535	1572	1506	1417	366	320	330	323	265
S.D.	282	220	239	323	373	138	40	61	65	38
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-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
RP5M01	109	332	132	192	159	70.5	61.9	48.7	48.4	45.9
RP5M02	122	95	101	100	102	80.6	69.9	54.0	57.4	50.2
RP5M03	80	79	108	110	108	52.6	46.9	40.5	42.4	39.3
RP5M04	112	114	129	119	137	50.7	47.7	42.9	46.5	44.7
Mean	106	155	118	130	127	63.6	56.6	46.5	48.7	45.0
S.D.	18	119	15	42	27	14.4	11.2	6.1	6.3	4.5
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 56

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-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
RP5M01	36	10	7	9	10	127	81	56	47	45
RP5M02	16	19	36	90	58	78	52	42	53	51
RP5M03	10	10	11	10	15	56	44	39	40	38
RP5M04	11	10	14	13	12	56	63	57	60	58
Mean	18	12	17	31	24	79	60	49	50	48
S.D.	12	5	13	40	23	33	16	9	9	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

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
RP5M01	68	60	64	66	73	0.12	0.14	0.14	0.07	0.07
RP5M02	97	75	101	103	101	0.28	0.20	0.10	0.07	0.07
RP5M03	96	68	81	82	89	0.29	0.27	0.12	0.12	0.13
RP5M04	79	59	57	66	80	0.11	0.09	0.07	0.06	0.08
Mean	85	66	76	79	86	0.20	0.18	0.11	0.08	0.09
S.D.	14	8	20	18	12	0.10	0.08	0.03	0.03	0.03
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 58

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-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
RP5M01	17.8	12.5	14.8	15.2	15.1	0.87	0.91	0.92	0.97	1.00
RP5M02	15.9	16.7	15.7	19.0	18.2	0.68	0.81	0.75	0.79	0.73
RP5M03	16.1	17.0	16.4	16.7	17.1	0.83	1.01	0.96	0.97	0.99
RP5M04	18.1	16.5	14.9	15.8	16.4	0.77	0.85	0.82	0.83	0.82
Mean	17.0	15.7	15.5	16.7	16.7	0.79	0.90	0.86	0.89	0.89
S.D.	1.1	2.1	0.8	1.7	1.3	0.08	0.09	0.10	0.09	0.13
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

Mid-High TM5509 80 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
RP5M01	78	84	66	73	77	18	33	27	23	28
RP5M02	150	128	112	125	111	13	31	52	61	86
RP5M03	126	111	106	112	101	15	24	37	27	31
RP5M04	131	120	100	120	112	20	30	44	48	38
Mean	121	111	96	108	100	17	30	40	40	46
S.D.	31	19	21	24	16	3	4	11	18	27
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 60

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-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
RP5M01	133	126	122	118	126	2.73	4.21	3.39	4.04	4.04
RP5M02	153	154	150	158	149	6.20	5.17	4.10	3.03	2.49
RP5M03	185	165	163	160	162	4.13	2.93	3.13	3.13	2.96
RP5M04	158	149	152	165	155	4.78	4.49	3.89	4.85	4.83
Mean	157	149	147	150	148	4.46	4.20	3.63	3.76	3.58
S.D.	21	16	17	22	16	1.44	0.94	0.45	0.86	1.06
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 7 Clinical chemistry (males)

Sex: Male 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
RP5M01	9.97	9.84	9.35	9.51	9.92	149.5	144.8	147.8	150.8	152.3
RP5M02	11.01	10.41	9.68	9.71	9.68	156.3	154.7	151.2	153.1	150.6
RP5M03	9.73	9.22	9.03	9.32	9.31	151.8	150.9	150.9	151.7	151.8
RP5M04	9.67	9.54	9.21	9.42	9.28	149.6	149.2	149.4	150.2	148.3
Mean	10.10	9.75	9.32	9.49	9.55	151.8	149.9	149.8	151.5	150.8
S.D.	0.62	0.51	0.27	0.17	0.31	3.2	4.1	1.6	1.3	1.8
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 62

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-High TM5509 80 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
RP5M01	3.86	3.94	3.51	3.59	3.82	107.9	109.5	110.6	114.1	112.4
RP5M02	4.59	4.87	4.33	4.38	4.43	107.9	116.2	111.7	109.2	111.3
RP5M03	3.98	3.58	3.61	3.45	3.27	108.1	113.2	110.5	112.1	111.4
RP5M04	3.59	4.12	3.73	3.83	3.79	103.9	111.2	109.1	108.2	108.9
Mean	4.01	4.13	3.80	3.81	3.83	107.0	112.5	110.5	110.9	111.0
S.D.	0.42	0.54	0.37	0.41	0.47	2.0	2.9	1.1	2.7	1.5
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

Mid-High TM5509 80 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
RP5M01	7.07	7.21	6.97	6.96	7.32	4.11	3.88	3.76	3.75	3.95
RP5M02	8.59	7.92	7.63	7.81	7.36	4.76	4.08	3.67	3.89	3.69
RP5M03	8.00	7.49	7.32	7.38	7.46	4.45	4.10	3.91	4.02	4.01
RP5M04	7.78	7.59	7.33	7.56	7.47	3.61	3.64	3.55	3.74	3.72
Mean	7.86	7.55	7.31	7.43	7.40	4.23	3.93	3.72	3.85	3.84
S.D.	0.63	0.29	0.27	0.36	0.07	0.49	0.21	0.15	0.13	0.16
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 64

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-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
RP5M01	1.39	1.17	1.17	1.17	1.17	16.9	4.1	2.9	2.0	1.8
RP5M02	1.24	1.06	0.93	0.99	1.01	3.4	0.5	1.9	2.8	3.0
RP5M03	1.25	1.21	1.15	1.20	1.16	5.0	1.4	11.2	2.0	4.1
RP5M04	0.87	0.92	0.94	0.98	0.99	0.5	1.9	1.6	1.4	1.8
Mean	1.19	1.09	1.05	1.08	1.08	6.5	2.0	4.4	2.1	2.7
S.D.	0.22	0.13	0.13	0.11	0.10	7.2	1.5	4.6	0.6	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

Mid-High TM5509 80 mg/kg/day	CRP (mg/dL)				
	-1	1	2	3	4
	RP5M01	0.05	0.03	0.07	0.06
RP5M02	0.03	0.07	0.08	0.04	0.03
RP5M03	0.17	0.16	0.27	0.20	0.24
RP5M04	0.29	0.24	0.39	0.35	0.36
Mean	0.14	0.13	0.20	0.16	0.17
S.D.	0.12	0.09	0.16	0.14	0.16
N	4	4	4	4	4