

TK13152

Page: 24

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	#Baso					#LUC				
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	0.03	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.01	0.02
RP2F02	0.04	0.02	0.03	0.02	0.03	0.05	0.03	0.05	0.03	0.06
RP2F03	0.05	0.02	0.03	0.04	0.02	0.04	0.03	0.04	0.04	0.02
RP2F04	0.03	0.01	0.02	0.02	0.03	0.02	0.03	0.03	0.03	0.03
Mean	0.04	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.03	0.03
S.D.	0.01	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.01	0.02
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	PT	PT	PT	PT	PT	APTT	APTT	APTT	APTT	APTT
	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
	-1	1	2	3	4	-1	1	2	3	4
RP2F01	10.1	10.2	10.3	10.3	9.9	24.4	25.4	24.4	25.4	22.8
RP2F02	9.4	9.7	9.9	9.6	9.9	23.9	23.8	23.7	24.4	23.4
RP2F03	10.5	10.5	10.4	10.4	10.8	21.3	22.0	19.5	21.0	21.3
RP2F04	10.7	10.7	10.6	10.7	10.2	26.5	26.6	25.7	25.4	24.0
Mean	10.2	10.3	10.3	10.3	10.2	24.0	24.5	23.3	24.1	22.9
S.D.	0.6	0.4	0.3	0.5	0.4	2.1	2.0	2.7	2.1	1.2
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low TM5509 2 mg/kg/day	Fib	Fib	Fib	Fib	Fib
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4
RP2F01	177.8	190.8	172.5	192.6	188.2
RP2F02	182.8	222.9	208.8	225.4	213.6
RP2F03	130.7	145.9	144.8	140.7	134.0
RP2F04	150.1	180.4	187.2	182.0	186.5
Mean	160.4	185.0	178.3	185.2	180.6
S.D.	24.4	31.7	26.9	34.9	33.4
N	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	RBC	RBC	RBC	RBC	RBC	HGB	HGB	HGB	HGB	HGB
	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	5.60	5.20	5.11	5.05	5.00	14.6	13.6	13.4	13.0	12.7
RP3F02	6.04	5.17	5.31	5.17	5.36	14.0	11.9	12.3	12.0	12.3
RP3F03	5.88	5.45	5.50	5.35	5.55	13.6	12.3	12.4	11.9	12.5
RP3F04	6.05	5.36	5.36	5.51	5.47	14.6	12.9	13.1	13.3	13.1
Mean	5.89	5.30	5.32	5.27	5.35	14.2	12.7	12.8	12.6	12.7
S.D.	0.21	0.13	0.16	0.20	0.24	0.5	0.7	0.5	0.7	0.3
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 28

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	HCT					MCV				
	HCT	HCT	HCT	HCT	HCT	MCV	MCV	MCV	MCV	MCV
	(%)	(%)	(%)	(%)	(%)	(fL)	(fL)	(fL)	(fL)	(fL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	45.8	41.7	41.2	40.7	41.3	81.8	80.3	80.5	80.6	82.6
RP3F02	48.4	40.2	42.0	41.7	42.5	80.2	77.8	79.0	80.6	79.4
RP3F03	44.0	40.0	40.9	40.2	43.0	74.8	73.5	74.2	75.2	77.4
RP3F04	48.0	42.3	41.0	43.8	43.2	79.4	78.9	76.4	79.5	78.9
Mean	46.6	41.1	41.3	41.6	42.5	79.1	77.6	77.5	79.0	79.6
S.D.	2.0	1.1	0.5	1.6	0.9	3.0	2.9	2.8	2.6	2.2
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	MCH	MCH	MCH	MCH	MCH	MCHC	MCHC	MCHC	MCHC	MCHC
	(pg)	(pg)	(pg)	(pg)	(pg)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	26.1	26.2	26.2	25.8	25.4	31.9	32.6	32.5	32.0	30.7
RP3F02	23.2	23.1	23.1	23.2	22.9	28.9	29.7	29.3	28.8	28.9
RP3F03	23.1	22.6	22.6	22.3	22.6	30.9	30.8	30.4	29.6	29.1
RP3F04	24.1	24.1	24.4	24.1	24.0	30.3	30.6	31.9	30.3	30.4
Mean	24.1	24.0	24.1	23.9	23.7	30.5	30.9	31.0	30.2	29.8
S.D.	1.4	1.6	1.6	1.5	1.3	1.3	1.2	1.4	1.4	0.9
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 30

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	%Retic	%Retic	%Retic	%Retic	%Retic	#Retic	#Retic	#Retic	#Retic	#Retic
	(%)	(%)	(%)	(%)	(%)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	1.2	1.8	1.5	1.7	2.6	66.5	93.4	79.2	87.3	131.7
RP3F02	1.2	2.6	3.6	2.3	2.4	74.7	134.7	192.6	118.7	125.9
RP3F03	1.1	0.5	0.9	0.9	1.5	61.9	27.5	50.9	48.3	81.2
RP3F04	0.9	1.9	1.9	2.6	2.4	53.9	101.6	103.1	140.7	132.6
Mean	1.1	1.7	2.0	1.9	2.2	64.3	89.3	106.5	98.8	117.9
S.D.	0.1	0.9	1.2	0.8	0.5	8.7	44.9	61.3	40.1	24.6
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	PLT	PLT	PLT	PLT	PLT	WBC	WBC	WBC	WBC	WBC
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	403	403	431	377	332	8.10	6.92	8.47	6.64	7.59
RP3F02	465	427	451	450	413	10.56	11.06	14.29	10.41	11.28
RP3F03	359	344	306	255	249	8.69	5.15	6.26	6.06	6.65
RP3F04	305	328	338	346	324	9.51	7.32	5.56	9.75	10.64
Mean	383	376	382	357	330	9.22	7.61	8.65	8.22	9.04
S.D.	68	47	70	81	67	1.07	2.48	3.96	2.18	2.27
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 32

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	%Neut					%Lymph				
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	36.3	39.9	40.8	43.4	36.5	59.6	55.6	54.6	53.1	59.5
RP3F02	30.1	27.6	47.8	38.8	34.5	59.6	61.0	43.7	50.5	55.0
RP3F03	49.5	21.2	31.6	48.7	22.4	44.8	72.9	62.8	47.2	72.0
RP3F04	54.0	34.8	26.0	60.9	39.6	41.3	60.3	68.4	34.1	54.4
Mean	42.5	30.9	36.6	48.0	33.3	51.3	62.5	57.4	46.2	60.2
S.D.	11.2	8.2	9.7	9.5	7.5	9.7	7.4	10.7	8.4	8.2
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	%Mono	%Mono	%Mono	%Mono	%Mono	%Eos	%Eos	%Eos	%Eos	%Eos
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	2.8	2.8	3.1	2.7	2.6	0.8	0.6	0.5	0.2	0.6
RP3F02	3.5	4.0	3.1	3.7	3.7	5.9	6.3	4.7	6.0	6.0
RP3F03	4.3	4.5	4.5	3.2	3.6	0.1	0.1	0.4	0.3	0.6
RP3F04	3.5	3.5	3.9	4.1	4.1	0.4	0.9	1.1	0.5	1.3
Mean	3.5	3.7	3.7	3.4	3.5	1.8	2.0	1.7	1.8	2.1
S.D.	0.6	0.7	0.7	0.6	0.6	2.7	2.9	2.0	2.8	2.6
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 34

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	%Baso	%Baso	%Baso	%Baso	%Baso	%LUC	%LUC	%LUC	%LUC	%LUC
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	0.2	0.5	0.4	0.2	0.2	0.4	0.6	0.6	0.4	0.5
RP3F02	0.4	0.4	0.3	0.4	0.3	0.4	0.6	0.4	0.5	0.5
RP3F03	0.6	0.4	0.3	0.3	0.4	0.8	0.9	0.4	0.4	1.0
RP3F04	0.3	0.2	0.2	0.2	0.3	0.5	0.3	0.4	0.2	0.3
Mean	0.4	0.4	0.3	0.3	0.3	0.5	0.6	0.5	0.4	0.6
S.D.	0.2	0.1	0.1	0.1	0.1	0.2	0.2	0.1	0.1	0.3
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	#Neut	#Neut	#Neut	#Neut	#Neut	#Lymph	#Lymph	#Lymph	#Lymph	#Lymph
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	2.94	2.76	3.46	2.88	2.77	4.83	3.84	4.63	3.52	4.52
RP3F02	3.18	3.06	6.84	4.04	3.89	6.30	6.75	6.24	5.26	6.20
RP3F03	4.30	1.09	1.98	2.95	1.49	3.89	3.75	3.93	2.86	4.79
RP3F04	5.14	2.55	1.44	5.94	4.21	3.93	4.41	3.80	3.32	5.78
Mean	3.89	2.37	3.43	3.95	3.09	4.74	4.69	4.65	3.74	5.32
S.D.	1.02	0.88	2.43	1.43	1.23	1.13	1.41	1.12	1.05	0.80
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 36

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	#Mono	#Mono	#Mono	#Mono	#Mono	#Eos	#Eos	#Eos	#Eos	#Eos
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	0.22	0.20	0.26	0.18	0.20	0.06	0.04	0.04	0.01	0.04
RP3F02	0.37	0.45	0.44	0.39	0.42	0.62	0.70	0.67	0.63	0.67
RP3F03	0.37	0.23	0.28	0.19	0.24	0.01	0.01	0.02	0.02	0.04
RP3F04	0.33	0.25	0.22	0.40	0.44	0.04	0.07	0.06	0.04	0.14
Mean	0.32	0.28	0.30	0.29	0.33	0.18	0.21	0.20	0.18	0.22
S.D.	0.07	0.11	0.10	0.12	0.12	0.29	0.33	0.32	0.30	0.30
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	#Baso	#Baso	#Baso	#Baso	#Baso	#LUC	#LUC	#LUC	#LUC	#LUC
	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)	(10 ³ /μL)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	0.02	0.04	0.03	0.01	0.02	0.03	0.04	0.05	0.03	0.04
RP3F02	0.04	0.04	0.04	0.04	0.03	0.05	0.07	0.06	0.06	0.06
RP3F03	0.05	0.02	0.02	0.02	0.02	0.07	0.04	0.02	0.02	0.06
RP3F04	0.03	0.02	0.01	0.02	0.03	0.05	0.02	0.02	0.02	0.04
Mean	0.04	0.03	0.03	0.02	0.03	0.05	0.04	0.04	0.03	0.05
S.D.	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.01
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 38

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	PT	PT	PT	PT	PT	APTT	APTT	APTT	APTT	APTT
	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
	-1	1	2	3	4	-1	1	2	3	4
RP3F01	9.8	10.1	10.2	10.1	10.3	22.3	23.8	22.4	22.6	22.7
RP3F02	9.5	9.3	9.3	9.3	9.6	25.6	25.4	24.9	26.0	25.7
RP3F03	9.6	9.9	10.2	10.4	9.9	20.7	21.8	20.9	21.3	21.3
RP3F04	9.8	9.3	9.6	9.6	9.4	23.6	24.1	23.7	23.7	23.3
Mean	9.7	9.7	9.8	9.9	9.8	23.1	23.8	23.0	23.4	23.3
S.D.	0.1	0.4	0.5	0.5	0.4	2.1	1.5	1.7	2.0	1.8
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Low-Mid TM5509 6 mg/kg/day	Fib	Fib	Fib	Fib	Fib
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4
RP3F01	171.5	172.5	166.7	166.7	180.0
RP3F02	153.7	177.1	177.1	185.4	171.0
RP3F03	156.2	151.4	144.8	146.9	176.9
RP3F04	182.8	236.1	202.4	208.8	205.1
Mean	166.1	184.3	172.8	177.0	183.3
S.D.	13.7	36.3	23.9	26.4	15.0
N	4	4	4	4	4

TK13152

Page: 40

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	RBC	RBC	RBC	RBC	RBC	HGB	HGB	HGB	HGB	HGB
	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(10 ⁶ /μL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	6.20	5.61	5.62	5.38	5.47	15.1	13.6	13.5	13.2	13.3
RP4F02	5.72	5.22	5.05	5.20	5.42	13.8	12.7	12.2	12.6	13.1
RP4F03	5.59	5.13	5.29	5.13	5.52	13.5	12.2	12.3	12.1	12.9
RP4F04	6.31	5.91	5.85	5.70	5.80	13.9	13.1	13.2	12.6	13.0
Mean	5.96	5.47	5.45	5.35	5.55	14.1	12.9	12.8	12.6	13.1
S.D.	0.35	0.36	0.35	0.25	0.17	0.7	0.6	0.6	0.4	0.2
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	HCT	HCT	HCT	HCT	HCT	MCV	MCV	MCV	MCV	MCV
	(%)	(%)	(%)	(%)	(%)	(fL)	(fL)	(fL)	(fL)	(fL)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	48.3	43.0	43.5	41.7	43.5	77.8	76.5	77.3	77.6	79.6
RP4F02	49.6	42.4	41.4	42.7	46.1	86.7	81.1	81.8	82.2	85.0
RP4F03	44.7	40.0	41.5	40.7	45.0	80.0	78.0	78.4	79.3	81.5
RP4F04	47.1	42.7	42.3	42.6	44.5	74.6	72.1	72.3	74.7	76.6
Mean	47.4	42.0	42.2	41.9	44.8	79.8	76.9	77.5	78.5	80.7
S.D.	2.1	1.4	1.0	0.9	1.1	5.1	3.7	3.9	3.1	3.5
N	4	4	4	4	4	4	4	4	4	4

TK13152

Page: 42

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	MCH					MCHC				
	(pg)	(pg)	(pg)	(pg)	(pg)	(g/dL)	(g/dL)	(g/dL)	(g/dL)	(g/dL)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	24.4	24.2	24.0	24.5	24.2	31.3	31.6	31.0	31.6	30.5
RP4F02	24.1	24.4	24.1	24.2	24.1	27.8	30.1	29.5	29.5	28.4
RP4F03	24.1	23.8	23.3	23.6	23.4	30.1	30.5	29.8	29.7	28.7
RP4F04	22.1	22.1	22.5	22.1	22.3	29.6	30.7	31.2	29.5	29.1
Mean	23.7	23.6	23.5	23.6	23.5	29.7	30.7	30.4	30.1	29.2
S.D.	1.1	1.0	0.7	1.1	0.9	1.5	0.6	0.9	1.0	0.9
N	4	4	4	4	4	4	4	4	4	4

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Mid TM5509 20 mg/kg/day	%Retic	%Retic	%Retic	%Retic	%Retic	#Retic	#Retic	#Retic	#Retic	#Retic
	(%)	(%)	(%)	(%)	(%)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)	(10 ⁹ /L)
	-1	1	2	3	4	-1	1	2	3	4
RP4F01	0.5	1.3	1.8	1.4	2.0	31.4	71.2	103.7	75.9	108.8
RP4F02	1.6	1.3	2.2	2.0	3.2	92.7	70.5	109.2	102.2	172.0
RP4F03	0.8	1.4	2.1	2.6	2.4	43.0	70.3	112.1	132.3	133.3
RP4F04	1.3	0.9	1.1	2.2	1.8	81.4	51.4	64.0	126.2	101.7
Mean	1.1	1.2	1.8	2.1	2.4	62.1	65.9	97.3	109.2	129.0
S.D.	0.5	0.2	0.5	0.5	0.6	29.5	9.6	22.4	25.7	31.7
N	4	4	4	4	4	4	4	4	4	4