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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 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
RP5M01	0.49	0.30	0.29	0.24	0.24	0.21	0.07	0.14	0.29	0.25
RP5M02	0.30	0.24	0.26	0.17	0.23	0.06	0.03	0.05	0.04	0.04
RP5M03	0.25	0.13	0.20	0.10	0.10	0.04	0.01	0.02	0.01	0.02
RP5M04	0.29	0.24	0.29	0.19	0.34	0.16	0.07	0.14	0.05	0.10
Mean	0.33	0.23	0.26	0.18	0.23	0.12	0.05	0.09	0.10	0.10
S.D.	0.11	0.07	0.04	0.06	0.10	0.08	0.03	0.06	0.13	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 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 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
RP5M01	0.04	0.01	0.02	0.02	0.03	0.10	0.04	0.07	0.09	0.07
RP5M02	0.05	0.03	0.04	0.03	0.02	0.07	0.03	0.07	0.04	0.06
RP5M03	0.08	0.02	0.04	0.02	0.02	0.08	0.02	0.02	0.02	0.02
RP5M04	0.04	0.02	0.03	0.02	0.03	0.05	0.03	0.04	0.04	0.06
Mean	0.05	0.02	0.03	0.02	0.03	0.08	0.03	0.05	0.05	0.05
S.D.	0.02	0.01	0.01	0.00	0.01	0.02	0.01	0.02	0.03	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 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 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
RP5M01	10.3	10.0	9.9	10.5	10.4	22.2	22.6	21.4	21.8	22.4
RP5M02	9.7	10.1	9.5	10.0	10.2	22.9	24.5	24.2	24.2	24.3
RP5M03	11.0	11.7	11.9	12.2	12.0	22.9	21.4	24.1	24.6	24.5
RP5M04	10.1	10.4	10.5	10.8	10.8	27.1	26.4	25.2	26.6	26.0
Mean	10.3	10.6	10.5	10.9	10.9	23.8	23.7	23.7	24.3	24.3
S.D.	0.5	0.8	1.1	0.9	0.8	2.2	2.2	1.6	2.0	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 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

Mid-High TM5509 80 mg/kg/day	Fib	Fib	Fib	Fib	Fib
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4
RP5M01	111.3	165.3	140.7	127.1	139.5
RP5M02	206.1	228.0	247.9	213.3	209.3
RP5M03	193.8	194.5	172.5	166.7	180.0
RP5M04	255.0	238.9	206.6	215.6	215.9
Mean	191.6	206.7	191.9	180.7	186.2
S.D.	59.7	33.4	46.0	42.2	34.8
N	4	4	4	4	4

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	RBC					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
RP6M01	5.56	4.87	4.80	4.62	4.83	12.9	11.5	11.4	11.4	12.0
RP6M02	5.53	5.54	4.48	.	.	13.8	13.7	10.9	.	.
RP6M03	5.86	5.93	5.85	5.15	5.02	14.8	14.9	14.7	13.1	12.4
RP6M04	5.34	4.96	5.05	5.04	4.90	13.8	12.5	12.6	12.8	12.3
Mean	5.57	5.33	5.05	4.94	4.92	13.8	13.2	12.4	12.4	12.2
S.D.	0.22	0.50	0.59	0.28	0.10	0.8	1.5	1.7	0.9	0.2
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	41.3	35.6	36.0	36.0	37.3	74.3	73.2	74.9	77.8	77.1
RP6M02	43.5	42.2	32.3	.	.	78.7	76.2	72.1	.	.
RP6M03	47.2	47.5	46.0	40.3	39.7	80.6	80.0	78.6	78.3	79.1
RP6M04	43.6	41.6	42.0	40.1	40.5	81.6	83.9	83.1	79.5	82.7
Mean	43.9	41.7	39.1	38.8	39.2	78.8	78.3	77.2	78.5	79.6
S.D.	2.4	4.9	6.1	2.4	1.7	3.2	4.6	4.8	0.9	2.8
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	23.2	23.5	23.8	24.6	24.8	31.2	32.1	31.8	31.6	32.2
RP6M02	24.9	24.6	24.4	.	.	31.7	32.4	33.9	.	.
RP6M03	25.2	25.1	25.1	25.3	24.6	31.3	31.4	31.9	32.4	31.1
RP6M04	25.8	25.2	25.0	25.4	25.0	31.6	30.1	30.0	31.9	30.3
Mean	24.8	24.6	24.6	25.1	24.8	31.5	31.5	31.9	32.0	31.2
S.D.	1.1	0.8	0.6	0.4	0.2	0.2	1.0	1.6	0.4	1.0
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	1.4	1.8	2.5	3.7	3.7	77.1	85.4	119.9	173.1	178.3
RP6M02	0.9	1.6	3.4	.	.	48.0	89.2	150.3	.	.
RP6M03	1.7	1.6	1.7	2.4	3.0	101.0	96.7	98.8	123.5	151.8
RP6M04	1.1	2.8	2.0	2.4	3.0	59.8	138.6	102.1	120.3	147.1
Mean	1.3	2.0	2.4	2.8	3.2	71.5	102.5	117.8	139.0	159.1
S.D.	0.4	0.6	0.7	0.8	0.4	23.0	24.5	23.6	29.6	16.8
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 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	PLT					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
RP6M01	505	437	505	496	605	7.23	4.94	7.38	4.75	6.00
RP6M02	396	426	654	.	.	6.50	3.67	7.63	.	.
RP6M03	323	356	498	458	436	8.96	9.62	8.78	11.03	9.75
RP6M04	341	333	476	391	409	10.14	10.21	11.97	17.14	14.19
Mean	391	388	533	448	483	8.21	7.11	8.94	10.97	9.98
S.D.	82	51	81	53	106	1.65	3.29	2.11	6.20	4.10
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	%Neut	%Neut	%Neut	%Neut	%Neut	%Lymph	%Lymph	%Lymph	%Lymph	%Lymph
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP6M01	20.3	54.4	59.0	48.3	57.0	74.9	41.8	36.6	47.7	40.1
RP6M02	15.4	42.2	73.0	.	.	80.7	52.8	22.3	.	.
RP6M03	23.0	50.3	33.9	51.9	38.6	72.0	44.5	59.1	43.4	53.2
RP6M04	34.7	53.0	56.7	70.5	69.6	62.8	44.6	40.5	27.1	28.0
Mean	23.4	50.0	55.7	56.9	55.1	72.6	45.9	39.6	39.4	40.4
S.D.	8.2	5.5	16.2	11.9	15.6	7.5	4.8	15.2	10.9	12.6
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	%Mono	%Mono	%Mono	%Mono	%Mono	%Eos	%Eos	%Eos	%Eos	%Eos
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP6M01	3.1	2.9	3.6	2.9	2.2	0.9	0.2	0.2	0.3	0.1
RP6M02	2.9	3.4	3.4	.	.	0.3	0.5	0.3	.	.
RP6M03	3.5	4.4	5.7	3.8	6.4	0.7	0.1	0.2	0.3	0.6
RP6M04	1.5	1.6	2.1	1.6	1.6	0.2	0.2	0.2	0.2	0.3
Mean	2.8	3.1	3.7	2.8	3.4	0.5	0.3	0.2	0.3	0.3
S.D.	0.9	1.2	1.5	1.1	2.6	0.3	0.2	0.1	0.1	0.3
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	%Baso	%Baso	%Baso	%Baso	%Baso	%LUC	%LUC	%LUC	%LUC	%LUC
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
	-1	1	2	3	4	-1	1	2	3	4
RP6M01	0.3	0.2	0.2	0.3	0.2	0.5	0.5	0.4	0.4	0.5
RP6M02	0.2	0.4	0.2	.	.	0.4	0.6	0.8	.	.
RP6M03	0.4	0.4	0.4	0.2	0.6	0.4	0.3	0.7	0.3	0.6
RP6M04	0.4	0.4	0.3	0.4	0.3	0.5	0.2	0.2	0.3	0.2
Mean	0.3	0.4	0.3	0.3	0.4	0.5	0.4	0.5	0.3	0.4
S.D.	0.1	0.1	0.1	0.1	0.2	0.1	0.2	0.3	0.1	0.2
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	1.47	2.69	4.35	2.29	3.42	5.41	2.06	2.70	2.26	2.41
RP6M02	1.00	1.55	5.57	.	.	5.24	1.94	1.70	.	.
RP6M03	2.06	4.84	2.98	5.73	3.76	6.45	4.28	5.19	4.78	5.19
RP6M04	3.52	5.41	6.79	12.09	9.87	6.36	4.55	4.85	4.65	3.98
Mean	2.01	3.62	4.92	6.70	5.68	5.87	3.21	3.61	3.90	3.86
S.D.	1.09	1.81	1.63	4.97	3.63	0.63	1.40	1.68	1.42	1.39
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	0.23	0.14	0.27	0.14	0.13	0.06	0.01	0.01	0.01	0.01
RP6M02	0.19	0.13	0.26	.	.	0.02	0.02	0.02	.	.
RP6M03	0.31	0.43	0.50	0.42	0.63	0.06	0.01	0.02	0.03	0.06
RP6M04	0.15	0.17	0.25	0.27	0.23	0.02	0.02	0.02	0.03	0.05
Mean	0.22	0.22	0.32	0.28	0.33	0.04	0.02	0.02	0.02	0.04
S.D.	0.07	0.14	0.12	0.14	0.26	0.02	0.01	0.00	0.01	0.03
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 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	0.02	0.01	0.02	0.01	0.01	0.04	0.03	0.03	0.02	0.03
RP6M02	0.02	0.01	0.01	.	.	0.02	0.02	0.06	.	.
RP6M03	0.03	0.04	0.03	0.02	0.06	0.04	0.02	0.06	0.04	0.06
RP6M04	0.04	0.04	0.03	0.06	0.04	0.05	0.02	0.03	0.04	0.02
Mean	0.03	0.03	0.02	0.03	0.04	0.04	0.02	0.05	0.03	0.04
S.D.	0.01	0.02	0.01	0.03	0.03	0.01	0.00	0.02	0.01	0.02
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 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
RP6M01	10.0	13.8	14.6	13.9	20.9	22.3	25.9	26.8	26.2	29.9
RP6M02	9.8	11.6	25.2	.	.	22.4	26.1	43.7	.	.
RP6M03	9.3	13.6	16.1	11.4	10.5	22.0	29.2	31.7	27.0	26.3
RP6M04	10.0	12.0	11.1	13.8	14.3	27.5	31.4	30.4	34.5	34.8
Mean	9.8	12.8	16.8	13.0	15.2	23.6	28.2	33.2	29.2	30.3
S.D.	0.3	1.1	6.0	1.4	5.3	2.6	2.6	7.3	4.6	4.3
N	4	4	4	3	3	4	4	4	3	3

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

Appendix 5 Hematology (males)

Sex: Male Week(s) Relative to Start Date

High TM5509 300 mg/kg/day	Fib	Fib	Fib	Fib	Fib
	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)	(mg/dL)
	-1	1	2	3	4
RP6M01	134.3	155.0	137.7	158.7	128.1
RP6M02	170.0	247.9	276.9	.	.
RP6M03	182.8	251.0	213.3	215.6	296.1
RP6M04	168.5	276.9	206.6	160.0	181.6
Mean	163.9	232.7	208.6	178.1	201.9
S.D.	20.8	53.4	56.9	32.5	85.8
N	4	4	4	3	3

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

Appendix 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1F01	5.97	5.72	5.79	5.66	5.88	13.8	13.0	13.2	12.9	13.3
RP1F02	5.50	5.28	5.57	5.40	5.51	13.1	12.6	13.3	12.9	13.3
RP1F03	5.59	5.18	5.50	5.42	5.66	14.1	13.1	13.8	13.7	14.0
RP1F04	6.05	5.47	5.71	5.51	5.61	13.2	12.3	12.7	12.3	12.4
Mean	5.78	5.41	5.64	5.50	5.67	13.6	12.8	13.3	13.0	13.3
S.D.	0.27	0.24	0.13	0.12	0.16	0.5	0.4	0.5	0.6	0.7
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 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1F01	45.7	44.4	44.7	45.2	47.2	76.6	77.8	77.2	79.9	80.4
RP1F02	42.1	42.0	44.0	43.5	44.9	76.6	79.5	78.9	80.7	81.4
RP1F03	47.3	44.8	46.8	48.1	50.1	84.7	86.4	85.1	88.7	88.5
RP1F04	45.9	42.6	43.0	42.7	44.0	75.8	77.8	75.3	77.6	78.4
Mean	45.3	43.5	44.6	44.9	46.6	78.4	80.4	79.1	81.7	82.2
S.D.	2.2	1.4	1.6	2.4	2.7	4.2	4.1	4.2	4.8	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 6 Hematology (females)

Sex: Female Week(s) Relative to Start Date

Control 0.5%CMC-Na	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
RP1F01	23.1	22.7	22.8	22.9	22.7	30.1	29.1	29.5	28.6	28.2
RP1F02	23.8	23.9	23.8	23.9	24.1	31.1	30.1	30.2	29.6	29.6
RP1F03	25.2	25.2	25.1	25.2	24.7	29.8	29.2	29.5	28.4	27.9
RP1F04	21.9	22.4	22.2	22.3	22.0	28.9	28.8	29.4	28.7	28.1
Mean	23.5	23.6	23.5	23.6	23.4	30.0	29.3	29.7	28.8	28.5
S.D.	1.4	1.3	1.3	1.3	1.2	0.9	0.6	0.4	0.5	0.8
N	4	4	4	4	4	4	4	4	4	4