SUPPLEMENTAL MATERIAL

List of investigators and study sites

List of Investigators	Site Number	Facility	Name of institutional review board
Shingo, Nakayamada	1001	Hospital of the University of Occupational and Environmental Health, Japan	Hospital of the University of Occupational and Environmental Health, Japan Institutional Review Board
Masanari, Kodera	1002	Japan Community Health Care Organization Chukyo Hospital	Japan Community Health Care Organization Chukyo Hospital Institutional Review Board
Yoichiro, Haji	1003	Daido Clinic	Daido Hospital Institutional Review Board
Kensuke, Oryoji (20May2022-25May2023)	1004	Matsuyama Red Cross Hospital	Institutional Review Board of Matsuyama Red Cross Hospital
Shinichi, Mizuki (26May2023-)			
Masaru Kato	1005	Hokkaido University Hospital	Hokkaido University Hospital Institutional Review Board
Tomonori, Ishii	1006	Tohoku University Hospital	Tohoku University Hospital Institutional Review Board
Naoto, Yokogawa	1007	Tokyo Metropolitan Tama Medical Center	Tokyo Metropolitan Hospital Organization Tokyo Metropolitan Tama Medical Center Institutional Review Board
Tomoya, Miyamura	1008	National Hospital Organization Kyushu Medical Center	National Hospital Organization Kyushu Medical Center Institutional Review Board
Yasuhiro, Kato	1009	Osaka University Hospital	Osaka University Hospital Institutional Review Board
Futoshi, Iwata	1010	St. Luke’s International Hospital	St. Luke's International Hospital Institutional Review Board
Hiroshi, Kaneko	1011	National Center for Global Health and Medicine	Certified Review Board of National Center for Global Health and Medicine
Kentaro Minowa	1012	Juntendo University Hospital	Juntendo university Hospital institutional review board

This study was approved by the Institutional Review Board for each study site. The numbers of the approval are not applicable on these study sites.

Supplemental Table S1 List of interferon gene signature evaluated in this study

Ensembl Gene ID	Gene Symbol
ENSG00000160710	ADAR
ENSG00000163568	AIM2
ENSG00000152766	ANKRD22
ENSG00000128383	APOBEC3A
ENSG00000100342	APOL1
ENSG00000140750	ARHGAP17
ENSG00000168062	BATF2
ENSG00000198604	BAZ1A
ENSG00000282851	BISPR
ENSG00000106605	BLVRA
ENSG00000130303	BST2
ENSG00000197536	C5orf56
ENSG00000163823	CCR1
ENSG00000086065	CHMP5
ENSG00000134326	CMPK2
ENSG00000137200	CMTR1
ENSG00000173198	CYSLTR1
ENSG00000107201	DDX58
ENSG00000137628	DDX60
ENSG00000181381	DDX60L
ENSG00000108771	DHX58
ENSG00000175550	DRAP1
ENSG00000163840	DTX3L
ENSG00000055332	EIF2AK2
ENSG00000133106	EPSTI1
ENSG00000010030	ETV7
ENSG00000116663	FBXO6
ENSG00000198019	FCGR1B
ENSG00000117228	GBP1
ENSG00000130589	HELZ2
ENSG00000138646	HERC5
ENSG00000138642	HERC6
ENSG00000163666	HESX1

Ensembl Gene ID	Gene Symbol
ENSG00000196684	HSH2D
ENSG00000163565	IFI16
ENSG00000165949	IFI27
ENSG00000068079	IFI35
ENSG00000137965	IFI44
ENSG00000137959	IFI44L
ENSG00000126709	IFI6
ENSG00000115267	IFIH1
ENSG00000185745	IFIT1
ENSG00000119922	IFIT2
ENSG00000119917	IFIT3
ENSG00000152778	IFIT5
ENSG00000185885	IFITM1
ENSG00000185201	IFITM2
ENSG00000142089	IFITM3
ENSG00000136689	IL1RN
ENSG00000185507	IRF7
ENSG00000213928	IRF9
ENSG00000187608	ISG15
ENSG00000172183	ISG20
ENSG00000165185	KIAA1958
ENSG00000127528	KLF2
ENSG00000130487	KLHDC7B
ENSG00000117009	KMO
ENSG00000078081	LAMP3
ENSG00000002549	LAP3
ENSG00000108679	LGALS3BP
ENSG00000168961	LGALS9
ENSG00000205837	LINC00487
ENSG00000160932	LY6E
ENSG00000140280	LYSMD2
ENSG00000157601	MX1
ENSG00000183486	MX2

Ensembl Gene ID	Gene Symbol
ENSG00000102921	N4BP1
ENSG00000124357	NAGK
ENSG00000111912	NCOA7
ENSG00000123609	NMI
ENSG00000089127	OAS1
ENSG00000111335	OAS2
ENSG00000111331	OAS3
ENSG00000135114	OASL
ENSG00000177989	ODF3B
ENSG00000115155	OTOF
ENSG00000178685	PARP10
ENSG00000059378	PARP12
ENSG00000173193	PARP14
ENSG00000138496	PARP9
ENSG00000136147	PHF11
ENSG00000145287	PLAC8
ENSG00000188313	PLSCR1
ENSG00000140464	PML
ENSG00000138035	PNPT1
ENSG00000105287	PRKD2
ENSG00000240065	PSMB9
ENSG00000092010	PSME1
ENSG00000100911	PSME2
ENSG00000266094	RASSF5
ENSG00000125826	RBCK1
ENSG00000143344	RGL1
ENSG00000134321	RSAD2
ENSG00000136514	RTP4
ENSG00000205413	SAMD9
ENSG00000177409	SAMD9L
ENSG00000284194	SCO2
ENSG00000149131	SERPING1
ENSG00000130813	SHFL

Ensembl Gene ID	Gene Symbol
ENSG00000164054	SHISA5
ENSG00000088827	SIGLEC1
ENSG00000135899	SP110
ENSG00000079263	SP140
ENSG00000196141	SPATS2L
ENSG00000115415	STAT1
ENSG00000170581	STAT2
ENSG00000168394	TAP1
ENSG00000196116	TDRD7
ENSG00000196664	TLR7
ENSG00000121858	TNFSF10
ENSG00000102524	TNFSF13B
ENSG00000136816	TOR1B
ENSG00000135148	TRAFD1
ENSG00000168016	TRANK1
ENSG00000132109	TRIM21
ENSG00000132274	TRIM22
ENSG00000121236	TRIM6
ENSG00000185880	TRIM69
ENSG00000025708	TYMP
ENSG00000156587	UBE2L6
ENSG00000184979	USP18
ENSG00000028116	VRK2
ENSG00000132530	XAF1
ENSG00000124256	ZBP1
ENSG00000105939	ZC3HAV1
ENSG00000141664	ZCCHC2
ENSG00000124201	ZNFX1

Supplemental Table S2 Mean (SD) percent change from baseline for each IGS at Week12

Gene Symbol	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
ADAR	6.631 (17.7196)	3.788 (43.7878)	-19.790 (30.2323)
AIM2	20.101 (36.4557)	32.826 (62.7625)	-18.679 (40.6946)
ANKRD22	17.456 (50.6162)	42.925 (68.8807)	26.035 (105.8585)
APOBEC3A	21.636 (36.2966)	-12.648 (48.4292)	-25.186 (52.4877)
APOL1	-3.934 (22.2349)	4.400 (46.8660)	-31.771 (24.5704)
ARHGAP17	6.606 (38.9281)	8.816 (45.4694)	-15.030 (33.2243)
BATF2	17.288 (62.0746)	-11.447 (65.1569)	-35.605 (70.1714)
BAZ1A	-0.421 (17.9550)	37.230 (46.7781)	21.057 (32.8672)
BISPR	24.022 (23.3060)	-41.287 (33.1931)	-36.816 (32.3473)
BLVRA	16.745 (33.7612)	-51.066 (25.3963)	-40.369 (26.0069)
BST2	17.671 (23.9812)	-41.165 (33.0467)	-53.275 (17.1502)
C5orf56	12.763 (28.4116)	1.560 (49.2481)	-27.874 (24.9438)
CCR1	8.141 (22.2527)	-41.282 (30.8854)	-52.675 (23.7220)
CHMP5	39.035 (46.2761)	-0.956 (73.6555)	-29.230 (36.7665)
CMPK2	58.787 (113.1709)	-59.075 (61.0848)	-80.693 (27.0592)
CMTR1	2.217 (17.5672)	-35.388 (30.3158)	-43.371 (17.8975)
CYSLTR1	19.453 (19.3655)	-4.760 (35.4830)	-36.403 (26.6787)
DDX58	14.361 (30.2349)	-29.377 (56.9362)	-43.849 (37.0803)
DDX60	25.612 (79.2378)	-53.230 (48.0923)	-66.767 (25.5314)
DDX60L	10.890 (18.3998)	-0.300 (58.9919)	-27.515 (42.5970)
DHX58	19.311 (42.4193)	-50.687 (50.4445)	-63.225 (23.9804)
DRAP1	7.311 (22.6291)	-19.979 (30.5517)	-40.314 (14.9702)
DTX3L	9.176 (15.4228)	-12.844 (32.5213)	-32.769 (23.2850)
EIF2AK2	25.127 (36.5537)	-40.794 (49.7523)	-54.307 (43.9799)
EPSTI1	42.669 (111.2747)	-55.727 (52.5601)	-69.869 (22.0689)
ETV7	8.644 (48.9638)	-26.308 (51.3666)	-47.752 (48.8921)
FBXO6	8.366 (24.5664)	-26.324 (29.0436)	-45.443 (26.4432)
FCGR1B	26.872 (58.7268)	65.427 (73.3871)	36.383 (119.3358)
GBP1	18.725 (39.8430)	-21.286 (47.4610)	-41.436 (33.3822)
HELZ2	10.033 (24.1189)	-31.268 (49.7941)	-48.164 (30.7095)
HERC5	33.004 (82.1430)	-40.742 (86.1107)	-72.245 (32.7781)
HERC6	16.029 (49.7051)	-60.526 (37.2956)	-68.114 (27.4332)
HESX1	31.430 (80.6653)	-73.594 (31.6283)	-86.131 (22.2527)

Gene Symbol	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
HSH2D	15.350 (24.0680)	-10.486 (51.4929)	-26.606 (44.0033)
IFI16	7.360 (17.8017)	-9.218 (44.9085)	-26.661 (31.8013)
IFI27	801.943 (2401.6551)	-94.531 (4.6051)	-71.682 (76.7512)
IFI35	18.455 (28.9240)	-32.196 (48.8292)	-55.885 (20.3163)
IFI44	58.373 (125.4265)	-64.693 (49.0628)	-77.303 (28.9327)
IFI44L	90.354 (239.3653)	-73.918 (40.9222)	-81.728 (33.8650)
IFI6	32.397 (43.6392)	-43.701 (77.1802)	-72.671 (29.9727)
IFIH1	19.042 (38.0529)	-45.080 (37.4962)	-55.737 (23.7398)
IFIT1	48.438 (80.7208)	-43.623 (88.5055)	-76.455 (39.4155)
IFIT2	29.609 (46.9090)	-32.308 (71.4207)	-54.166 (53.1133)
IFIT3	41.471 (72.7251)	-37.923 (79.3497)	-66.161 (45.9052)
IFIT5	24.449 (30.1389)	-37.995 (68.5305)	-59.974 (32.1354)
IFITM1	12.568 (28.7817)	-14.671 (58.5806)	-41.608 (26.5534)
IFITM2	13.722 (45.8862)	65.152 (73.0890)	-0.864 (44.5569)
IFITM3	15.917 (41.7243)	4.985 (75.9127)	-41.670 (32.9008)
IL1RN	10.624 (27.1833)	-10.599 (53.7216)	-31.991 (36.6761)
IRF7	17.252 (29.4464)	-50.373 (38.6746)	-58.184 (29.6506)
IRF9	3.560 (13.3204)	-3.312 (42.0878)	-33.074 (17.2595)
ISG15	49.147 (92.3495)	-53.507 (67.6979)	-85.624 (18.5411)
ISG20	7.481 (24.0030)	13.918 (55.6759)	-31.255 (24.5743)
KIAA1958	13.527 (23.0633)	-47.602 (25.7536)	-49.283 (31.2475)
KLF2	1.198 (20.4372)	16.085 (24.7895)	3.032 (16.4008)
KLHDC7B	31.135 (99.6856)	-69.625 (19.7848)	-64.728 (38.0027)
KMO	8.654 (39.9395)	-30.522 (28.0824)	-11.404 (31.0517)
LAMP3	4.262 (66.8047)	-40.176 (82.7888)	-71.084 (17.0738)
LAP3	17.619 (27.8000)	-53.688 (24.1515)	-53.025 (25.0913)
LGALS3BP	-7.563 (20.5879)	-59.154 (15.4861)	-65.965 (18.2341)
LGALS9	12.763 (16.7663)	-36.644 (28.4018)	-36.960 (18.6334)
LINC00487	30.437 (73.8612)	-70.435 (41.3770)	-90.345 (14.1573)
LY6E	78.372 (201.7218)	-60.017 (61.0589)	-86.911 (14.2909)
LYSMD2	16.875 (21.7297)	10.203 (58.8860)	-27.705 (19.0866)
MX1	25.811 (69.9133)	-58.294 (55.9666)	-74.926 (32.2853)
MX2	13.284 (18.3889)	-10.711 (57.9542)	-28.034 (49.7251)
N4BP1	2.008 (11.3412)	48.110 (42.9674)	15.342 (30.2513)

Gene Symbol	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
NAGK	12.921 (15.9570)	-14.154 (20.5629)	-25.435 (23.1437)
NCOA7	12.263 (23.7210)	-21.701 (13.8080)	-24.612 (12.6748)
NMI	20.159 (22.1666)	15.608 (47.0092)	-10.688 (41.2578)
OAS1	67.289 (153.7253)	-60.592 (54.8040)	-76.050 (31.2300)
OAS2	51.465 (138.5131)	-59.427 (51.8581)	-74.259 (27.8742)
OAS3	72.473 (178.3071)	-55.339 (67.2478)	-78.521 (30.5349)
OASL	40.018 (62.8736)	-38.931 (71.9035)	-65.921 (49.5261)
ODF3B	0.303 (21.5859)	-33.794 (39.9616)	-39.163 (29.0420)
OTOF	193.169 (555.8496)	-89.754 (14.8489)	-77.117 (56.4388)
PARP10	4.522 (19.7853)	-34.506 (35.2744)	-44.449 (23.4168)
PARP12	19.376 (37.4004)	-44.918 (43.2701)	-56.790 (22.9286)
PARP14	12.652 (30.5853)	-27.529 (39.2058)	-38.515 (30.3318)
PARP9	7.769 (16.6404)	-18.802 (41.1671)	-36.458 (35.9599)
PHF11	10.537 (16.1336)	-25.905 (32.4907)	-37.815 (21.8334)
PLAC8	3.972 (27.0533)	-30.649 (21.0603)	-28.205 (19.0074)
PLSCR1	11.786 (26.3625)	-37.671 (45.5996)	-45.302 (45.5631)
PML	8.788 (28.1304)	-28.016 (36.1026)	-37.154 (30.6970)
PNPT1	29.035 (31.4807)	-50.712 (31.3598)	-50.890 (18.6845)
PRKD2	-3.509 (17.9489)	30.458 (53.8902)	-13.912 (24.6736)
PSMB9	5.959 (24.0234)	7.341 (38.4598)	-20.753 (28.8982)
PSME1	6.232 (19.3847)	14.425 (34.1968)	-10.215 (17.6706)
PSME2	10.260 (29.4712)	-19.920 (21.5986)	-21.230 (28.5841)
RASSF5	3.629 (9.6377)	28.542 (19.7947)	3.797 (12.9670)
RBCK1	3.973 (11.8400)	4.596 (35.2295)	-24.236 (18.7995)
RGL1	78.638 (137.9630)	-30.409 (26.2402)	-37.226 (31.6868)
RSAD2	106.492 (274.3871)	-53.392 (79.7677)	-82.077 (34.0946)
RTP4	60.174 (103.3296)	-60.499 (39.3630)	-69.459 (26.6843)
SAMD9	25.788 (19.1969)	-36.043 (48.0949)	-15.137 (75.2094)
SAMD9L	15.149 (27.3646)	-43.684 (42.2201)	-39.060 (50.1739)
SCO2	5.456 (28.7290)	-44.379 (28.1531)	-50.339 (20.6048)
SERPING1	41.338 (85.1136)	-26.769 (84.9900)	-51.960 (59.4306)
SHFL	14.792 (30.9751)	-30.705 (27.7162)	-48.997 (13.9230)
SHISA5	13.664 (23.7542)	-0.738 (49.3486)	-40.308 (22.4638)
SIGLEC1	51.540 (139.5216)	-85.603 (24.9920)	-94.777 (5.3380)

Gene Symbol	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
SP110	11.992 (23.7348)	6.750 (49.8026)	-21.421 (22.6796)
SP140	0.492 (18.6981)	-19.968 (32.7564)	-33.230 (23.9293)
SPATS2L	40.320 (104.3396)	-62.338 (42.1336)	-73.499 (33.9410)
STAT1	5.738 (20.2394)	-19.276 (31.2473)	-32.015 (24.1946)
STAT2	11.795 (25.6191)	-36.687 (30.2129)	-43.748 (25.9971)
TAP1	6.800 (17.9455)	1.168 (40.3459)	-25.852 (24.4424)
TDRD7	9.981 (20.0102)	-22.330 (46.0686)	-36.454 (31.1352)
TLR7	6.160 (30.4240)	-48.502 (19.8360)	-27.422 (28.2067)
TNFSF10	24.929 (26.0080)	-5.136 (48.5063)	-22.480 (43.9721)
TNFSF13B	10.755 (31.6052)	-6.049 (50.5334)	-18.514 (44.2826)
TOR1B	23.252 (16.0854)	-31.374 (45.0671)	-39.797 (34.5782)
TRAFD1	7.643 (17.9921)	6.433 (34.5301)	-25.611 (29.7275)
TRANK1	4.914 (16.8165)	27.074 (54.8120)	-9.534 (35.1995)
TRIM21	8.620 (16.1460)	6.058 (39.2621)	-14.478 (36.7376)
TRIM22	17.390 (25.7923)	-30.696 (55.0349)	-39.312 (46.2415)
TRIM6	14.917 (35.5697)	-43.449 (50.2069)	-65.375 (47.6346)
TRIM69	11.913 (13.5516)	-16.403 (25.1214)	-24.781 (28.5598)
TYMP	4.786 (20.3706)	-29.815 (29.8182)	-36.858 (20.6992)
UBE2L6	14.305 (26.3289)	-4.073 (48.2935)	-44.612 (22.4474)
USP18	59.583 (137.0477)	-74.957 (30.9949)	-82.952 (20.6929)
VRK2	5.144 (19.8816)	-18.328 (18.9702)	-14.041 (18.2966)
XAF1	27.495 (59.0520)	-56.825 (46.8146)	-69.147 (26.5821)
ZBP1	19.378 (28.8967)	-30.426 (64.5760)	-52.511 (39.1452)
ZC3HAV1	11.849 (15.7822)	0.801 (39.6796)	-19.333 (26.7610)
ZCCHC2	18.610 (38.7913)	-36.142 (55.0791)	-59.060 (29.9112)
ZNFX1	0.773 (13.1730)	16.777 (39.8217)	-9.128 (28.7274)

Only subjects with non-missing data at both baseline and the relevant post-baseline visit are included in the change/percent change from baseline summary statistics.

For percent change from baseline calculations, subjects with 0 at baseline are excluded.

Supplemental Table S3 Median percent change from baseline for IGS score

Visit	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
Baseline			
n	9	8	9
Median Percentage	100	100	100
Week 2			
n	9	8	9
Median Percentage	115	12	15
Week 4			
n	9	8	9
Median Percentage	151	11	11
Week 8			
n	9	8	9
Median Percentage	124	15	11
Week 12			
n	9	8	8
Median Percentage	114	13	13
Follow-up			
n	9	8	9
Median Percentage	136	146	92

Supplemental Table S4 Mean percent change from baseline for R848-mediated ex-vivo induction of blood cytokines

Visit / Timepoint Statistics	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
Interleukin-1β (ng/L)			
Day 1 / pre-dose (Baseline)			
n	9	8	9
Mean (SD)	0	0	0
Day 1 / 1 hr post-dose			
n	9	8	9
Mean (SD)	12.872 (50.3489)	-99.530 (1.0091)	-99.471 (0.8017)
Day 1 / 2 hrs post-dose			
n	9	8	9
Mean (SD)	7.409 (58.1975)	-99.704 (0.5501)	-99.757 (0.3921)
Day 1 / 3 hrs post-dose			
n	9	8	9
Mean (SD)	39.749 (88.3659)	-99.449 (1.0818)	-99.669 (0.6047)
Day 1 / 6 hrs post-dose			
n	9	8	9
Mean (SD)	90.754 (103.6237)	-99.229 (1.5020)	-99.500 (1.5000)
Day 15 / pre-dose			
n	9	8	9
Mean (SD)	-12.961 (54.2801)	-97.337 (2.0642)	-85.065 (39.8342)
Day 15 / 1 hr post-dose			
n	9	8	9
Mean (SD)	40.400 (96.9953)	-99.113 (1.3800)	-99.804 (0.2574)
Day 15 / 2 hrs post-dose			
n	9	8	9
Mean (SD)	52.855 (100.7442)	-99.539 (0.5360)	-99.827 (0.3185)
Day 15 / 3 hrs post-dose			
n	9	8	9
Mean (SD)	58.409 (119.9955)	-99.884 (0.3274)	-99.353 (1.2534)
Day 15 / 6 hrs post-dose			
n	9	8	9
Mean (SD)	102.605 (172.5928)	-99.722 (0.5472)	-99.609 (0.8670)
Interleukin-6 (ng/L)			
Day 1 / pre-dose (Baseline)			
n	9	8	9
Mean (SD)	0	0	0
Day 1 / 1 hr post-dose			
n	9	8	9
Mean (SD)	1.014 (42.0451)	-95.615 (11.6667)	-97.877 (5.5573)

Visit / Timepoint Statistics	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
Day 1 / 2 hrs post-dose			
n	9	8	9
Mean (SD)	-3.625 (50.1343)	-98.216 (3.3470)	-98.812 (2.0384)
Day 1 / 3 hrs post-dose			
n	9	8	9
Mean (SD)	8.364 (47.0364)	-99.312 (0.9373)	-98.008 (4.9924)
Day 1 / 6 hrs post-dose			
n	9	8	9
Mean (SD)	40.270 (70.4681)	-97.444 (4.7430)	-95.809 (11.6223)
Day 15 / pre-dose			
n	9	8	9
Mean (SD)	-28.732 (32.4104)	-73.919 (33.1609)	-73.110 (65.7286)
Day 15 / 1 hr post-dose			
n	9	8	9
Mean (SD)	-11.394 (51.1945)	-94.890 (9.5397)	-99.787 (0.2984)
Day 15 / 2 hrs post-dose			
n	9	8	9
Mean (SD)	-5.813 (59.5118)	-99.524 (0.8172)	-99.808 (0.3493)
Day 15 / 3 hrs post-dose			
n	9	8	9
Mean (SD)	-6.693 (65.1702)	-99.562 (0.7422)	-98.306 (4.9029)
Day 15 / 6 hrs post-dose			
n	9	8	9
Mean (SD)	40.340 (104.7373)	-97.808 (5.9400)	-99.884 (0.1039)
Tumor Necrosis Factor-α (ng/L)			
Day 1 / pre-dose (Baseline)			
n	9	8	9
Mean (SD)	0	0	0
Day 1 / 1 hr post-dose			
n	9	8	9
Mean (SD)	7.035 (34.0620)	-99.650 (0.8967)	-99.708 (0.3022)
Day 1 / 2 hrs post-dose			
n	9	8	9
Mean (SD)	6.927 (64.5909)	-99.670 (0.5194)	-99.749 (0.1755)
Day 1 / 3 hrs post-dose			
n	9	8	9
Mean (SD)	17.264 (77.0445)	-99.856 (0.1141)	-99.613 (0.6064)
Day 1 / 6 hrs post-dose			
n	9	8	9
Mean (SD)	73.479 (114.4272)	-99.564 (0.7004)	-99.391 (1.2838)
Day 15 / pre-dose			

Visit / Timepoint Statistics	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)
n	9	8	9
Mean (SD)	-13.886 (70.0234)	-94.934 (9.0841)	-81.991 (51.9123)
Day 15 / 1 hr post-dose			
N	9	8	9
Mean (SD)	16.311 (86.2430)	-99.513 (0.7714)	-99.752 (0.3110)
Day 15 / 2 hrs post-dose			
n	9	8	9
Mean (SD)	24.837 (99.9210)	-99.882 (0.1546)	-99.843 (0.1576)
Day 15 / 3 hrs post-dose			
n	9	8	9
Mean (SD)	44.159 (124.3807)	-99.937 (0.0966)	-99.500 (1.3060)
Day 15 / 6 hrs post-dose			
n	9	8	9
Mean (SD)	105.575 (189.5408)	-99.775 (0.3418)	-99.812 (0.2987)

Only subjects with non-missing data at both baseline and the relevant post-baseline visit are included in the change/percent change from baseline summary statistics.

For the purpose of all descriptive statistics the median measured concentration in the analytical sample (n=3) is used. If 1/3 measurements were below the limit of quantification (BLQ), the BLQ was assigned as zero and the median value was used; if 2/3 were BLQ, the lower limit of quantification was used; if all measurements were BLQ, zero was used.

Supplemental Table S5 Clinical outcomes after treatment with E6742 at Week 12

Outcomes	Placebo (N=9)	E6742 100 mg BID (N=8)	E6742 200 mg BID (N=9)*
Change from baseline at Week 12 †, Mean (SD)			
SLEDAI-2K total score	-2.2 (2.11)	-1.6 (2.26)	-2.3 (2.25)
PGA score	-0.4 (0.45)	-0.6 (0.45)	-0.7 (0.38)
CLASI activity score	-1.3 (2.18)	-1.1 (1.13)	-2.4 (4.78)
Tender joint counts (out of 68 joints)	-0.9 (9.97)	-2.4 (7.84)	-5.3 (7.17)
Swollen joint counts (out of 66 joints)	0.1 (1.27)	-3.8 (4.98)	-1.5 (2.33)
Anti-dsDNA IgG antibody (IU/mL)	2.3 (6.78)	-7.7 (12.89)	-2.7 (5.35)
Complement C3 (g/L)	0.02 (0.16)	0.06 (0.072)	0.06 (0.16)
Complement C4 (g/L)	-0.008 (0.032)	0.009 (0.024)	0.004 (0.038)
Responder rate at Week 12, n/m (%)			
CLASI-50 response ‡	2/6 (33.3)	4/7 (57.1)	4/8 (50.0)

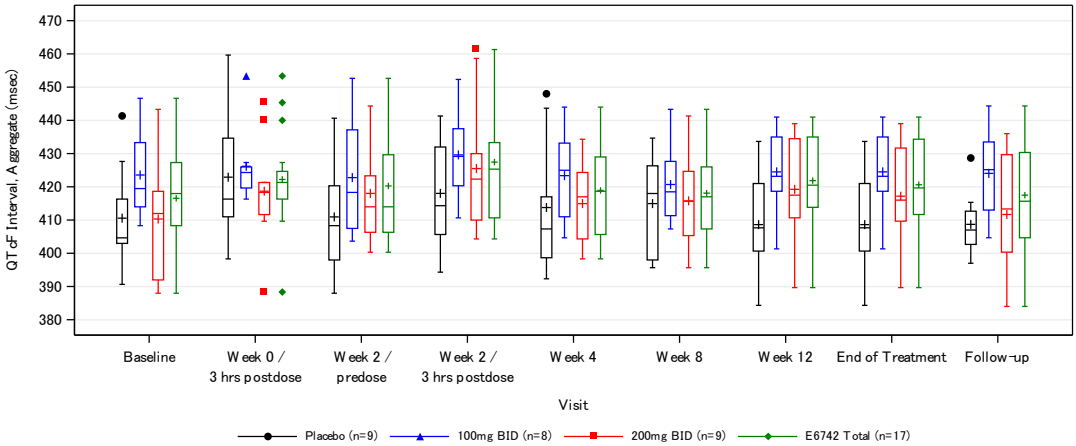
*Includes one participant with missing data due to early discontinuation.

†Only patients with non-missing data at both baseline and the relevant post-baseline visit were included in the change from baseline summary statistics.

‡Response rate analyzed a decrease of ≥ 50% from baseline Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) activity score for patients with ≥ 1 point in CLASI anti-dsDNA, anti-double-stranded DNA; PGA, Physician's Global Assessment; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

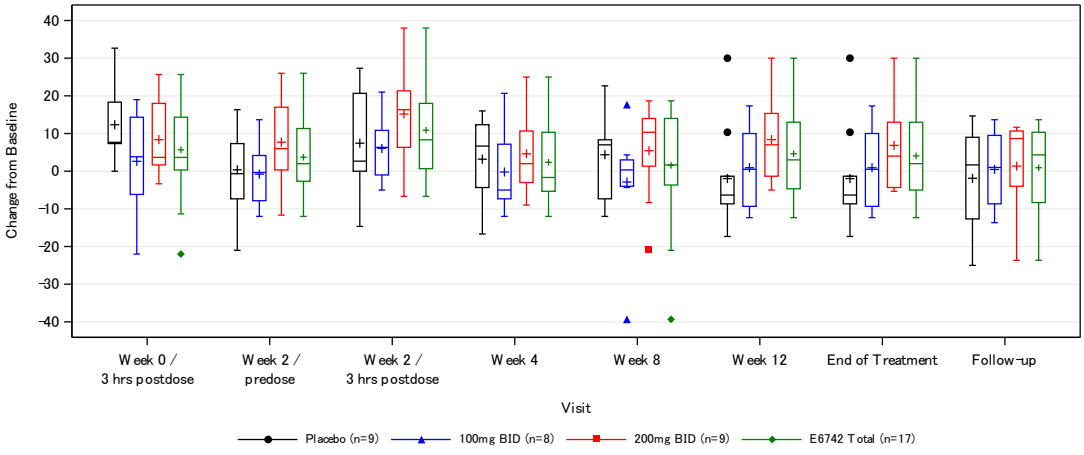
Supplemental Figure S1 Box plots of changes in QTcF values among systemic lupus erythematosus patients under treatment with E6742.

The upper plot shows aggregated changes in QTcF values and the lower plot shows changes from baseline after multiple doses of placebo or E6742 (100 or 200 mg) administered twice daily (BID). Whiskers extend to the minimum and maximum values, or 1.5 × the interquartile range. QTcF, corrected QT interval using Fridericia's formula.



Number of Subjects at Visit

Placebo	9	9	9	9	9	9	9	9	9
100mg BID	8	8	8	8	8	8	8	8	8
200mg BID	9	9	9	9	9	9	8	9	9
E6742 Total	17	17	17	17	17	17	16	17	17

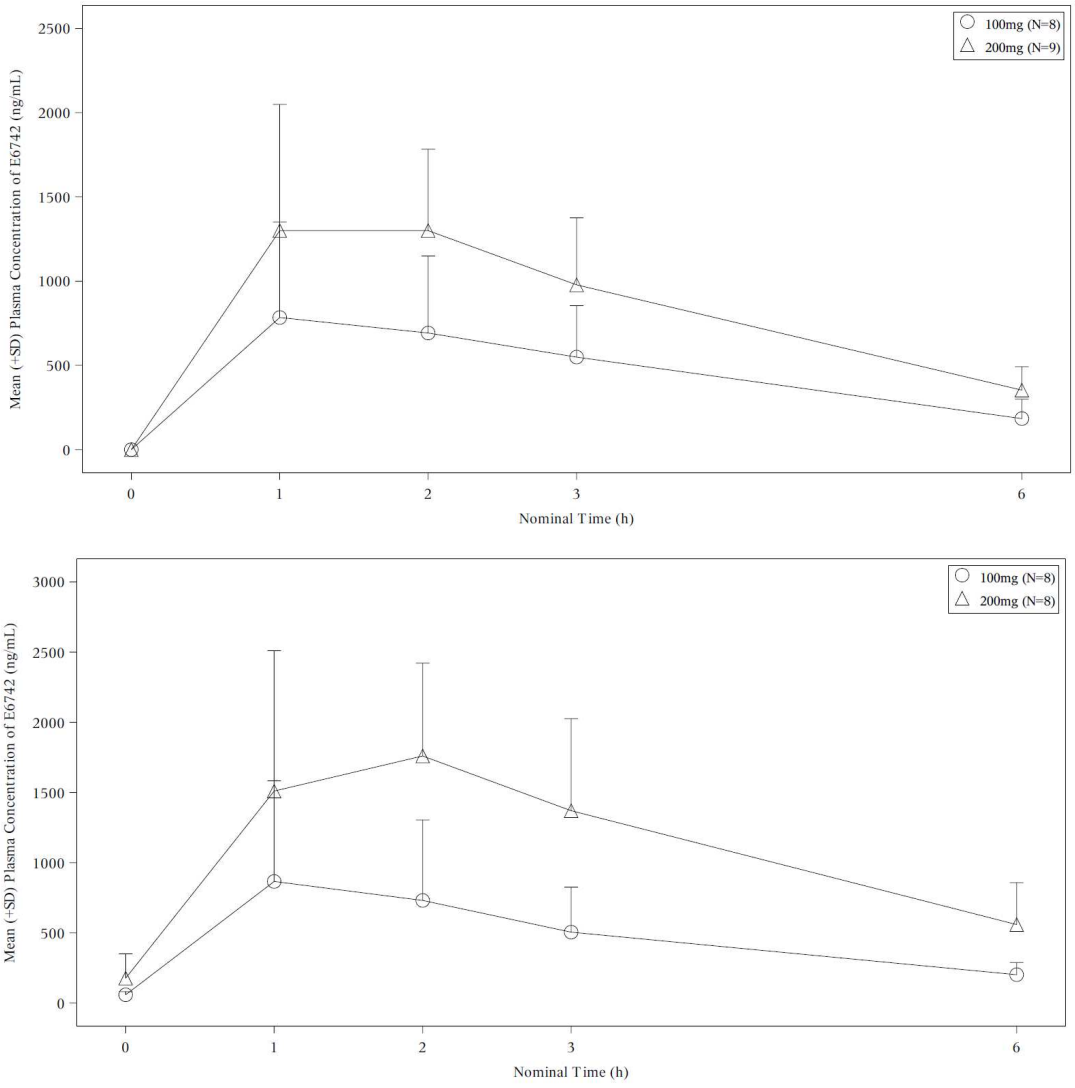


Number of Subjects at Visit

Placebo	9	9	9	9	9	9	9	9	9
100mg BID	8	8	8	8	8	8	8	8	8
200mg BID	9	9	9	9	9	9	8	9	9
E6742 Total	17	17	17	17	17	17	16	17	17

Supplemental Figure S2 Linear-scale plasma concentration-time curve and summary of pharmacokinetic parameters of E6742 in trial patients with SLE.

Mean (+ standard deviation [SD]) plasma concentrations of E6742 following a single dose (Day 1; upper graph) or multiple doses (Day 15; lower graph) at 100 and 200 mg administered twice daily (BID) in the pharmacokinetic analysis set of patients (N = 17). One patient in the 200 mg BID group did not take the study drug from Days 8–14, and was thus excluded from the data shown on Day 15.



	Pharmacokinetic Parameter	E6742	
		100 mg (N=8)	**200 mg (N=9)**
Day 1	C_{max} (ng/mL)	768 (60.5) 875±460	1350 (51.9) 1490±655
	t_{max} (h)	1.44 (0.83 – 3.10)	1.87 (0.83 – 3.10)
	$AUC_{(0\text{-}6h)}$ (ng•h/mL)	2300 (61.0) 2660±1610	4390 (43.9) 4730±1880
Day 15	$C_{ss,max}$ (ng/mL)	793 (65.6) 941±653	1960 (36.8) 2080±788 [a]
	$t_{ss,max}$ (h)	1.11 (0.88 – 3.02)	1.42 (0.80 – 3.12) [a]
	$AUC_{(0\text{-}6h)ss}$ (ng•h/mL)	2410 (53.9) 2750±1790	6040 (40.6) 6470±2790 [a]
	R_{ac} (C_{max})	1.03 (27.2) 1.06±0.273	1.32 (25.2) 1.36±0.341 [a]
	R_{ac} (AUC)	1.04 (24.4) 1.07±0.258	1.28 (20.4) 1.30±0.257 [a]

Data are shown as geometric mean (%CV) and arithmetic mean±SD except t_{max} and $t_{ss,max}$; for t_{max} and $t_{ss,max}$, median (min-max) is shown.
%CV = sqrt(exp[SD**2 of log-transformed data]–1)*100

$AUC_{(0\text{-}6h)}$ = area under the concentration-time curve from zero time to fixed time point 6 hour, $AUC_{(0\text{-}6h)ss}$ = area under the concentration-time curve from zero time to fixed time point 6 hour at steady state, C_{max} = maximum drug concentration, $C_{ss,max}$ = maximum observed concentration at steady state, R_{ac} (AUC) = accumulation ratio for AUC, R_{ac} (C_{max}) = accumulation ratio for C_{max}, t_{max} = time at which the highest drug concentration occurs, $t_{ss,max}$ = time at which the highest drug concentration occurs at steady state**.**
a: n=8, One subject in the 200 mg cohort did not take the study drug from Day 8 to Day 14, therefore this subject was not included in the summary statistics on Day 15.