SUPPLEMENTAL MATERIAL

Supplemental Table S1. Demographics and baseline characteristics (intent-to-treat population)[a]

Characteristic	Cohort 1: 750 mg MEDI8852 + OS (*n* = 31)	Cohort 2: 3,000 mg MEDI8852 + OS (*n* = 31)	Cohort 3: placebo + OS (*n* = 32)	Cohort 4: 3,000 mg MEDI8852 (*n* = 32)	Cohorts 1, 2, and 4 combined: total MEDI8852 (*n* = 94)
Hemisphere					
Northern	23 (74.2)	25 (80.6)	24 (75.0)	23 (71.9)	71 (75.5)
Southern	8 (25.8)	6 (19.4)	8 (25.0)	9 (28.1)	23 (24.5)
Age, y (median [range])	40.0 (21–61)	43.0 (19–64)	42.0 (18–59)	44.5 (22–65)	43.0 (19–65)
Sex					
Female	13 (41.9)	18 (58.1)	20 (62.5)	15 (46.9)	46 (48.9)
Race					
Asian	0	0	1 (3.1)	0 (0)	0 (0)
Black or African American	8 (25.8)	3 (9.7)	5 (15.6)	5 (15.6)	16 (17.0)
White	23 (74.2)	28 (90.3)	26 (81.3)	27 (84.4)	78 (83.0)
Ethnicity					
Hispanic or Latino	17 (54.8)	20 (64.5)	16 (50.0)	17 (53.1)	54 (57.4)
Duration of illness at baseline					
≤48 h	15 (48.4)	18 (58.1)	14 (43.8)	18 (56.3)	51 (54.3)
>48 h	16 (51.6)	13 (41.9)	18 (56.3)	14 (43.8)	43 (45.7)
Body temperature, ˚C (median [range])	38.00 (36.1–39.6)	38.15 (35.8–39.7)	38.10 (36.5–39.3)	38.00 (36.1–39.6)	38.00 (35.8–39.7)
Solicited influenza symptoms, total score (median [range])	17.0 (7–21)	16.0 (7–21)	16.0 (6–21)	17.0 (10-21)	17.0 (7–21)
Confirmed influenza by viral subtype via RT-PCR					
A/H1N1	22 (71.0)	21 (67.7)	26 (81.3)	20 (62.5)	63 (67.0)
A/H3N2	5 (16.1)	2 (6.5)	4 (12.5)	3 (9.4)	10 (10.6)

[a] Data are presented as *n* (%) unless otherwise noted.

OS = oseltamivir; RT-PCR = reverse transcription–polymerase chain reaction.

Supplemental Table S2. Subject samples containing influenza A neuraminidase amino acid changes in last sequenced sample relative to baseline

Subject gender/age (y)	Subtype	Treatment group	NA amino acid at baseline (day 1)	NA amino acid change at last day sequenced		Change in known OS-susceptible site[a]
				Change	Study day	
Male/24	H1N1	MEDI8852 750 mg + OS	M15 F115	M15V F115L	Day 5	None
Male/24	H1N1	MEDI8852 750 mg + OS	V321	V321I	Day 7	None
Female/56	H1N1	MEDI8852 3,000 mg + OS	W33	W33R	Day 5	None
Female/40	H1N1	Placebo + OS	D199	D199N	Day 5	None
Female/57	H1N1	Placebo + OS	I23	I23T	Day 3	None
Female/58	H1N1	Placebo + OS	M15 T350	M15V T350S	Day 3	None
Male/39	H1N1	Placebo + OS	S334	S334N	Day 3	None
Male/45	H1N1	Placebo + OS	S299	S299[b]	Day 3	None
Female/54	H1N1	MEDI8852 3,000 mg	S229	S229F	Day 7	None
Male/22	H1N1	MEDI8852 3,000 mg	T55	T55N	Day 11	None
Male/36	H3N2	MEDI8852 3,000 mg	T157 S416	T157A S416N	Day 3	None
Male/51	H1N1	MEDI8852 3,000 mg	R107	R107G	Day 3	None

[a]No amino acid change was observed within a known oseltamivir-resistant site (H1N1-E119, H275, R293 and N295 [N1 numbering], and H3N2-E119, H274, R292, and N294 [N2 numbering]).

[b]A stop codon was observed at this site.

NA = neuraminidase; OS = oseltamivir.

Supplemental Table S3. Baseline samples with unique influenza A hemagglutinin amino acid changes in the MEDI8852 binding site[a]

Subject gender/age (y)	Treatment group	Subtype	Baseline (day 1)
Female/42	MEDI8852 750 mg + OS	H1N1	L382Q
Female/54	MEDI8852 750 mg + OS	H1N1	L382Q
Male/24	MEDI8852 750 mg + OS	H1N1	L382Q
Male/40	MEDI8852 3,000 mg + OS	H1N1	V47F
Male/48	MEDI8852 3,000 mg + OS	H1N1	L382Q
Female/48	Placebo + OS	H1N1	V47I
Female/52	Placebo + OS	H1N1	L382Q
Female/51	MEDI8852 3,000 mg	H1N1	L382Q
Female/64	MEDI8852 3,000 mg	H1N1	L382Q
Male/40	MEDI8852 3,000 mg	H1N1	L382L/Q

[a]MEDI8852 binding site (30 amino acids) changes are relative to a reference sequence (A/Bolivia/559/2013 [H1N1] and A/Hong Kong/4801/2014 [H3N2]).

OS = oseltamivir.

Supplemental Table S4. Subject samples containing influenza A hemagglutinin amino acid changes in the last sequenced sample relative to baseline

Subject gender/age (y)	Subtype	Treatment group	HA amino acid at baseline (day 1)	HA amino acid change at last day sequenced		Change within MEDI8852 binding region[a]
				Change	Study day	
Male/36	H1N1	MEDI8852 750 mg + OS	T500	T5001	Day 3	None
Male/43	H1N1	MEDI8852 3,000 mg + OS	S102	S102L	Day 3	None
Male/21	H1N1	Placebo + OS	N245	N245D	Day 3	None
Male/39	H1N1	Placebo + OS	H486	H486Y	Day 3	None
Male/45	H1N1	Placebo + OS	P199	P199Q	Day 3	None
Female/54	H1N1	MEDI8852 3,000 mg	R276	R276K	Day 5	None

[a]No amino acid change was observed within the putative MEDI8852 binding regions. MEDI8852 binding regions consist of 30 amino acids identified by crystallographic structure analysis and in vitro analyses of monoclonal antibody–resistant mutants.

HA = hemagglutinin; OS = oseltamivir.

Supplemental Table S5. Time to resolution and duration and severity of illness, influenza A–infected subjects confirmed by RT-PCR (intent-to-treat population)

Parameter[a]	Cohort 1: 750 mg MEDI8852 + OS (*n* = 27)	Cohort 2: 3,000 mg MEDI8852 + OS (*n* = 23)	Cohort 3: placebo + OS (*n* = 31)	Cohort 4: 3,000 mg MEDI8852 (*n* = 25)	Cohorts 1, 2, and 4 combined: total MEDI8852 (*n* = 75)
Cough					
Time to resolution (h)	71.58 (26.50–107.25)	92.37 (44.25–96.50)	81.77 (43.58–132.00)	92.00 (46.38–151.58)	87.60 (59.40–103.22)
Duration and severity (score-h)	284.30 (0–525.00)	304.30 (51.20–648.00)	287.80 (0–667.50)	281.80 (24.50–620.40)	289.50 (0–648.00)
Nasal obstruction					
Time to resolution (h)	48.17 (22.23–67.07)	29.25 (12.67–55.97)	52.45 (22.83–62.75)	59.40 (21.67–94.40)	48.10 (27.67–59.17)
Duration and severity (score-h)	179.50 (12.00–434.80)	190.60 (16.50–577.50)	203.20 (0–451.60)	228.80 (0–432.70)	202.30 (0–577.50)
Sore throat					
Time to resolution (h)	10.42 (7.73–27.67)	45.17 (17.25–55.97)	31.00 (10.77–56.97)	22.45 (9.75–57.50)	23.08 (10.58–44.17)
Duration and severity (score-h)	87.60 (0–550.80)	154.00 (0–534.00)	136.60 (0–379.70)	107.80 (0–515.80)	119.10 (0–550.80)
Fatigue					
Time to resolution (h)	24.42 (12.00–66.33)	55.28 (32.47–69.45)	50.30 (32.50–80.83)	46.82 (34.08–67.17)	46.23 (32.47–56.78)
Duration and severity (score-h)	150.40 (12.10–476.80)	154.50 (46.90–534.00)	137.00 (16.90–661.20)	162.50 (58.50–490.70)	154.50 (12.10–534.00)
Headache					
Time to resolution (h)	24.17 (10.42–30.33)	31.28 (20.05–32.67)	42.33 (20.50–45.77)	21.25 (10.67–28.17)	23.40 (20.05–28.17)

Parameter[a]	Cohort 1: 750 mg MEDI8852 + OS (*n* = 27)	Cohort 2: 3,000 mg MEDI8852 + OS (*n* = 23)	Cohort 3: placebo + OS (*n* = 31)	Cohort 4: 3,000 mg MEDI8852 (*n* = 25)	Cohorts 1, 2, and 4 combined: total MEDI8852 (*n* = 75)
Duration and severity (score-h)	65.30 (0–334.80)	118.90 (6.00–391.50)	112.80 (0–505.20)	58.10 (0–419.50)	81.50 (0–419.50)
Myalgia					
Time to resolution (h)	24.17 (10.42–43.67)	56.40 (20.67–77.25)	44.08 (31.75–58.08)	33.25 (23.40–51.25)	32.25 (23.40–45.25)
Duration and severity (score-h)	106.40 (10.60–311.50)	131.70 (17.80–417.00)	156.40 (29.60–553.00)	124.20 (46.80–516.70)	115.80 (10.60–516.70)
Feverishness					
Time to resolution (h)	22.45 (8.08–33.02)	29.55 (18.50–40.17)	43.58 (32.00–50.62)	21.67 (18.23–33.00)	22.75 (18.50–29.55)
Duration and severity (score-h)	56.20 (3.80–323.40)	74.90 (18.00–378.00)	97.80 (10.60–305.10)	53.80 (1.90–365.50)	66.80 (1.90–378.00)

[a]Data on time to resolution are presented as median (95% confidence interval); duration and severity data are presented as median (range). Confidence intervals were calculated based on the median obtained from Kaplan-Meier analysis. Score-hours were assessed by area-under-the-curve analysis derived on a by-subject basis, using the linear trapezoidal rule with all available data from baseline to the last time point with influenza symptoms measurement up to day 13.

OS = oseltamivir; RT-PCR = reverse transcriptase-polymerase chain reaction.

Supplemental Table S6. Time to resolution of illness in subjects with baseline severity score greater than the median score at baseline, influenza A–infected subjects confirmed by RT-PCR (intent-to-treat population)

	Time to resolution (median [95% CI])[a]						
Cohort	**Cough**	**Nasal obstruction**	**Sore throat**	**Fatigue**	**Headache**	**Myalgia**	**Feverishness**
Cohort 1: 750 mg MEDI8852 + OS (*n* = 12)	104.25 (14.10–159.42)	68.42 (27.67–101.62)	41.42 (7.33–114.05)	66.19 (24.42–94.50)	29.00 (17.17–42.45)	49.42 (23.08–101.62)	36.28 (6.17–57.12)
Cohort 2: 3,000 mg MEDI8852 + OS (*n* = 11)	80.83 (45.25–96.50)	44.25 (11.80–119.75)	48.08 (32.67–56.40)	53.17 (17.75-69.45)	31.50 (11.80–43.98)	31.97 (8.17-69.45)	32.17 (11.80–55.97)
Cohort 3: placebo + OS (*n* = 11)	161.75 (22.00–255.82)	88.33 (10.00–171.62)	60.13 (10.00–76.75)	63.07 (22.00–101.99)	51.07 (20.50–88.75)	53.50 (22.00–99.07)	51.07 (22.00–77.33)
Cohort 4: 3,000 mg MEDI8852 (*n* = 14)	75.70 (43.92–148.50)	66.54 (28.17–114.73)	38.46 (10.25–67.62)	45.37 (28.17–88.58)	22.26 (8.08–45.25)	38.58 (18.83–92.95)	30.58 (18.50-53.00)
Cohorts 1, 2 and 4 combined: total MEDI8852 (*n* = 37)	92.00 (62.25–118.17)	59.58 (45.12–90.33)	45.90 (28.17–57.50)	55.17 (33.12–66.33)	28.17 (23.08–32.17)	43.67 (27.67–59.17)	32.17 (23.40–43.98)

[a]The median time to resolution of influenza symptoms were summarized by Kaplan-Meier curves. Subjects with missing data were censored. Confidence intervals were calculated based on the median obtained from the Kaplan-Meier analysis.

CI = confidence interval; OS = oseltamivir; RT-PCR = reverse transcriptase-polymerase chain reaction.