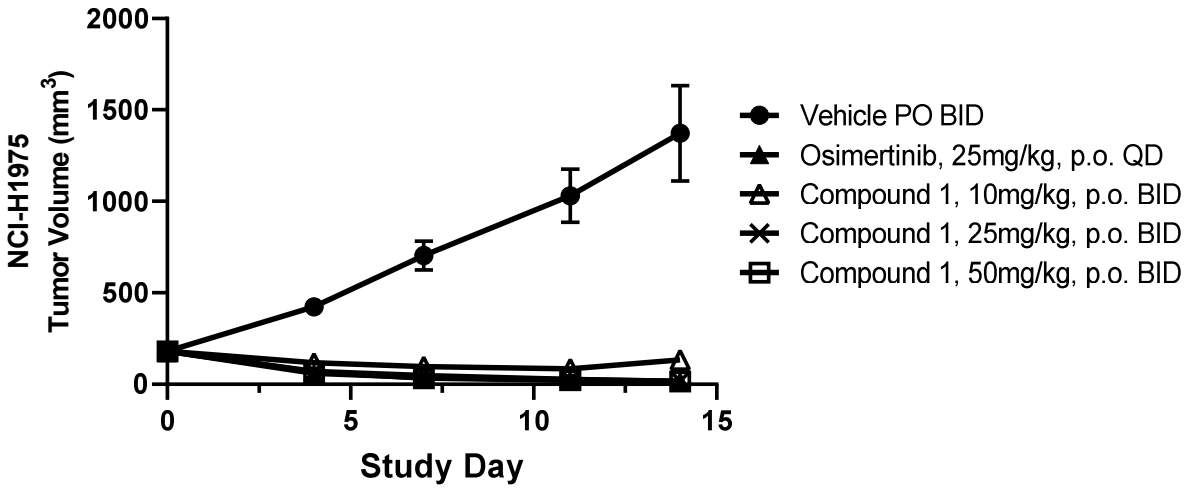

NCI-H1975
Tumor Volume (mm3)
2000
1500
1000
500
0
0
5
10
15
Study Day
Vehicle PO BID
Osimertinib, 25mg/kg, p.o. QD
Compound 1, 10mg/kg, p.o. BID
Compound 1, 25mg/kg, p.o. BID
Compound 1, 50mg/kg, p.o. BID

FIG. 1A

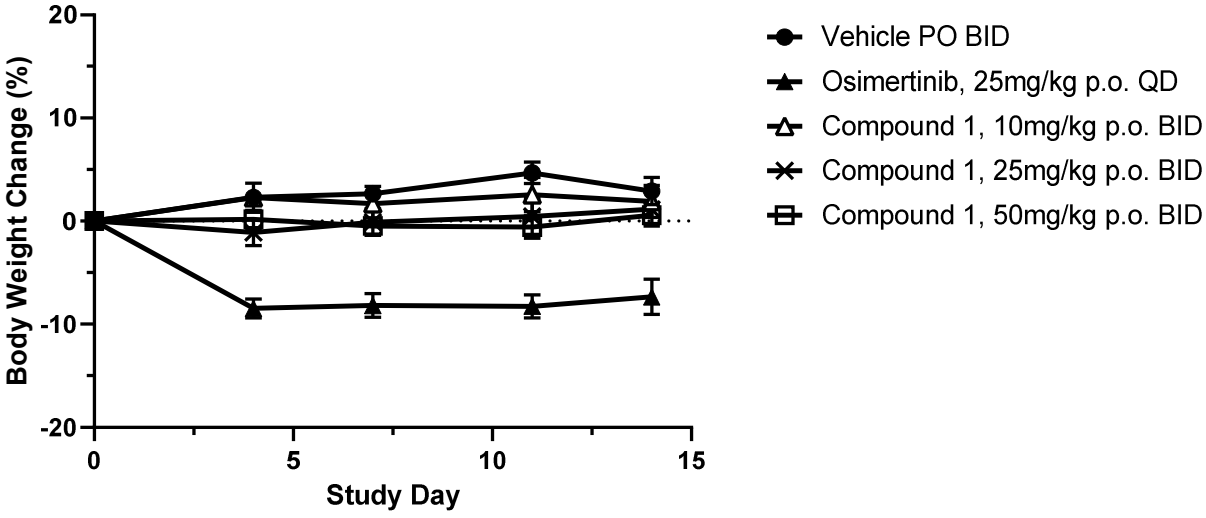

Body Weight Change (%)
20
10
0
-10
-20
0
5
10
15
Study Day
Vehicle PO BID
Osimertinib, 25mg/kg p.o. QD
Compound 1, 10mg/kg p.o. BID
Compound 1, 25mg/kg p.o. BID
Compound 1, 50mg/kg p.o. BID

FIG. 1B

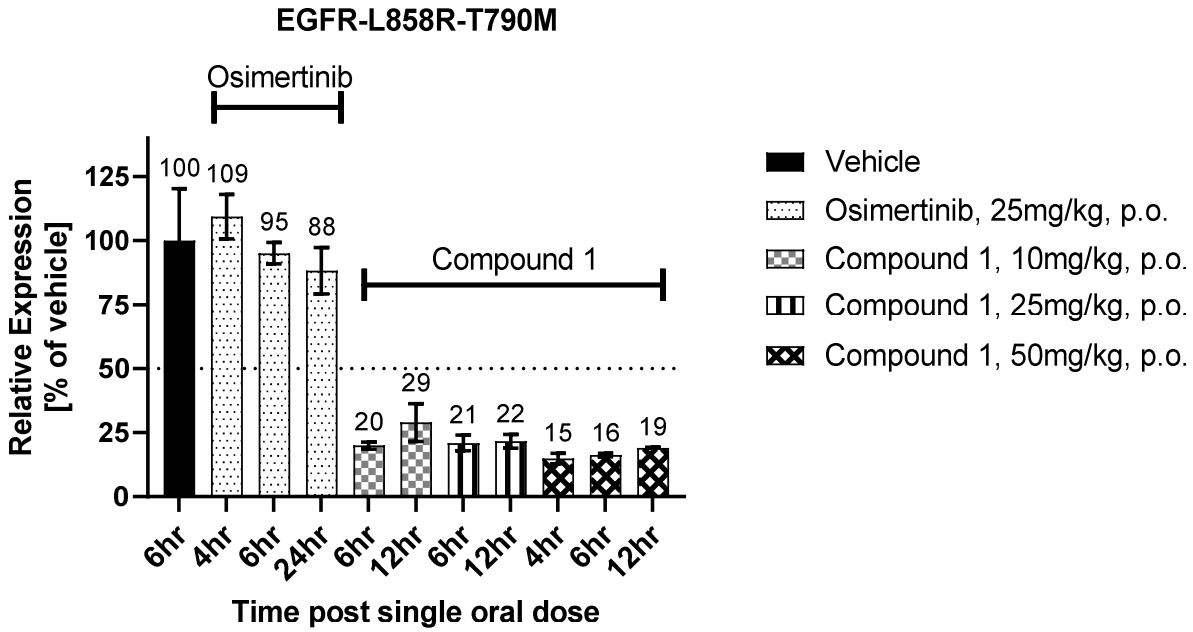

EGFR-L858R-T790M
Osimertinib
Compound 1
Relative Expression [% of vehicle]
125
100
75
50
25
0
100
109
95
88
20
29
21
22
15
16
19
6hr
4hr
6hr
24hr
6hr
12hr
6hr
12hr
4hr
6hr
12hr
Time post single oral dose
Vehicle
Osimertinib, 25mg/kg, p.o.
Compound 1, 10mg/kg, p.o.
Compound 1, 25mg/kg, p.o.
Compound 1, 50mg/kg, p.o.

FIG. 2A

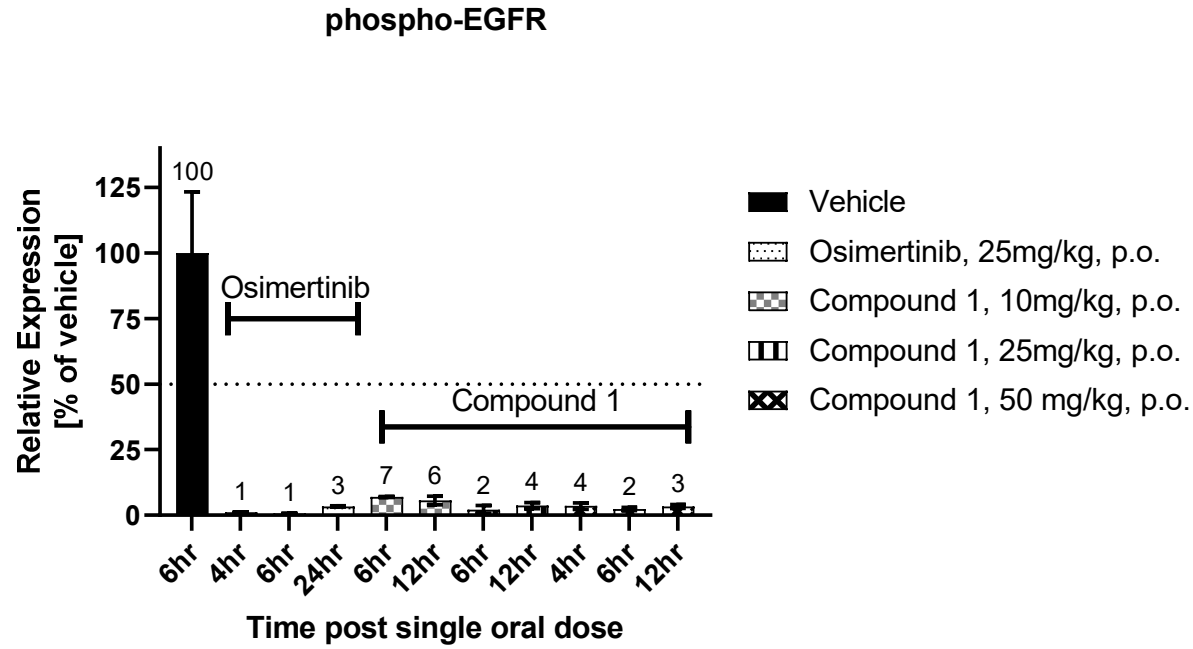

phospho-EGFR
Relative Expression [% of vehicle]
125
100
75
50
25
0
100
Osimertinib
Compound 1
1
1
3
7
6
2
4
4
2
3
6hr
4hr
6hr
24hr
6hr
12hr
6hr
12hr
4hr
6hr
12hr
Time post single oral dose
Vehicle
Osimertinib, 25mg/kg, p.o.
Compound 1, 10mg/kg, p.o.
Compound 1, 25mg/kg, p.o.
Compound 1, 50 mg/kg, p.o.

FIG. 2B

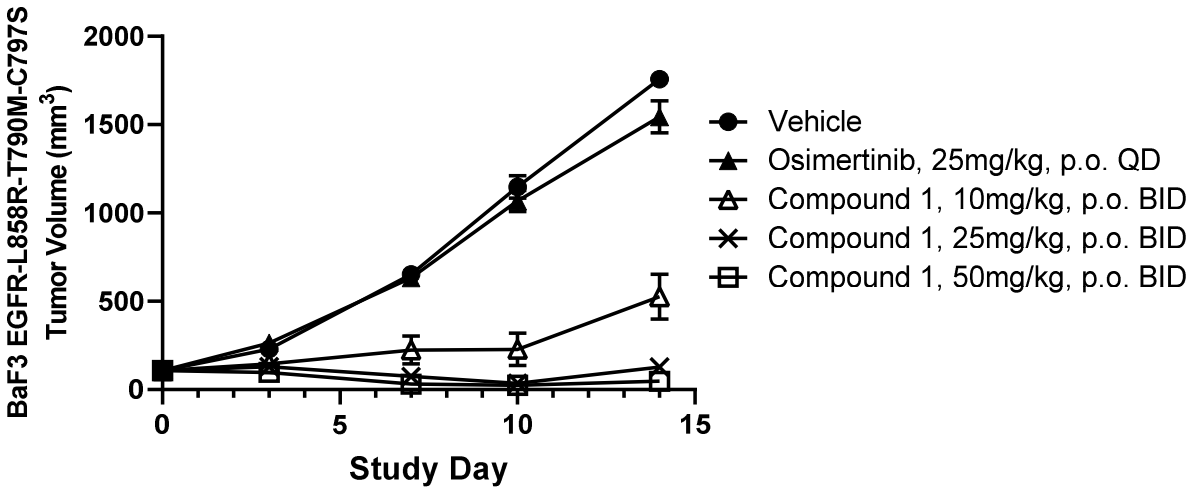

BaF3 EGFR-L858R-T790M-C797S
Tumor Volume (mm3)
2000
1500
1000
500
0
0
5
10
15
Study Day
Vehicle
Osimertinib, 25mg/kg, p.o. QD
Compound 1, 10mg/kg, p.o. BID
Compound 1, 25mg/kg, p.o. BID
Compound 1, 50mg/kg, p.o. BID

FIG. 3A

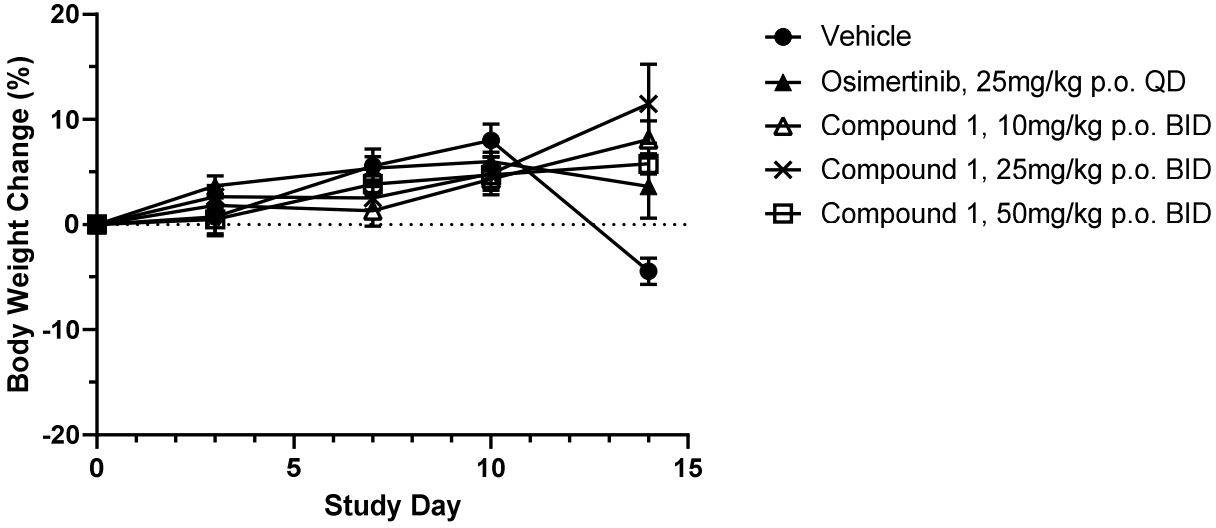

Body Weight Change (%)
20
10
0
-10
-20
0
5
10
15
Study Day
Vehicle
Osimertinib, 25mg/kg p.o. QD
Compound 1, 10mg/kg p.o. BID
Compound 1, 25mg/kg p.o. BID
Compound 1, 50mg/kg p.o. BID

FIG. 3B

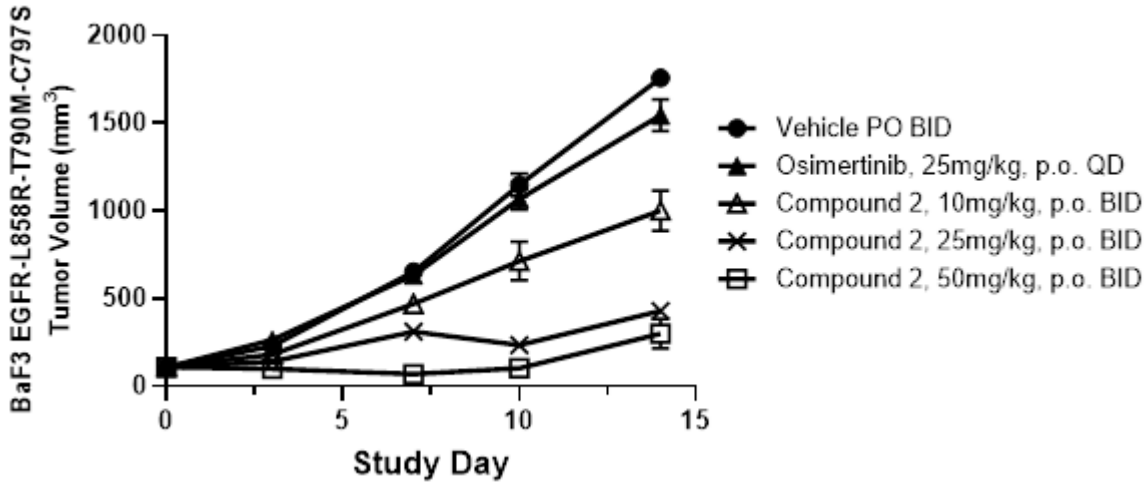

BaF3 EGFR-L858R-T790M-C797S
Tumor Volume (mm3)
2000
1500
1000
500
0
0
5
10
15
Study Day
Vehicle PO BID
Osimertinib, 25mg/kg, p.o. QD
Compound 2, 10mg/kg, p.o. BID
Compound 2, 25mg/kg, p.o. BID
Compound 2, 50mg/kg, p.o. BID

FIG. 4A

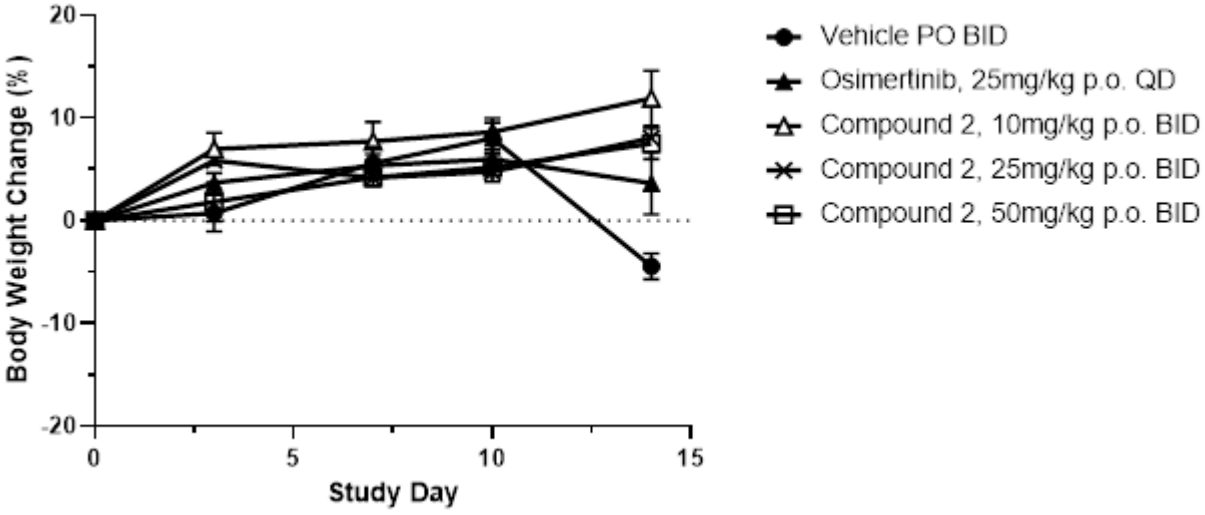

Body Weight Change (%)
20
10
0
-10
-20
0
5
10
15
Study Day
Vehicle PO BID
Osimertinib, 25mg/kg p.o. QD
Compound 2, 10mg/kg p.o. BID
Compound 2, 25mg/kg p.o. BID
Compound 2, 50mg/kg p.o. BID

FIG. 4B

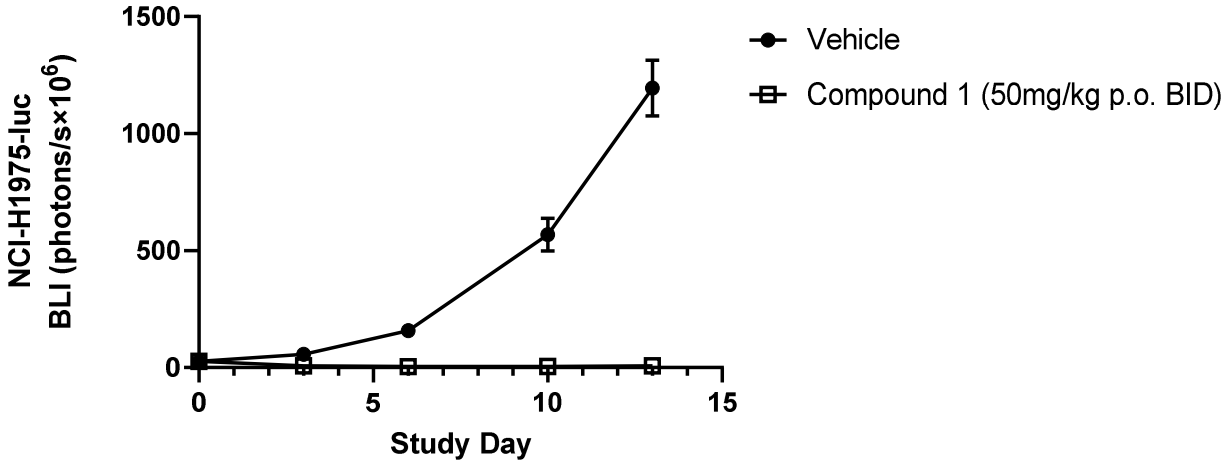
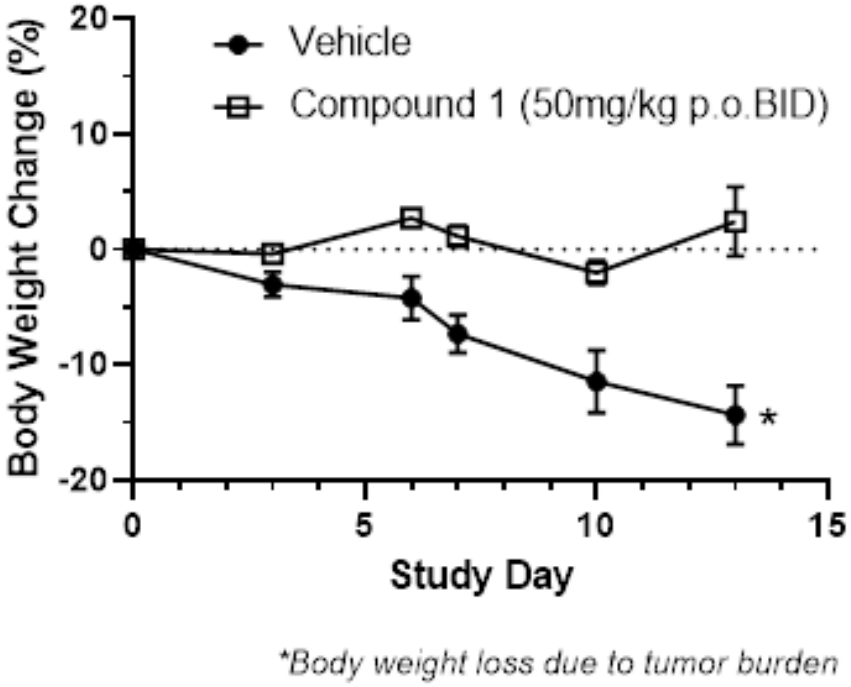


FIG. 5A



*Body weight loss due to tumor burden

FIG. 5B

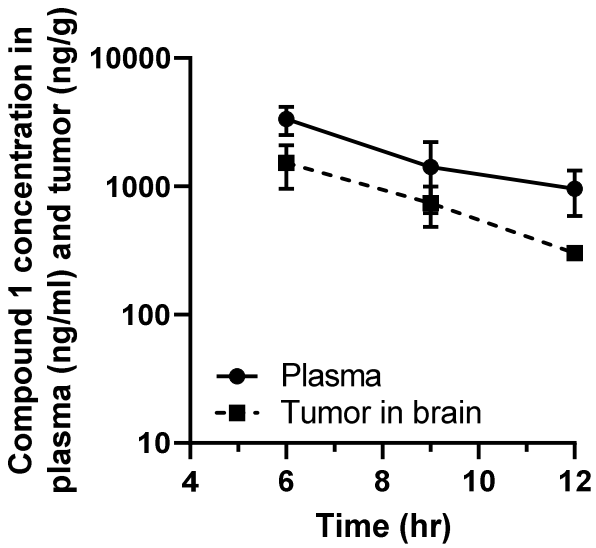

Compound 1 concentration in plasma (ng/ml) and tumor (ng/g)
10000
1000
100
10
Plasma
Tumor in brain
4
6
8
10
12
Time (hr)

FIG. 6

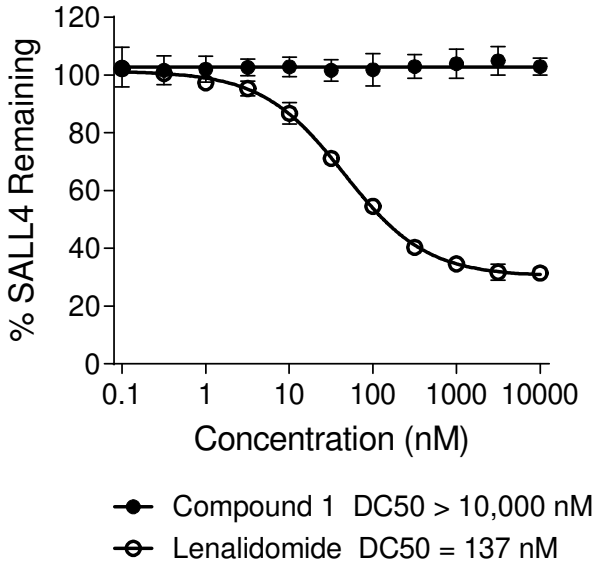

120
100
80
60
40
20
0
% SALL4 Remaining
0.1
1
10
100
1000
10000
Concentration (nM)
Compound 1 DC50 > 10,000 nM
Lenalidomide DC50 = 137 nM

FIG. 7

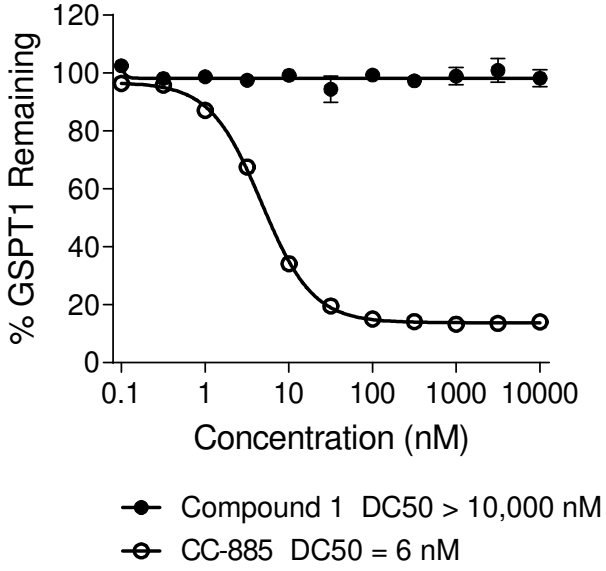

120
100
80
60
40
20
0
% GSPT1 Remaining
0.1
1
10
100
1000
10000
Concentration (nM)
Compound 1 DC50 > 10,000 nM
CC-885 DC50 = 6 nM

FIG. 8

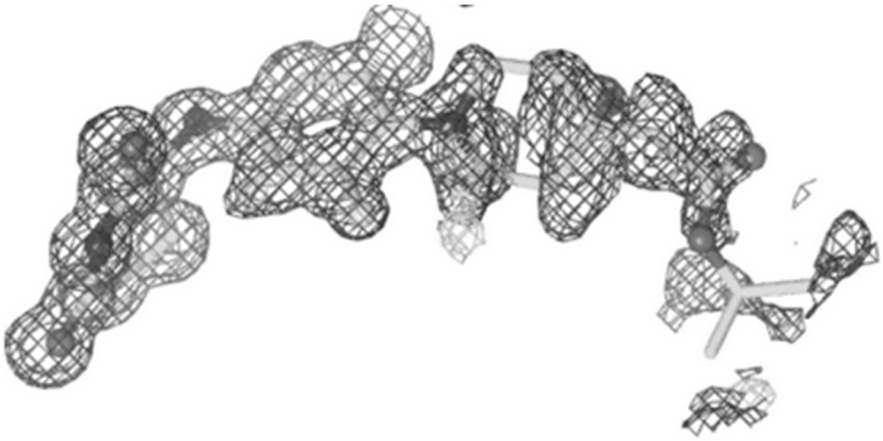


FIG. 9

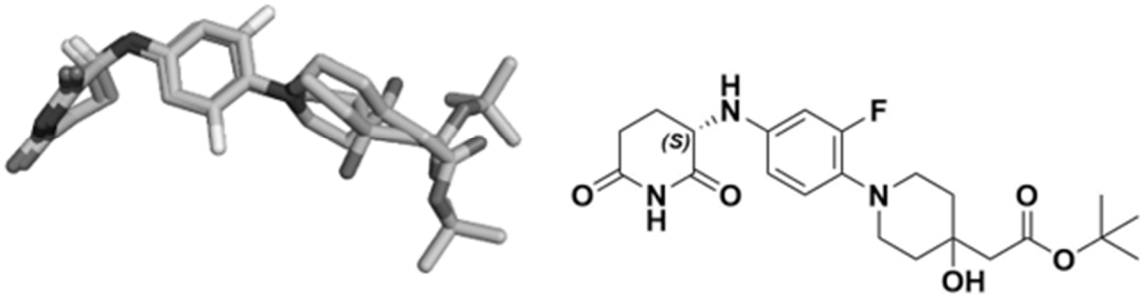


FIG. 10

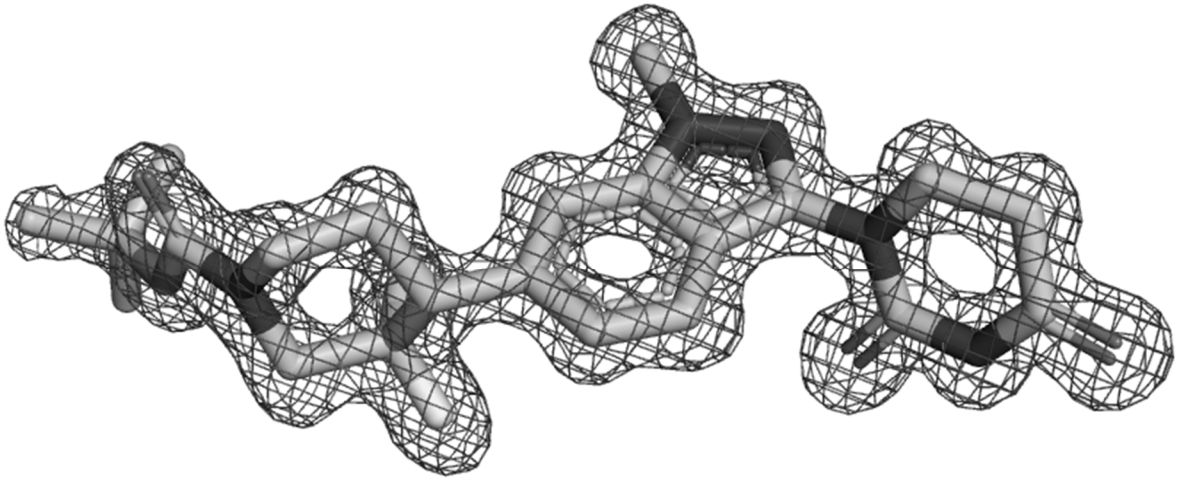


FIG. 11

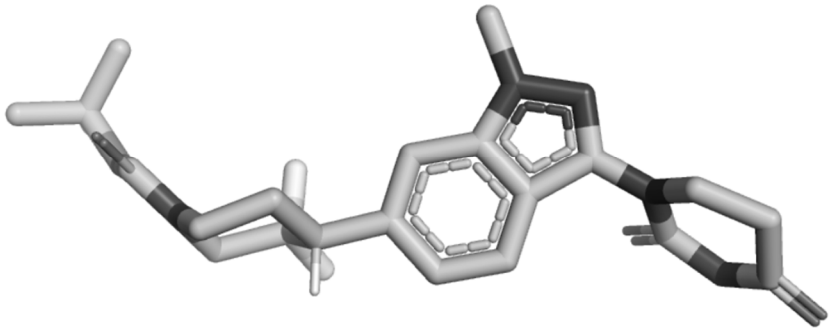


FIG. 12

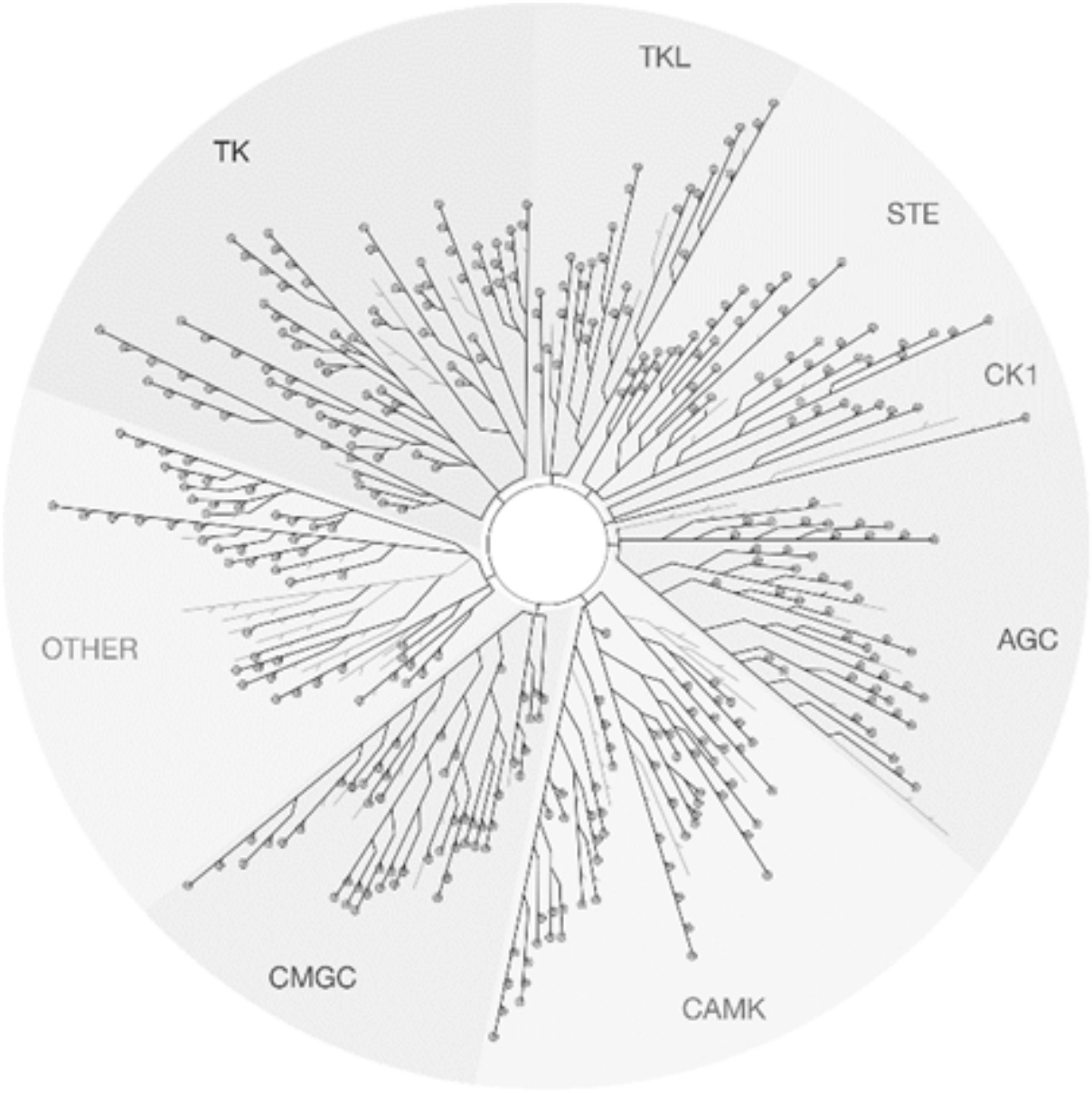


FIG. 13A

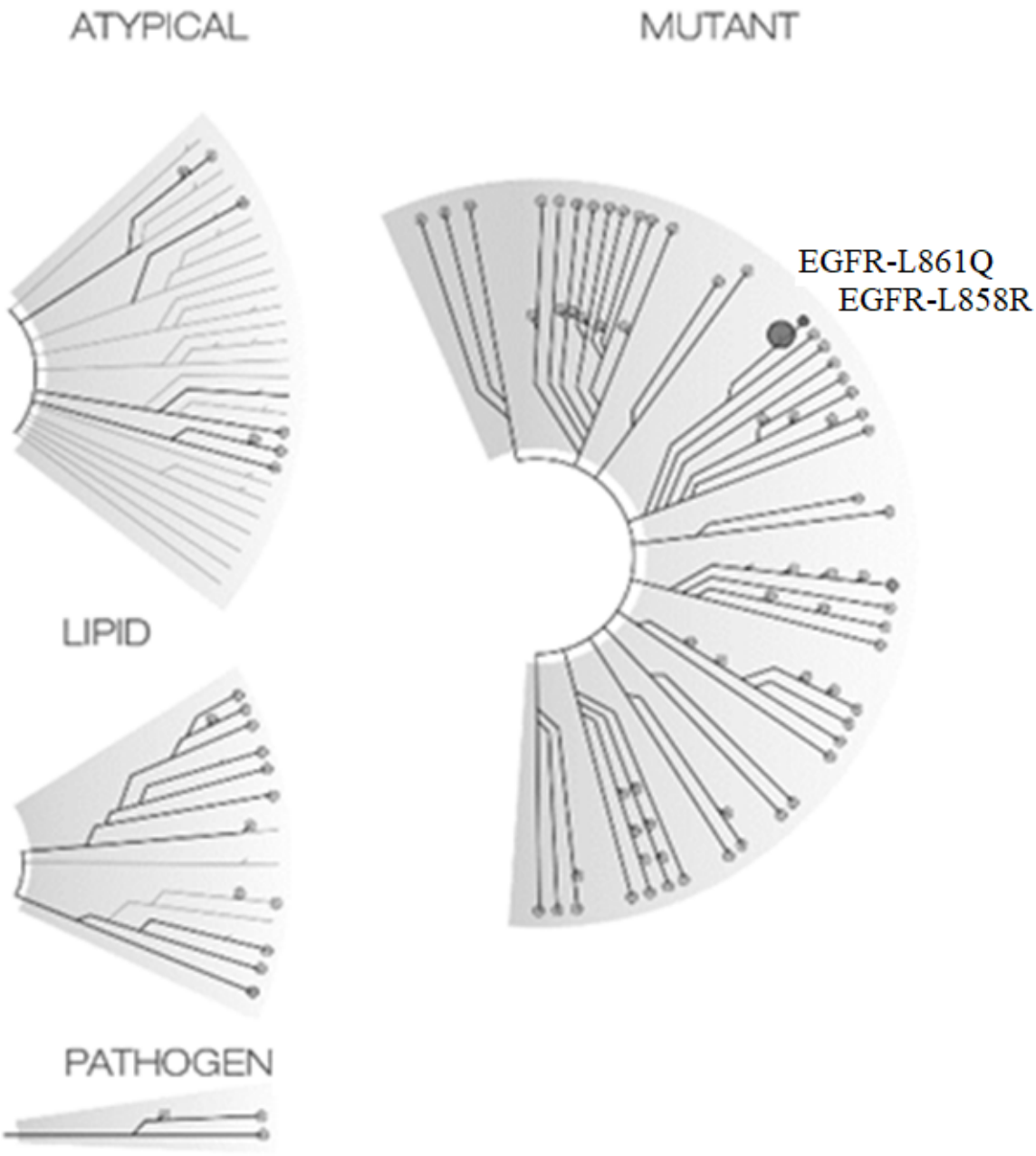


FIG. 13B

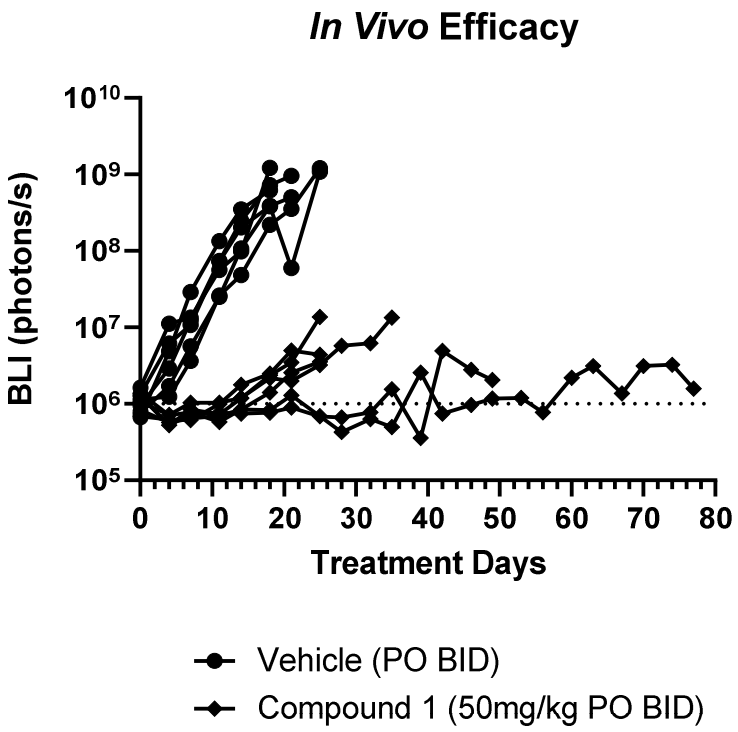

In Vivo Efficacy
BLI (photons/s)
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
0
10
20
30
40
50
60
70
80
Treatment Days
Vehicle (PO BID)
Compound 1 (50mg/kg PO BID)

FIG 14

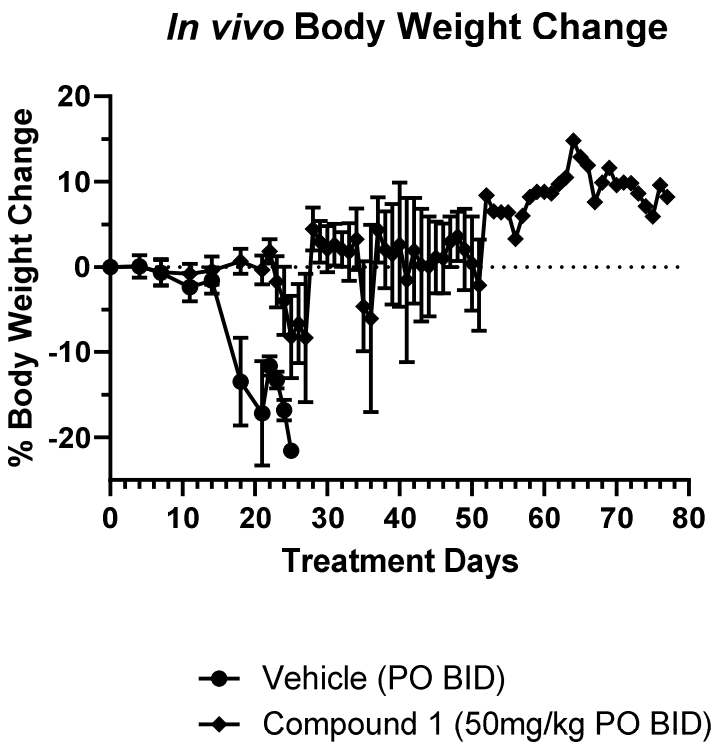

In vivo Body Weight Change
% Body Weight Change
20
10
0
-10
-20
0
10
20
30
40
50
60
70
80
Treatment Days
Vehicle (PO BID)
Compound 1 (50mg/kg PO BID)

FIG 15

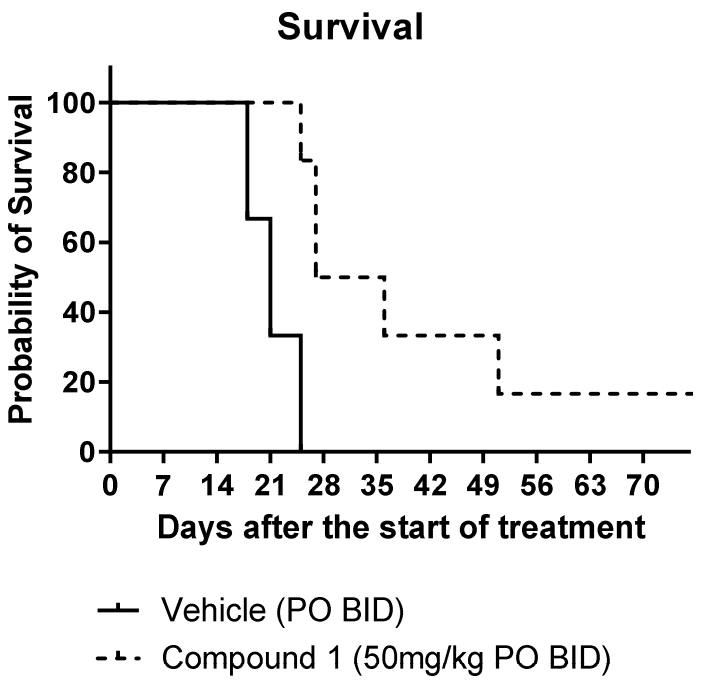

Survival
Probability of Survival
100
80
60
40
20
0
0 7 14 21 28 35 42 49 56 63 70
Days after the start of treatment
Vehicle (PO BID)
Compound 1 (50mg/kg PO BID)

FIG. 16



FIG. 17

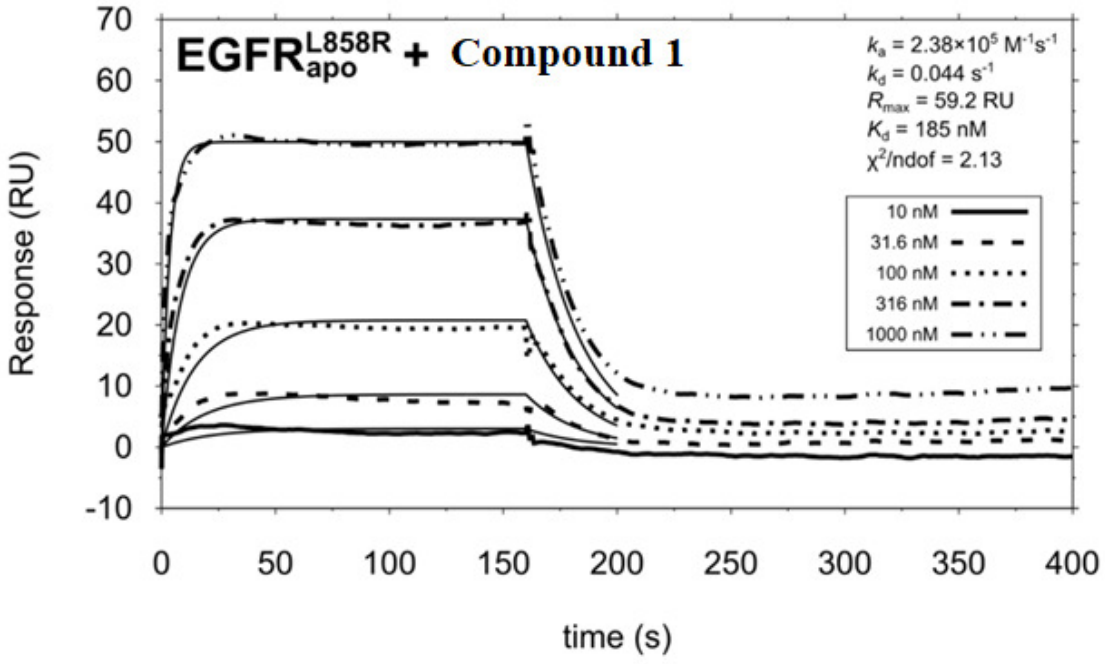


FIG. 18A

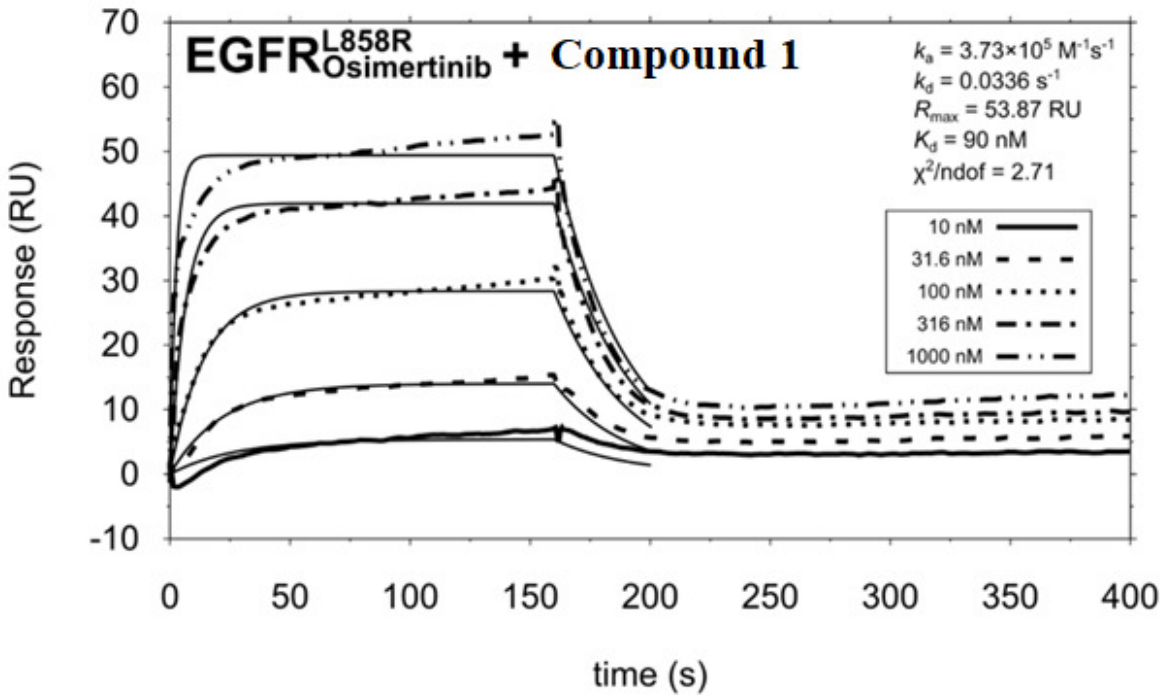


FIG. 18B

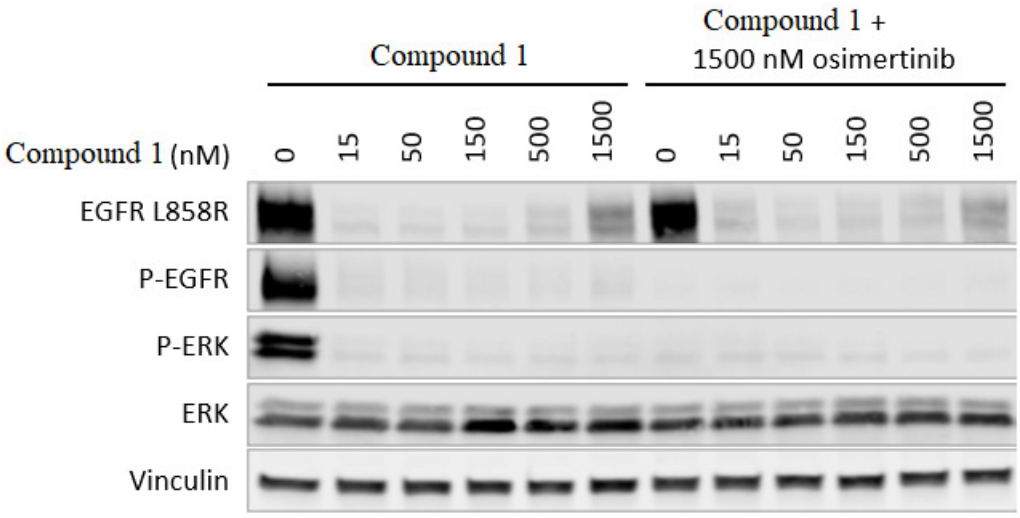

Compound 1
Compound 1 +
1500 nM osimertinib
Compound 1 (nM)
0
15
50
150
500
1500
0
15
50
150
500
1500
EGFR L858R
P-EGFR
P-ERK
ERK
Vinculin

FIG. 19