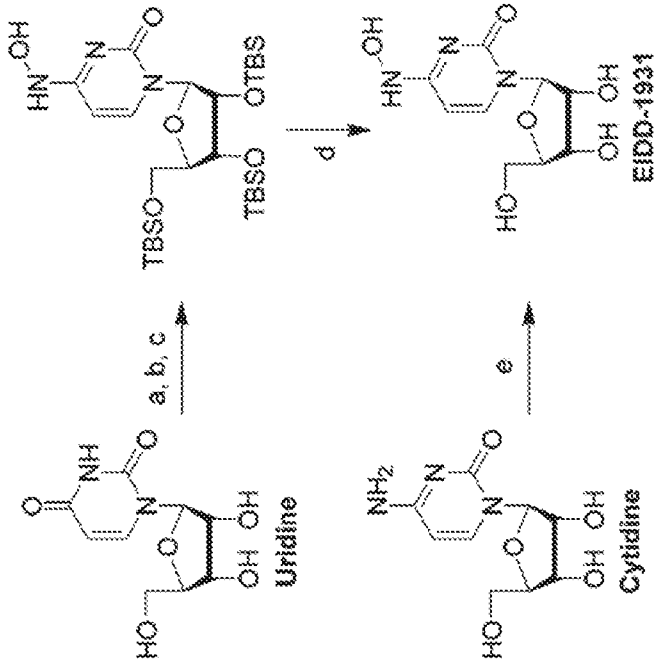

FIG. 1

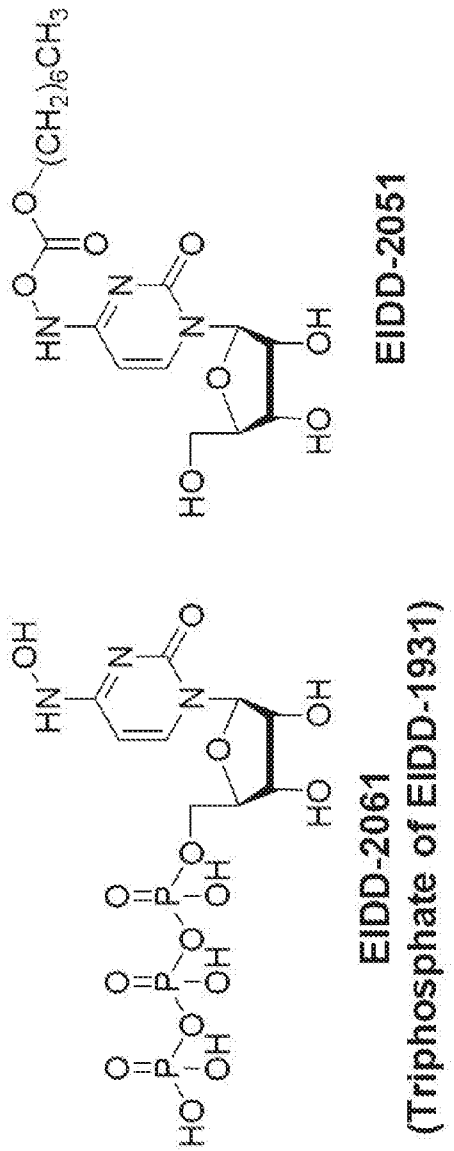

FIG. 2

W = CH2, CF2, CD2
Q = O, NH
R1 = H, F, Cl, Br, I, CH3, CF3, SMe, D, alkyl, alkenyl, allenyl, alkynyl
R2 = H, OH, CH3, alkyl, alkenyl, allenyl, alkynyl
R3 = OH, H, F, Cl
R4, R5 = H,
where X = CH2, O, S, or NH, and
lipid = n-C6H13 through C16H33
phospholipid,
phosphoramidate,
cycloSal phosphotriester
where R6 = H or OBn, and
lipid = n-C6H13 through C16H33

FIG. 3

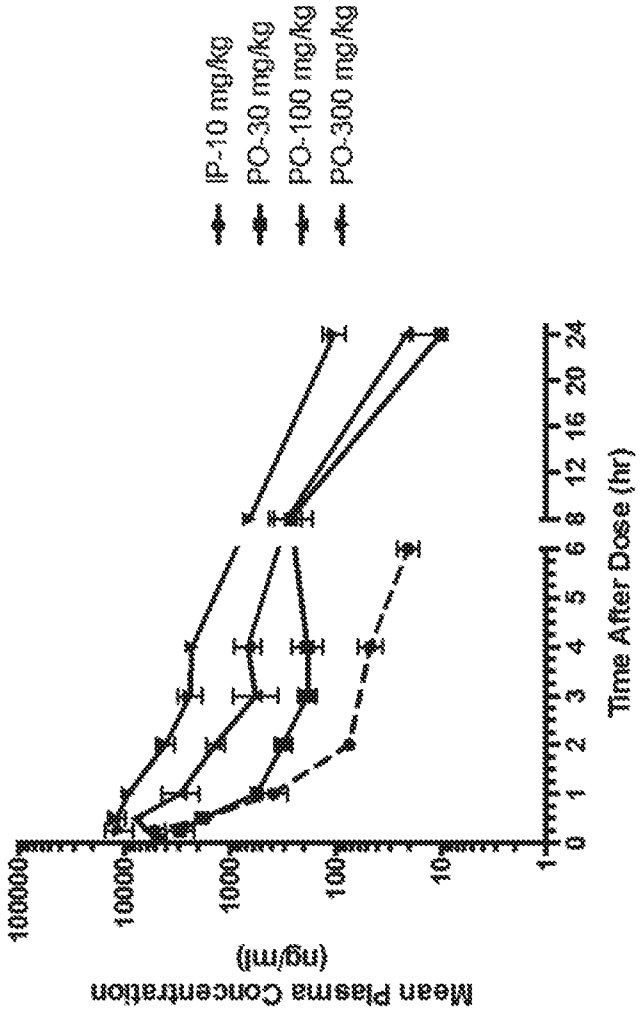
IP-10 mg/kg
PO-30 mg/kg
PO-100 mg/kg
PO-300 mg/kg
Mean Plasma Concentration (ng/ml)
100000
10000
1000
100
10
1
0 1 2 3 4 5 6 8 12 16 20 24
Time After Dose (hr)

FIG. 4

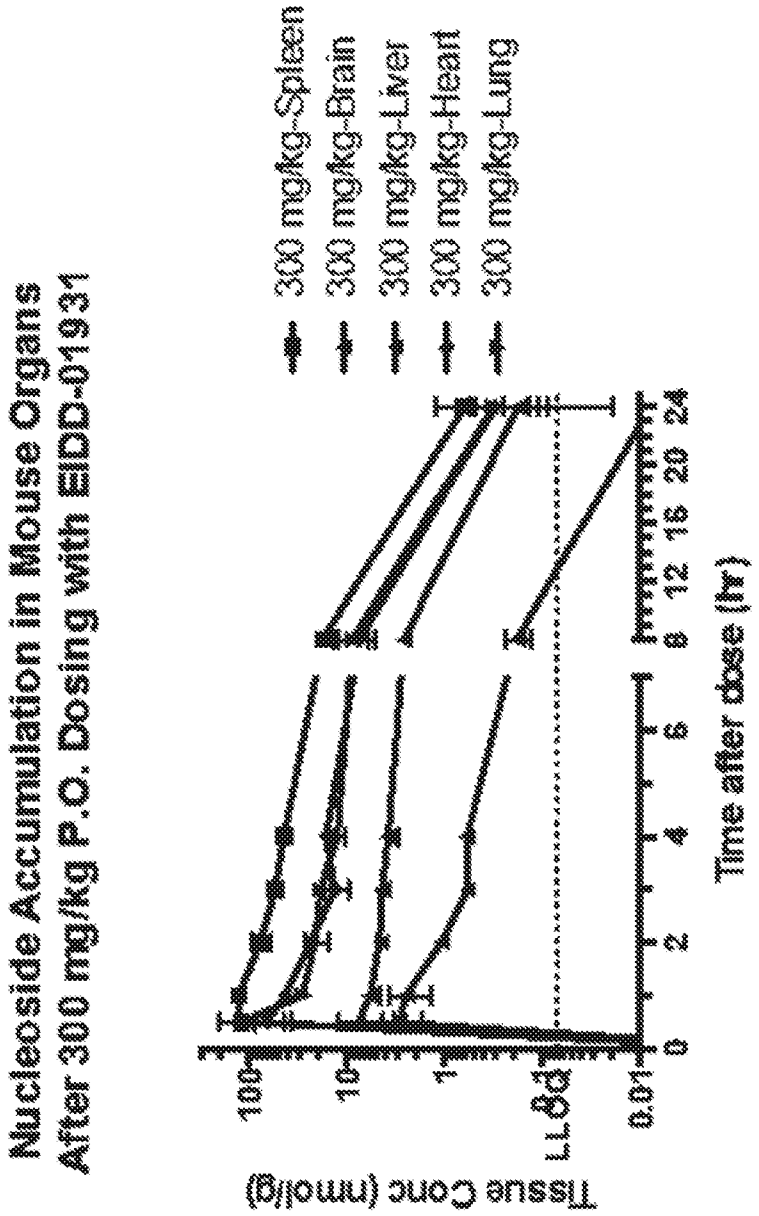
Nucleoside Accumulation in Mouse Organs
After 300 mg/kg P.O. Dosing with EIDD-01931
300 mg/kg-Spleen
300 mg/kg-Brain
300 mg/kg-Liver
300 mg/kg-Heart
300 mg/kg-Lung
Tissue Conc (nmol/g)
100
10
1
LLOQ
0.01
0
2
4
6
8
12
16
20
24
Time after dose (hr)

Fig. 5

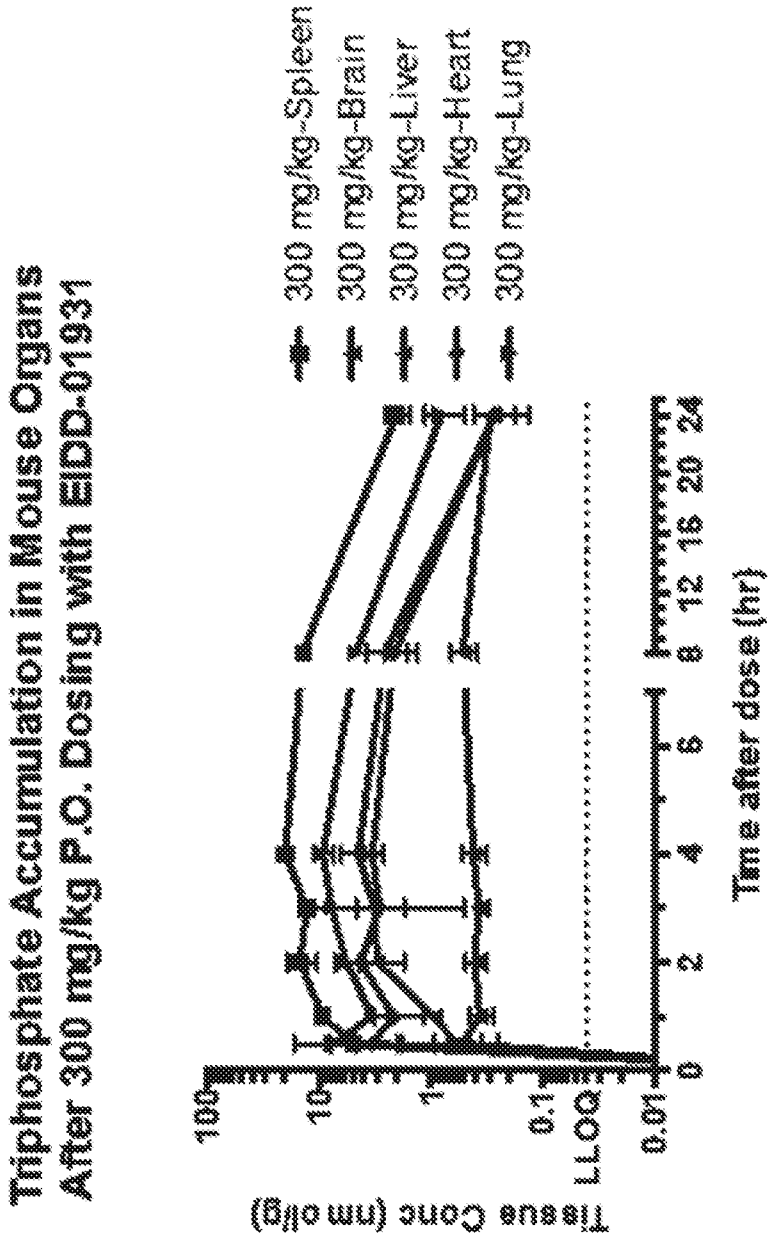
Triphosphate Accumulation in Mouse Organs
After 300 mg/kg P.O. Dosing with EIDD-01931
300 mg/kg-Spleen
300 mg/kg-Brain
300 mg/kg-Liver
300 mg/kg-Heart
300 mg/kg-Lung
Tissue Conc (nm o/g)
100
10
1
0.1
0.01
LLOQ
0
2
4
6
8
12
16
20
24
Time after dose (hr)

Fig. 6

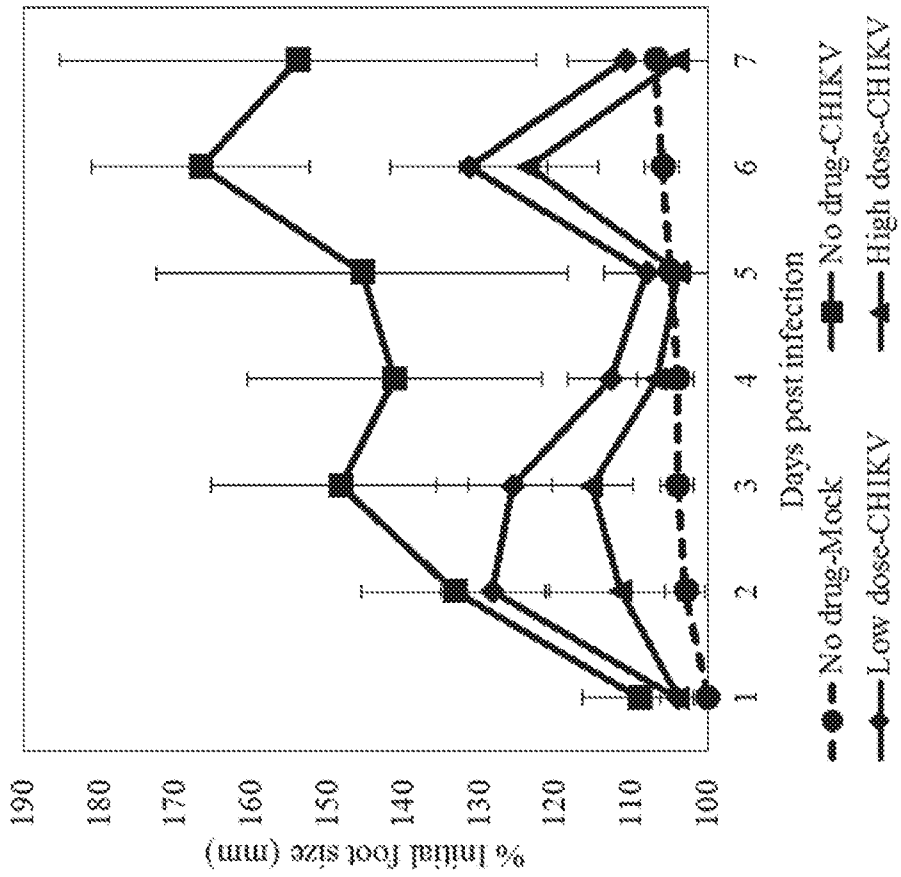
% Initial foot size (mm)
190
180
170
160
150
140
130
120
110
100
1
2
3
4
5
6
7
Days post infection
No drug-Mock
No drug-CHIKV
Low dose-CHIKV
High dose-CHIKV

Fig. 7

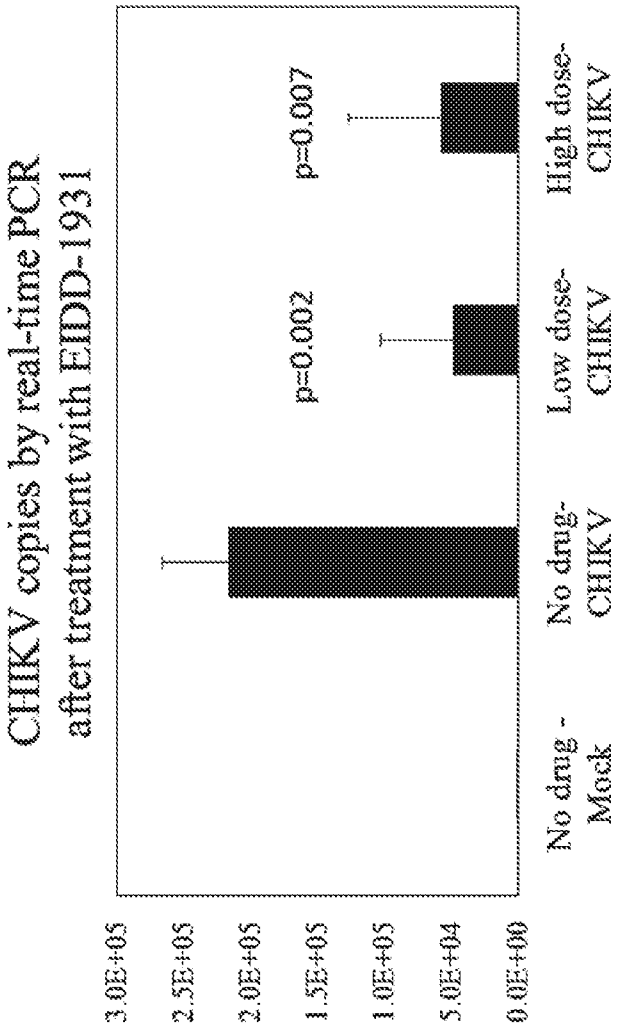
CHIKV copies by real-time PCR
after treatment with EIDD-1931
3.0E+05
2.5E+05
2.0E+05
1.5E+05
1.0E+05
5.0E+04
0.0E+00
p=0.002
p=0.007
No drug - Mock
No drug-CHIKV
Low dose-CHIKV
High dose-CHIKV

Fig. 8