Figure 1

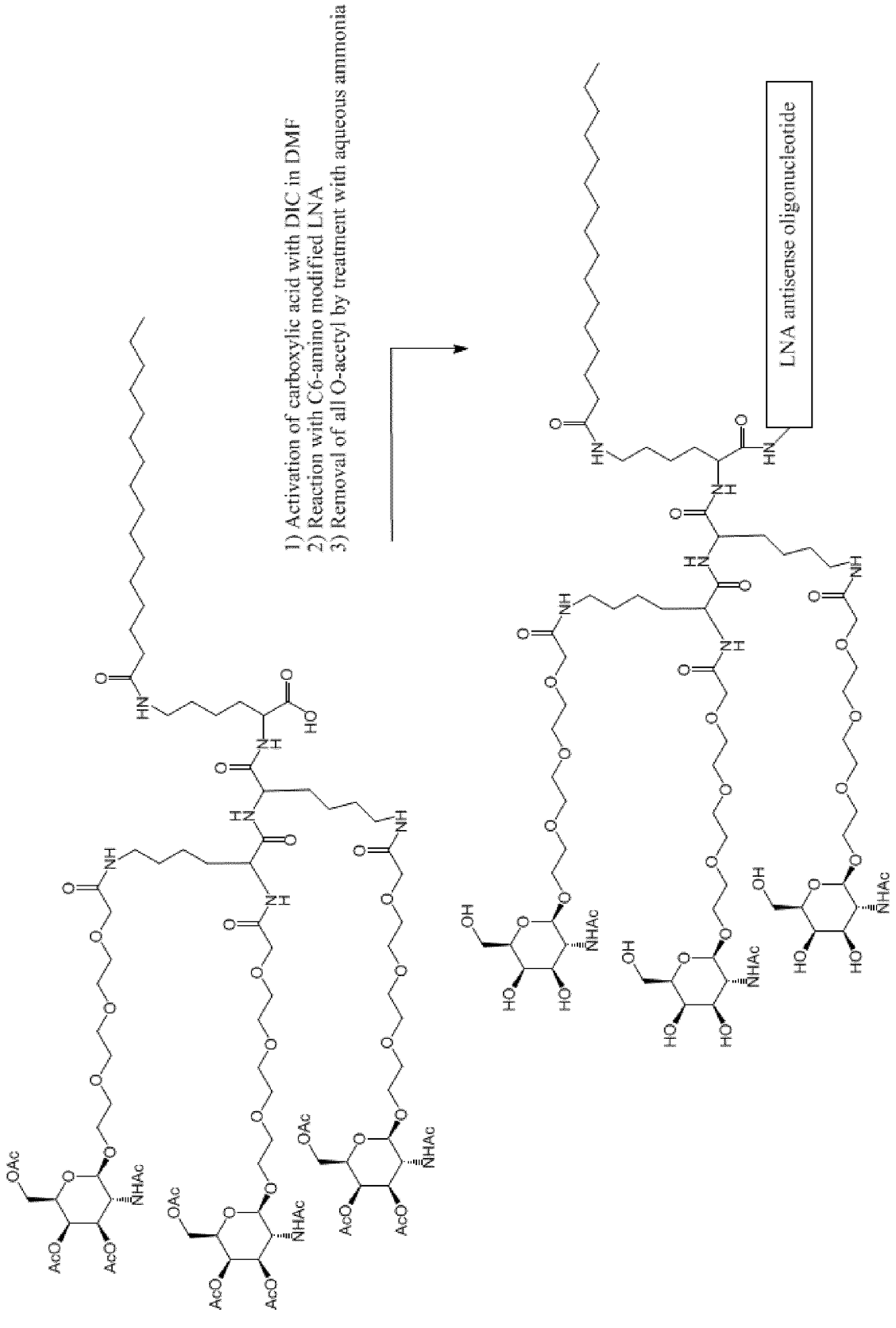

1) Activation of carboxylic acid with DIC in DMF
2) Reaction with C6-amino modified LNA
3) Removal of all O-acetyl by treatment with aqueous ammonia
LNA antisense oligonucleotide

Figure 2

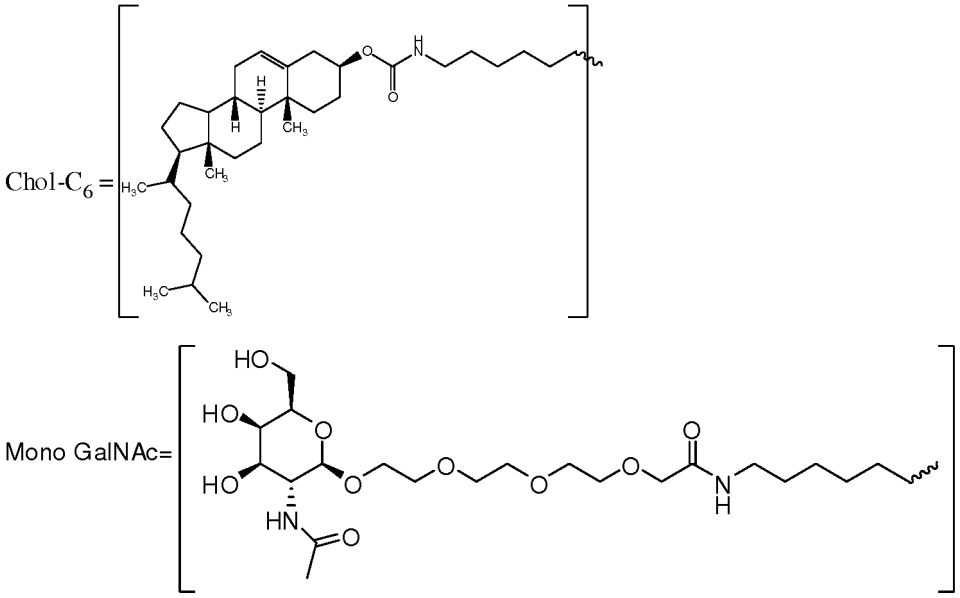


Figure 3

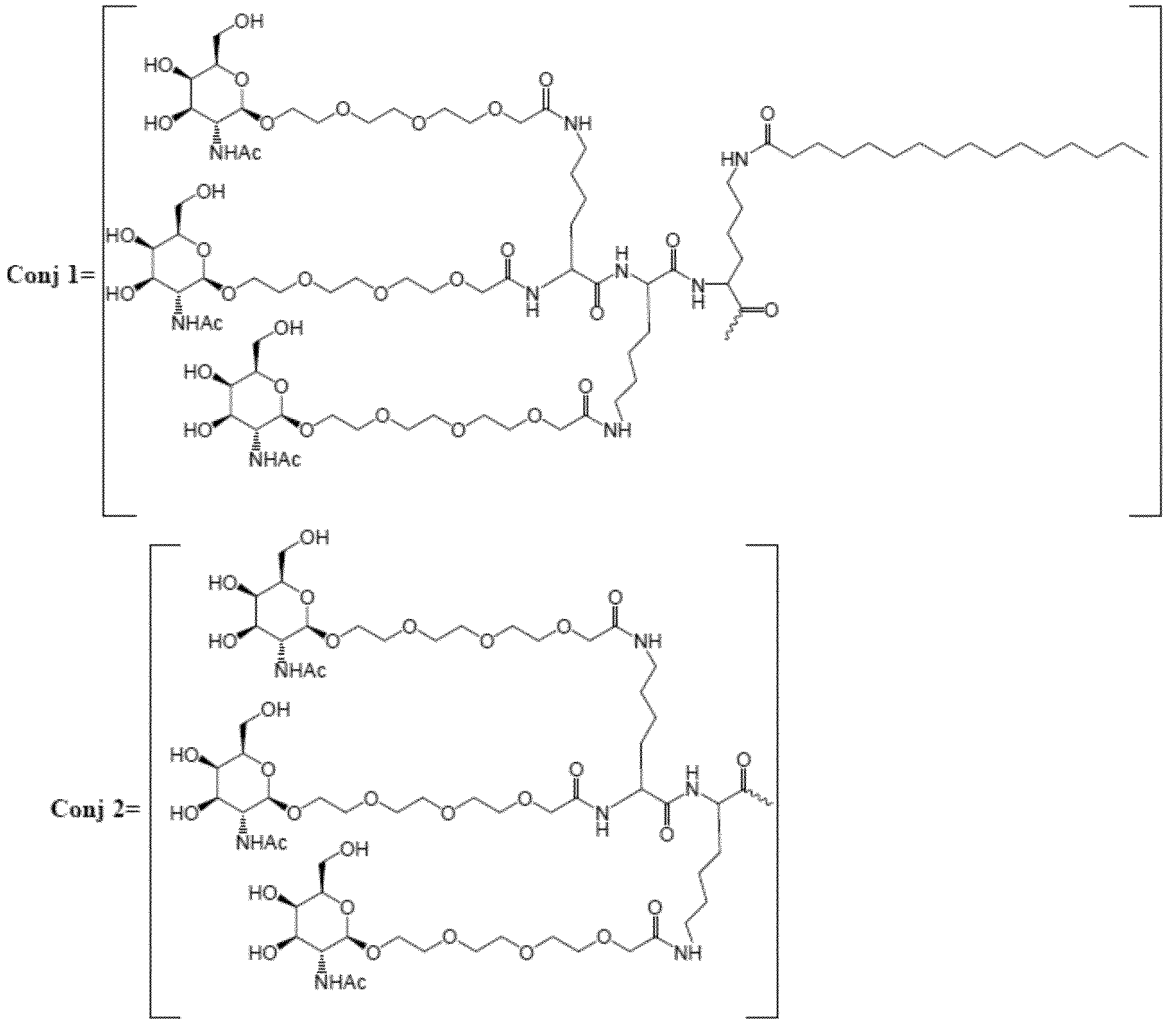
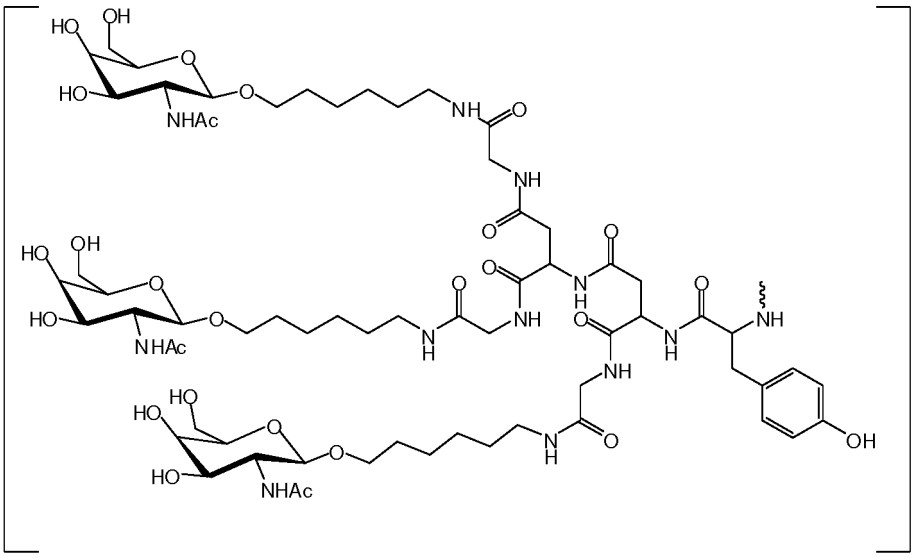


Figure 3 (cont)

Conj 3=



Conj 4=

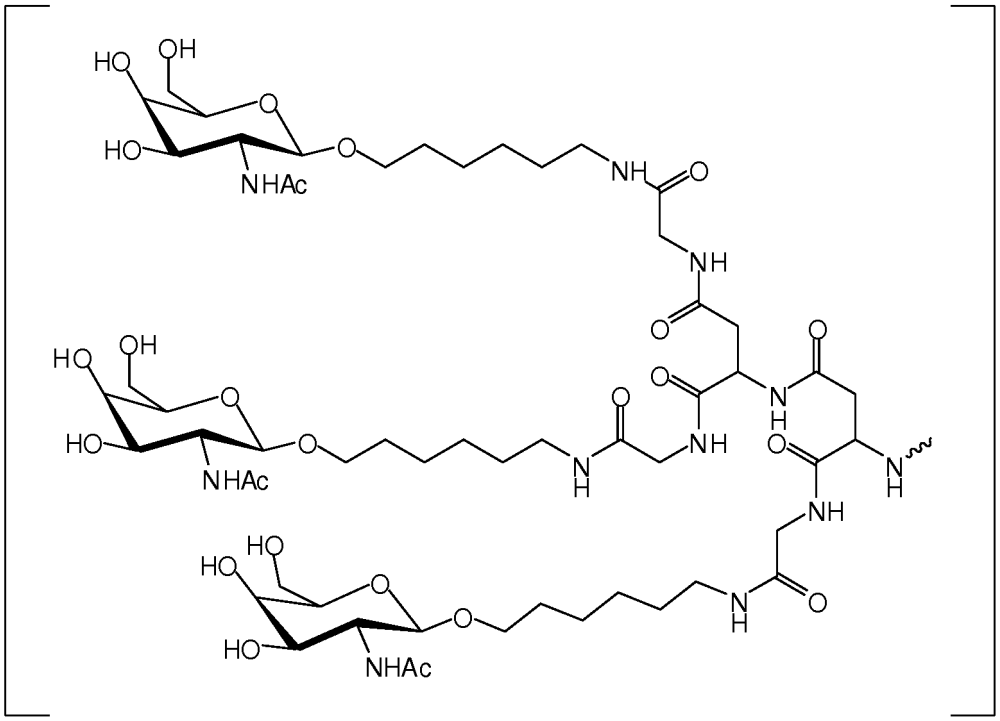
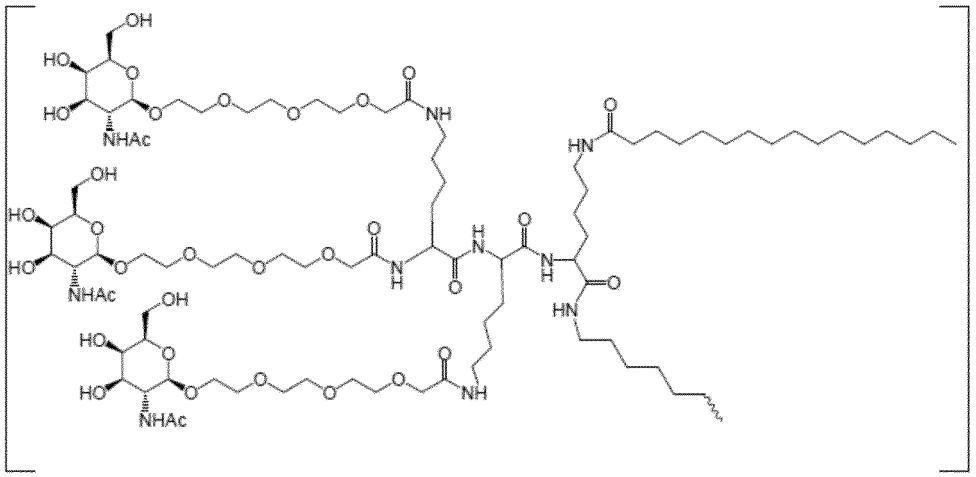


Figure 3 (cont)

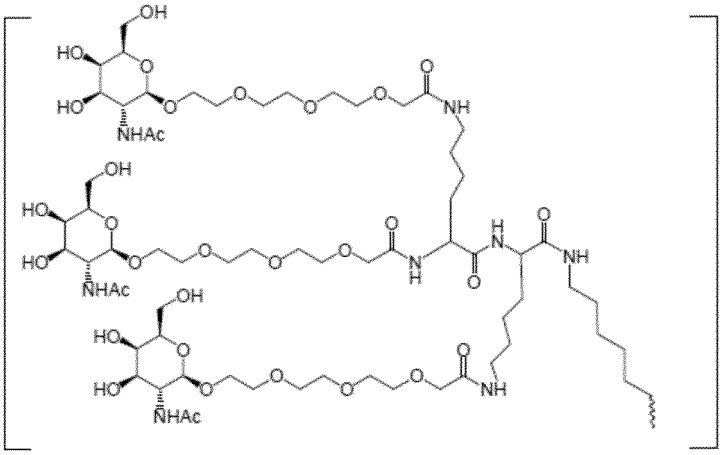
Conj 1a=

GalNAc1



Conj 2a=

GalNAc2



Conj 3a=

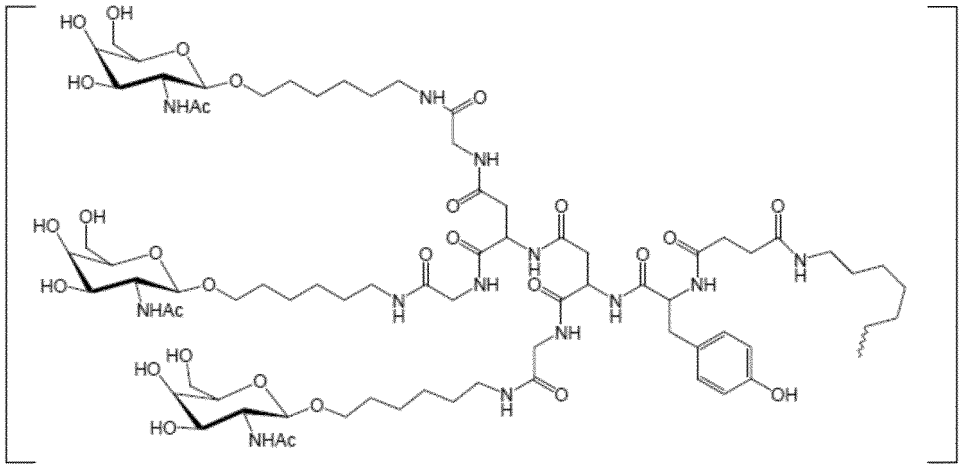


Figure 3 (cont)

Conj 4a=

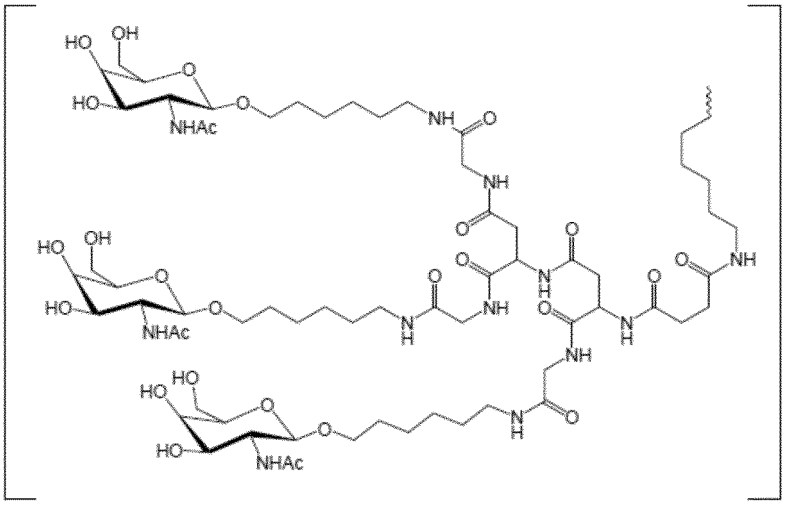


Figure 4

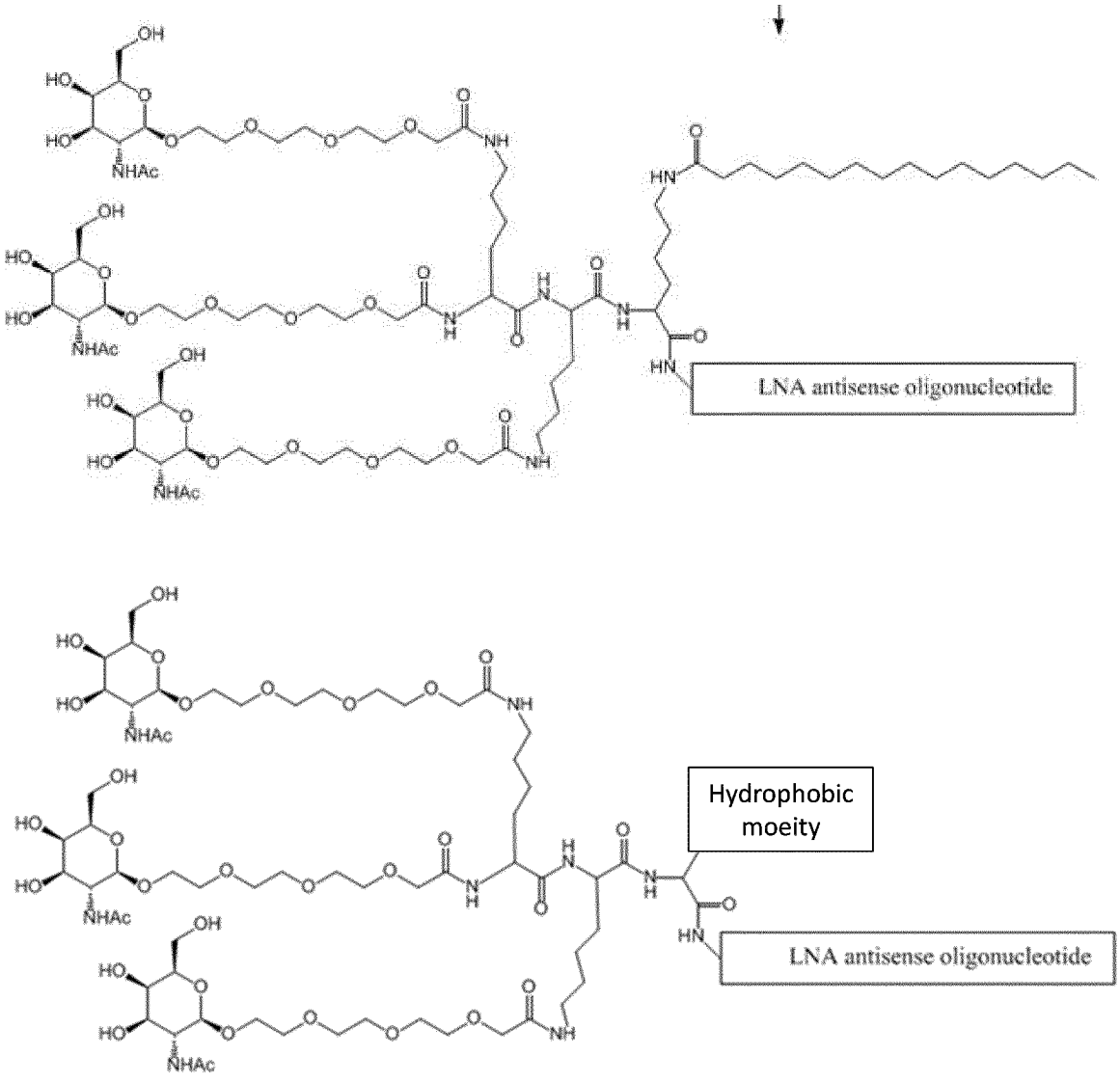
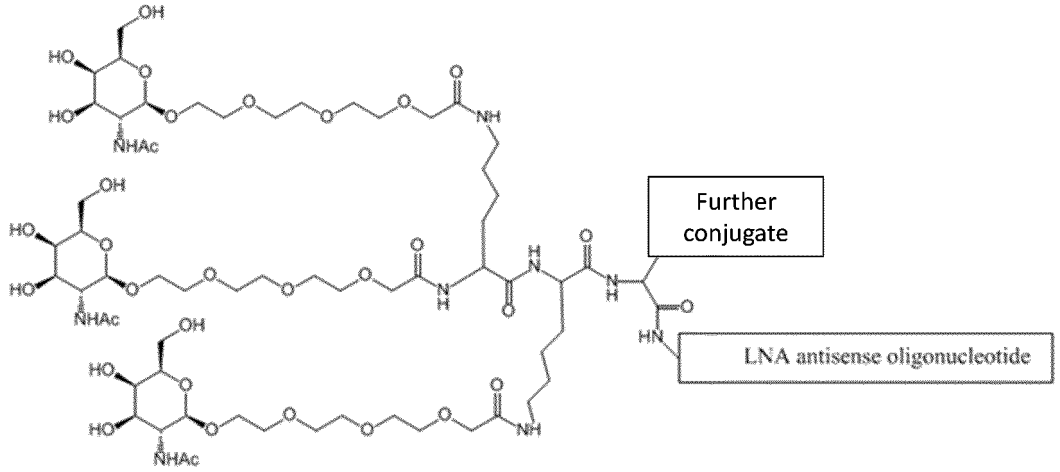


Figure 4 (Cont.)



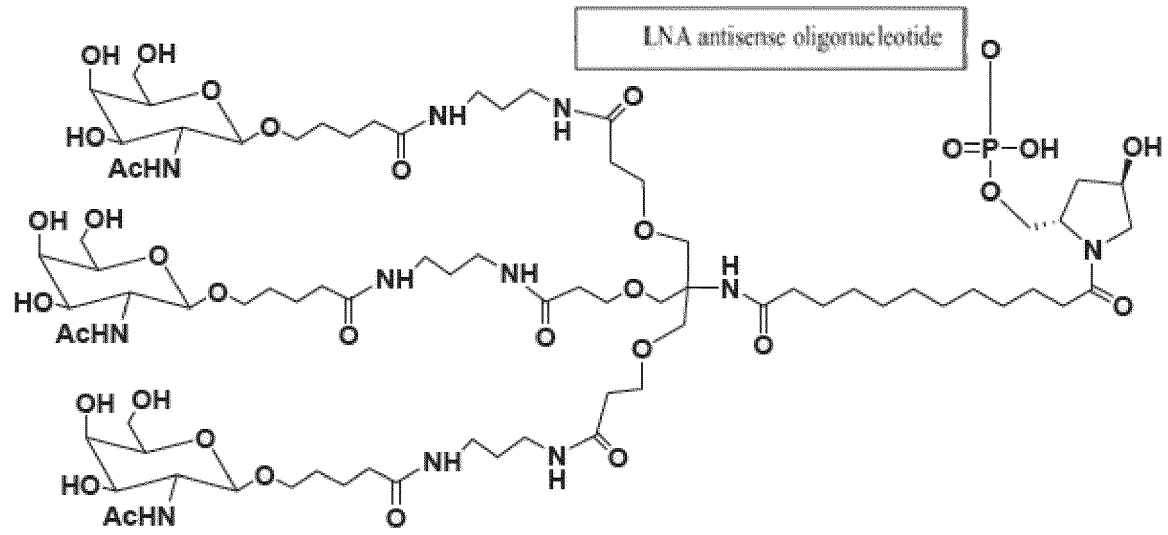
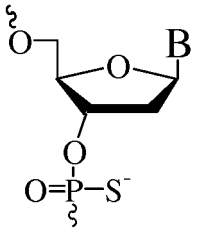
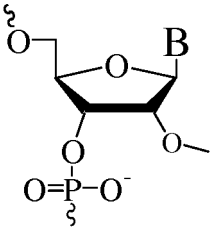


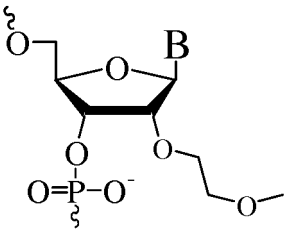
Figure 5



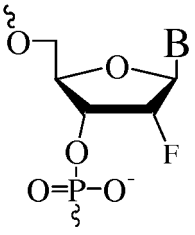
Phosphorthioate



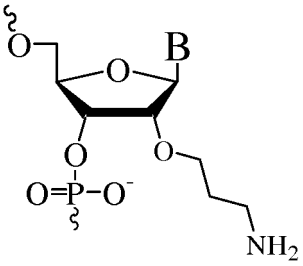
2'-O-Methyl



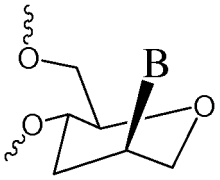
2'-MOE



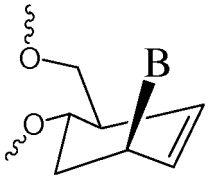
2'-Fluoro



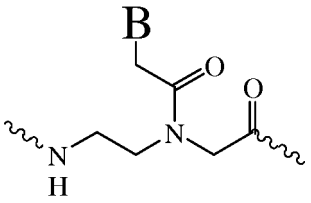
2'-AP



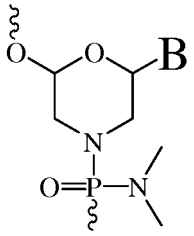
HNA



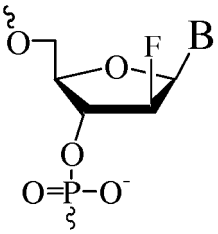
CeNA



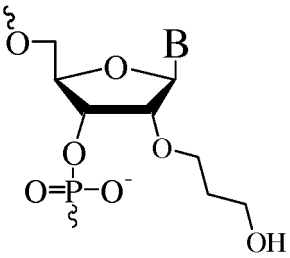
PNA



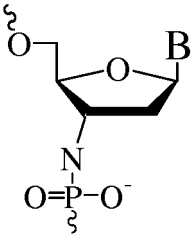
Morpholino



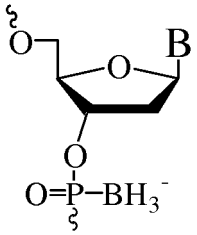
2'-F-ANA



2'-(3-hydroxy)propyl



3'-Phosphoramidate



Boranophosphates

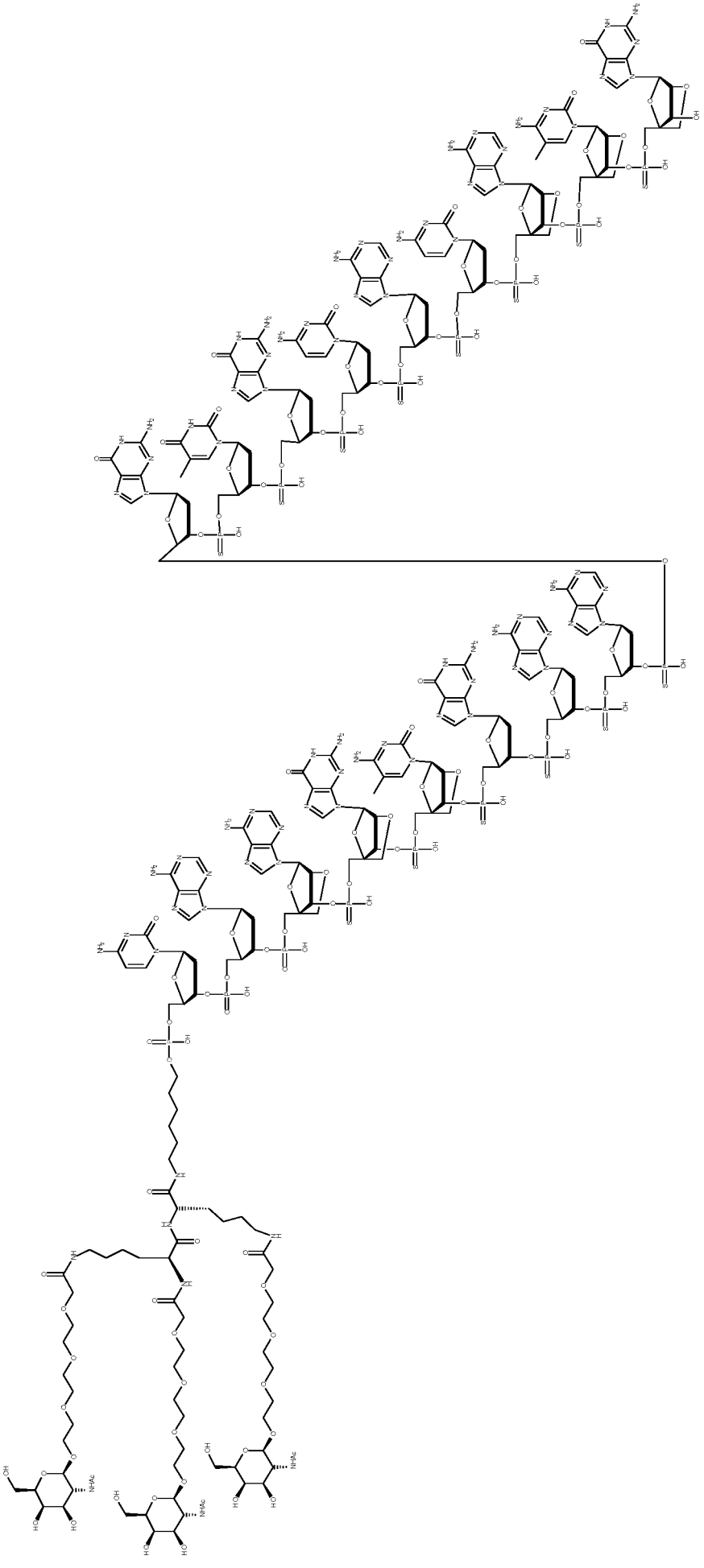


Figure 6
SEQ ID NO: 808

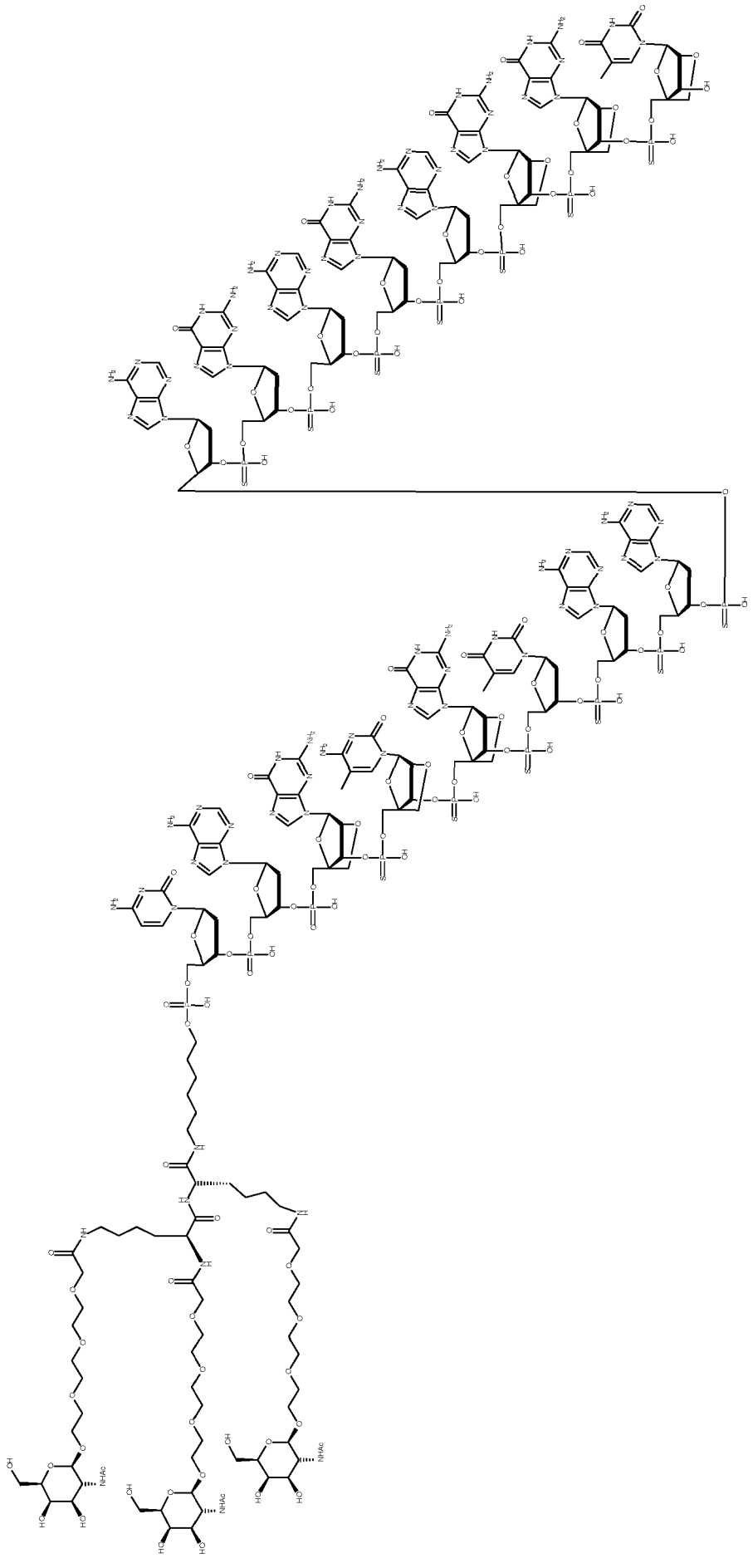


Figure 7
SEQ ID NO: 814

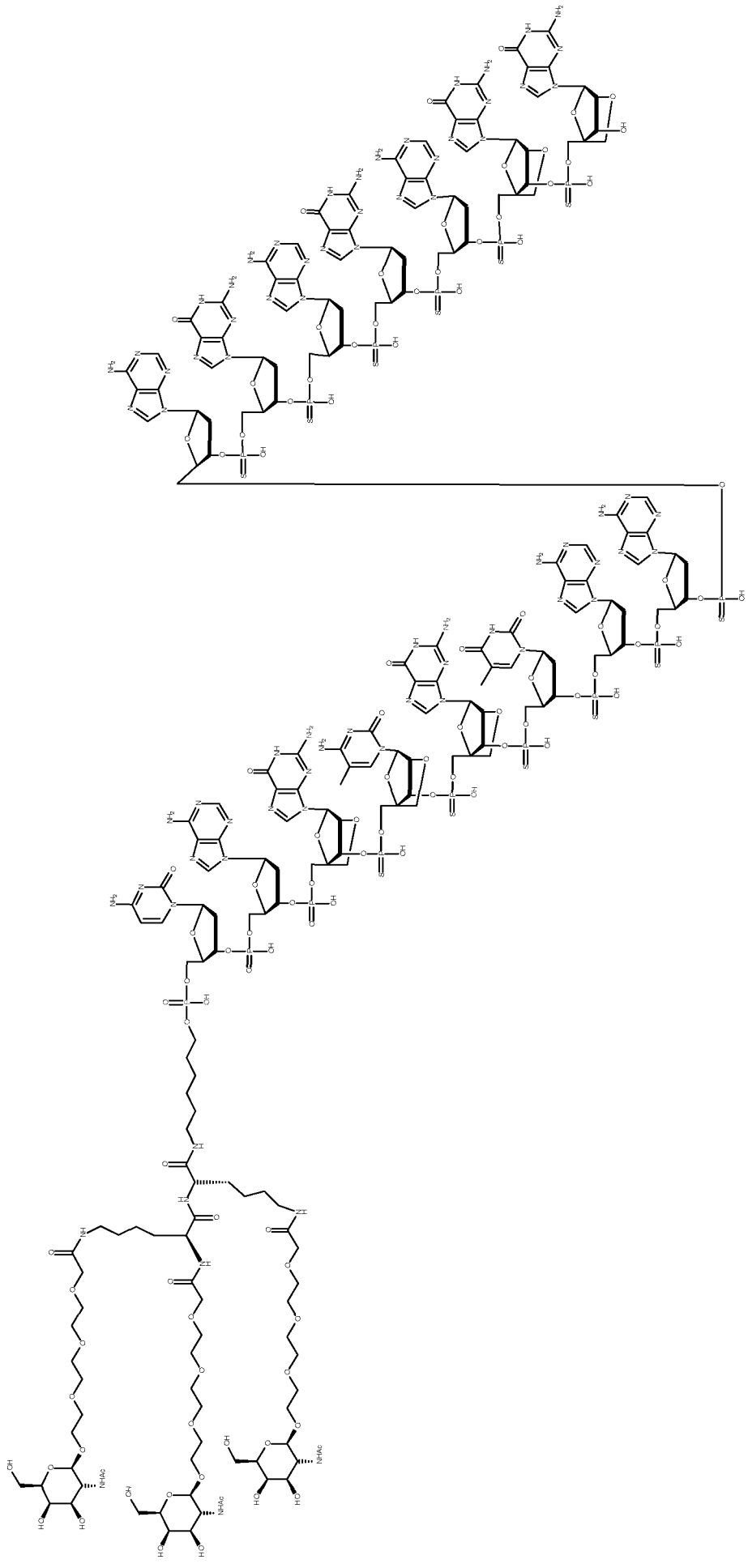


Figure 8
SEQ ID NO: 815

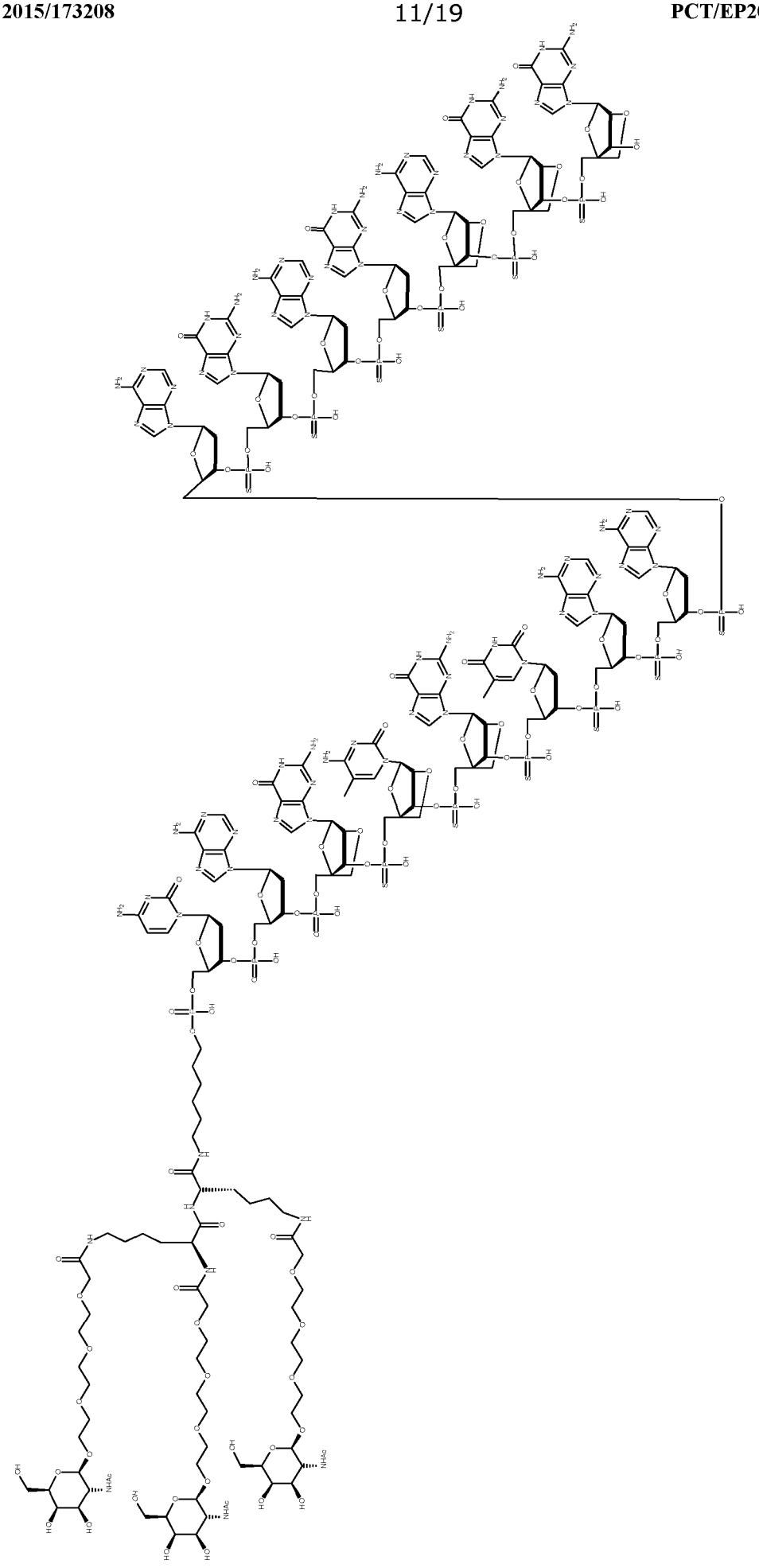


Figure 9
SEQ ID NO: 825

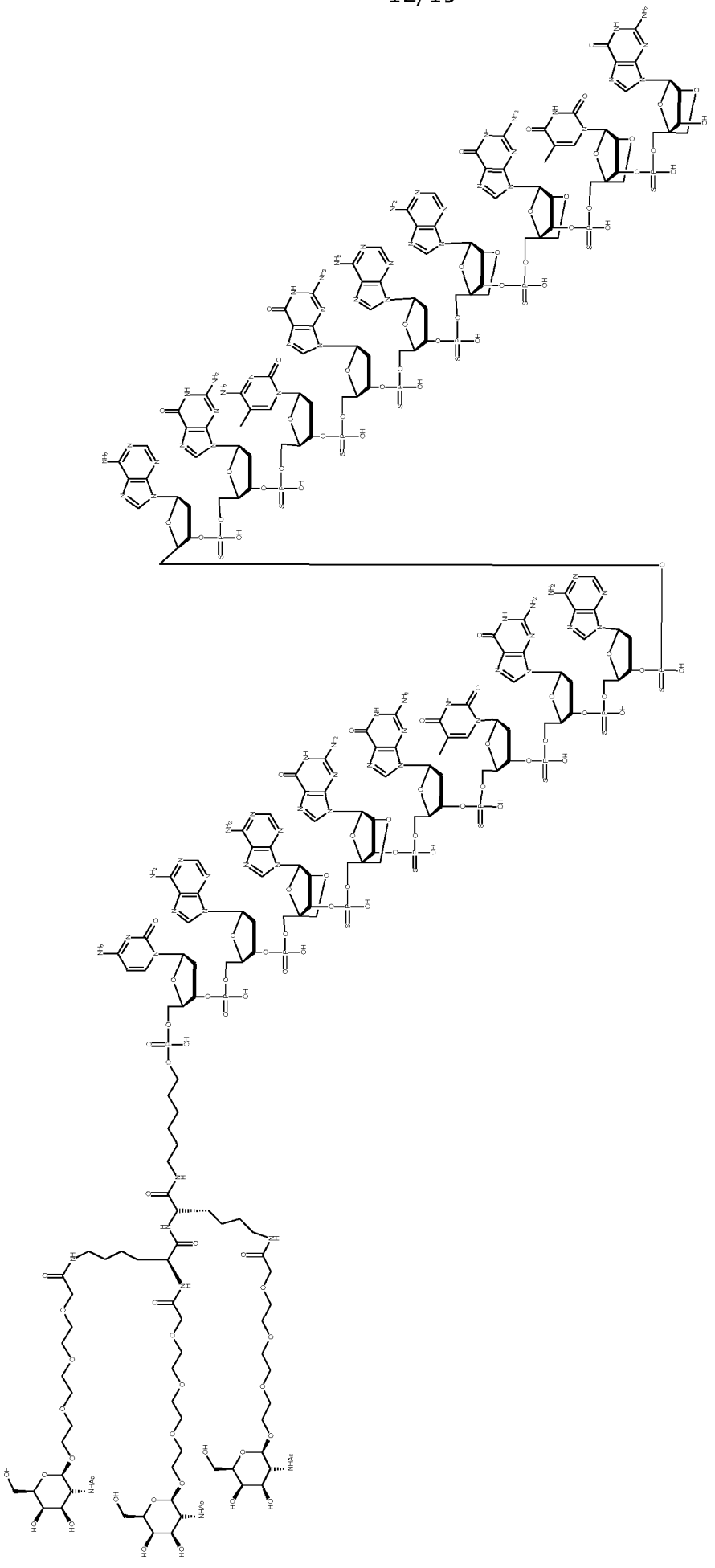


Figure 10
SEQ ID NO: 826

Figure 11

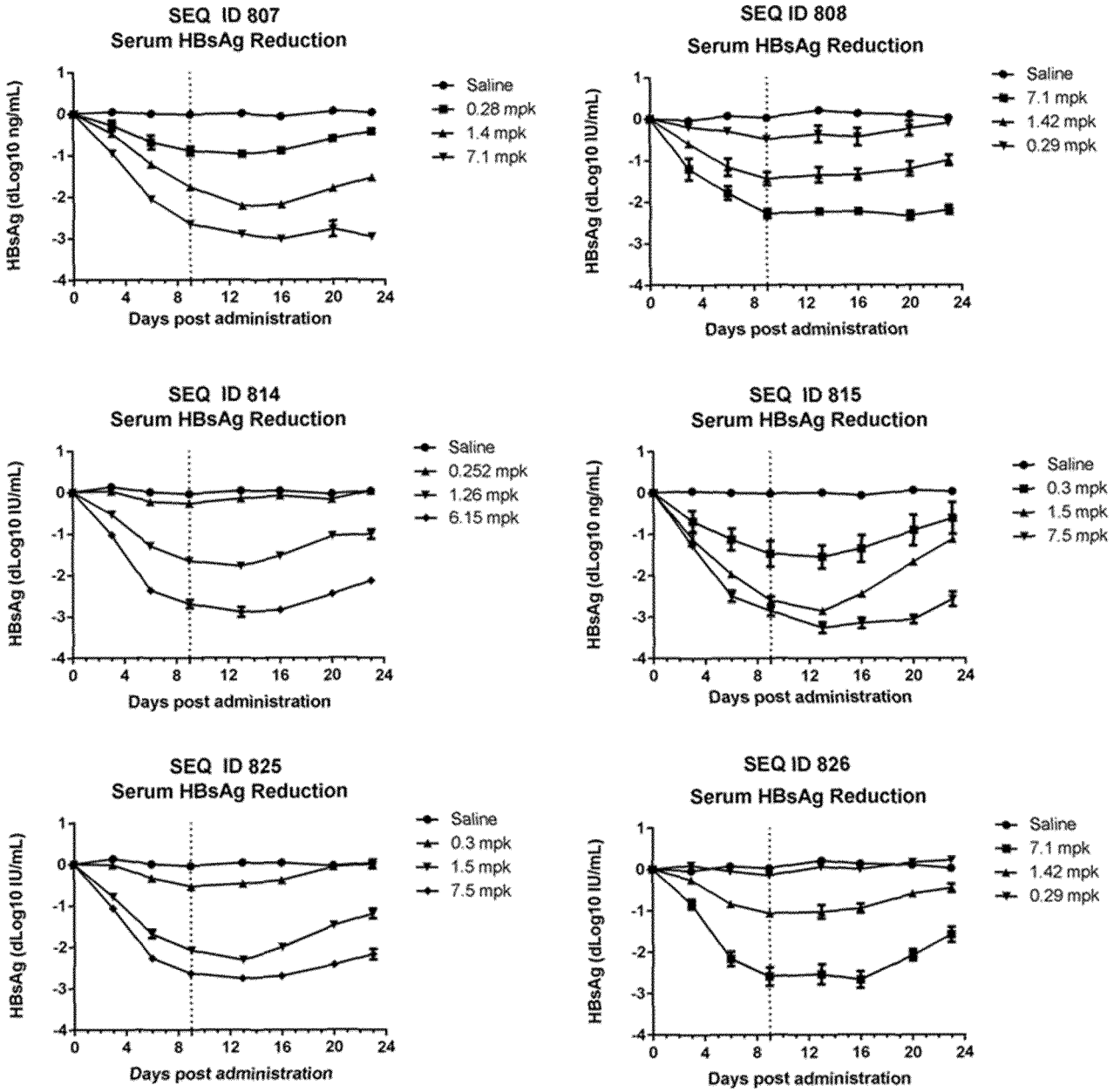

SEQ ID 807
Serum HBsAg Reduction
HBsAg (dLog10 ng/mL)
Days post administration
Saline
0.28 mpk
1.4 mpk
7.1 mpk
SEQ ID 808
Serum HBsAg Reduction
HBsAg (dLog10 IU/mL)
Days post administration
Saline
7.1 mpk
1.42 mpk
0.29 mpk
SEQ ID 814
Serum HBsAg Reduction
HBsAg (dLog10 IU/mL)
Days post administration
Saline
0.252 mpk
1.26 mpk
6.15 mpk
SEQ ID 815
Serum HBsAg Reduction
HBsAg (dLog10 ng/mL)
Days post administration
Saline
0.3 mpk
1.5 mpk
7.5 mpk
SEQ ID 825
Serum HBsAg Reduction
HBsAg (dLog10 IU/mL)
Days post administration
Saline
0.3 mpk
1.5 mpk
7.5 mpk
SEQ ID 826
Serum HBsAg Reduction
HBsAg (dLog10 IU/mL)
Days post administration
Saline
7.1 mpk
1.42 mpk
0.29 mpk

Figure 12

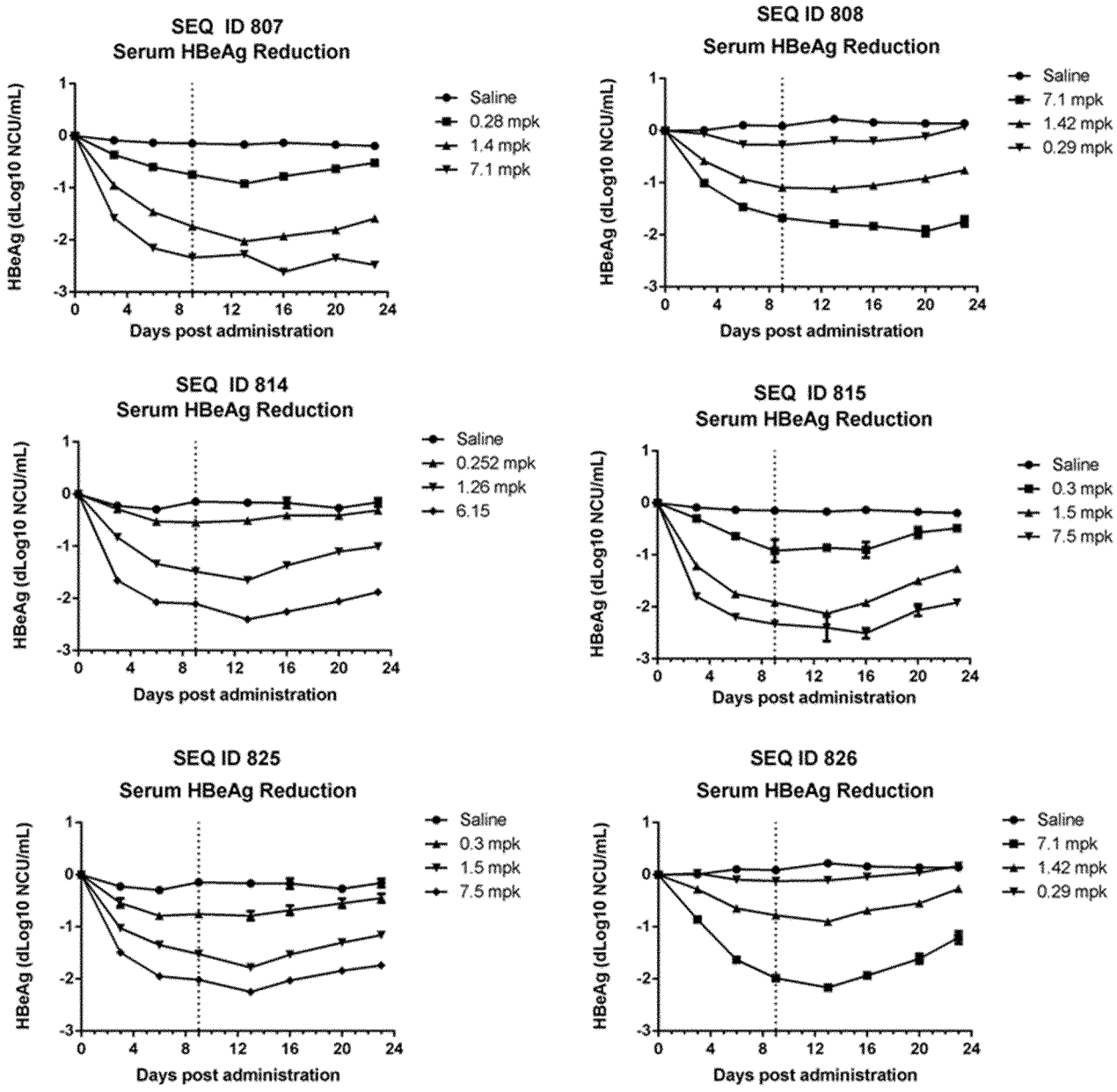

SEQ ID 807
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
0.28 mpk
1.4 mpk
7.1 mpk
SEQ ID 808
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
7.1 mpk
1.42 mpk
0.29 mpk
SEQ ID 814
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
0.252 mpk
1.26 mpk
6.15
SEQ ID 815
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
0.3 mpk
1.5 mpk
7.5 mpk
SEQ ID 825
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
0.3 mpk
1.5 mpk
7.5 mpk
SEQ ID 826
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
7.1 mpk
1.42 mpk
0.29 mpk

Figure 13

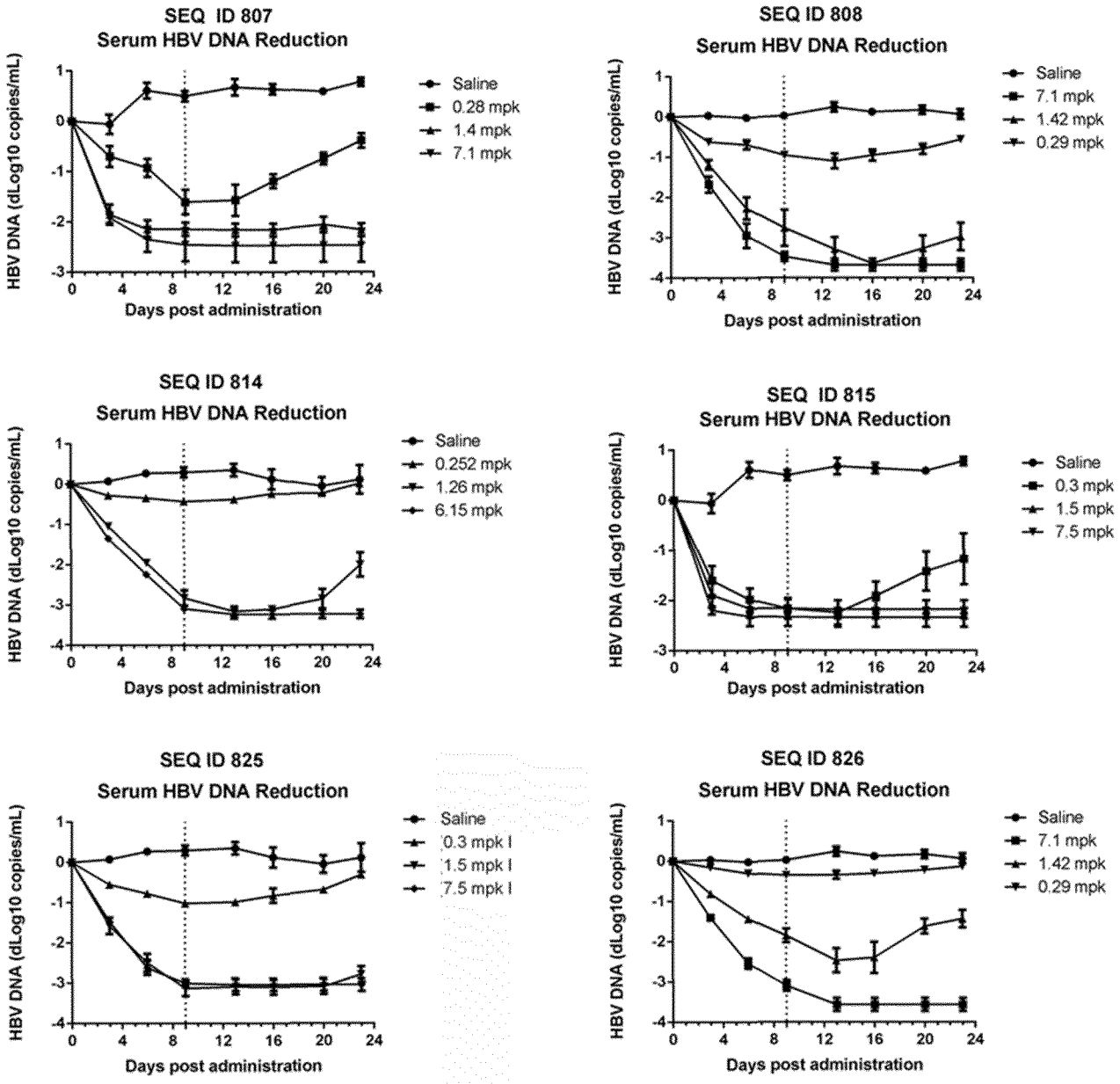
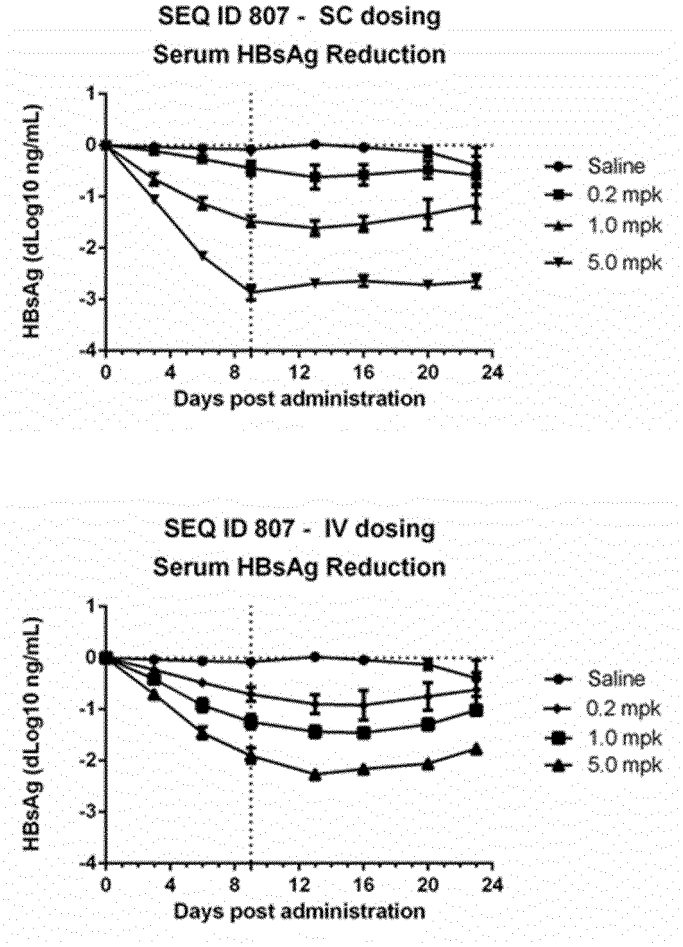

SEQ ID 807
Serum HBV DNA Reduction
HBV DNA (dLog10 copies/mL)
Days post administration
Saline
0.28 mpk
1.4 mpk
7.1 mpk
SEQ ID 808
Serum HBV DNA Reduction
HBV DNA (dLog10 copies/mL)
Days post administration
Saline
7.1 mpk
1.42 mpk
0.29 mpk
SEQ ID 814
Serum HBV DNA Reduction
HBV DNA (dLog10 copies/mL)
Days post administration
Saline
0.252 mpk
1.26 mpk
6.15 mpk
SEQ ID 815
Serum HBV DNA Reduction
HBV DNA (dLog10 copies/mL)
Days post administration
Saline
0.3 mpk
1.5 mpk
7.5 mpk
SEQ ID 825
Serum HBV DNA Reduction
HBV DNA (dLog10 copies/mL)
Days post administration
Saline
0.3 mpk I
1.5 mpk I
7.5 mpk I
SEQ ID 826
Serum HBV DNA Reduction
HBV DNA (dLog10 copies/mL)
Days post administration
Saline
7.1 mpk
1.42 mpk
0.29 mpk

Figure 14

A)


SEQ ID 807 - SC dosing
Serum HBsAg Reduction
HBsAg (dLog10 ng/mL)
Days post administration
Saline
0.2 mpk
1.0 mpk
5.0 mpk
SEQ ID 807 - IV dosing
Serum HBsAg Reduction
HBsAg (dLog10 ng/mL)
Days post administration
Saline
0.2 mpk
1.0 mpk
5.0 mpk

B)

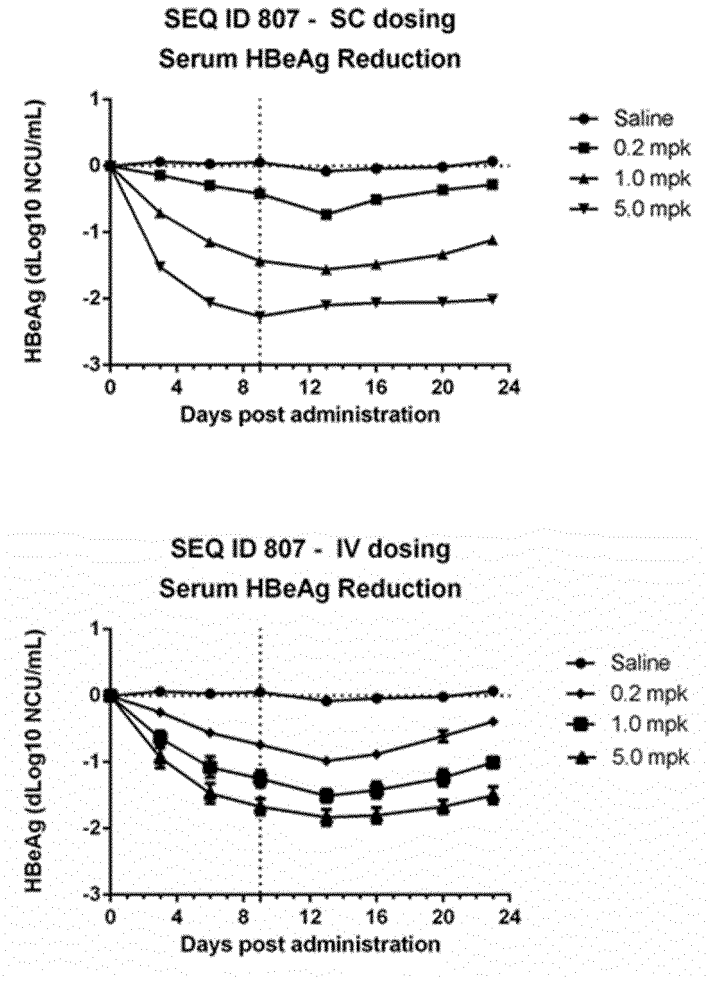
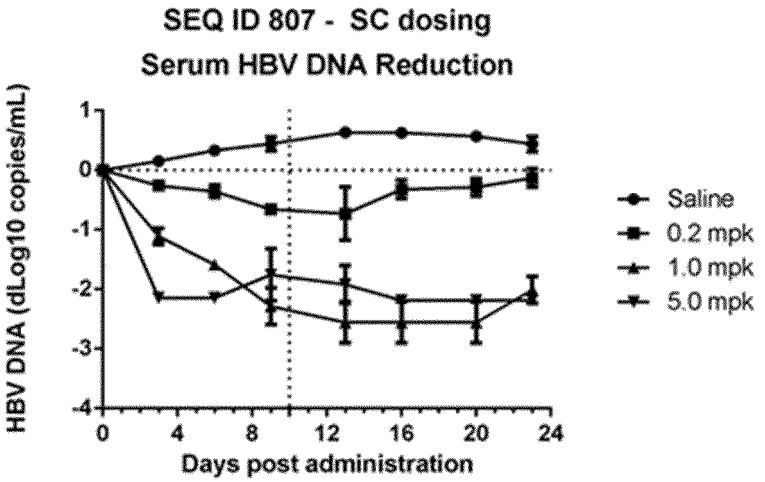

SEQ ID 807 - SC dosing
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
0.2 mpk
1.0 mpk
5.0 mpk
SEQ ID 807 - IV dosing
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
Days post administration
Saline
0.2 mpk
1.0 mpk
5.0 mpk

Figure 14 Cont'd

C



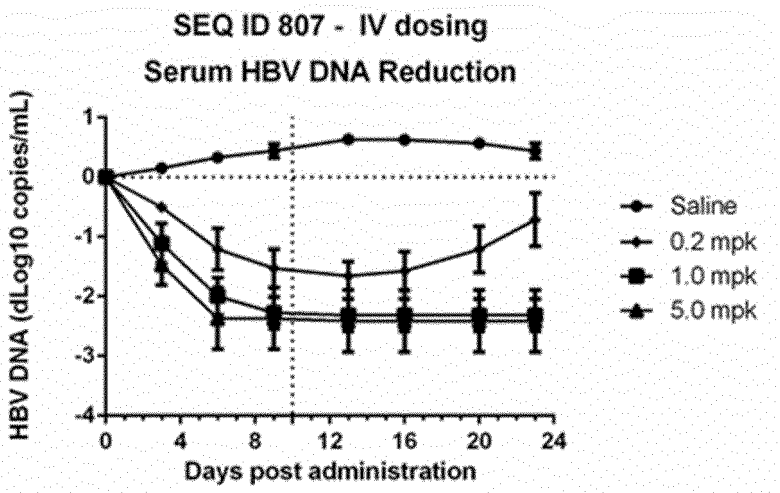
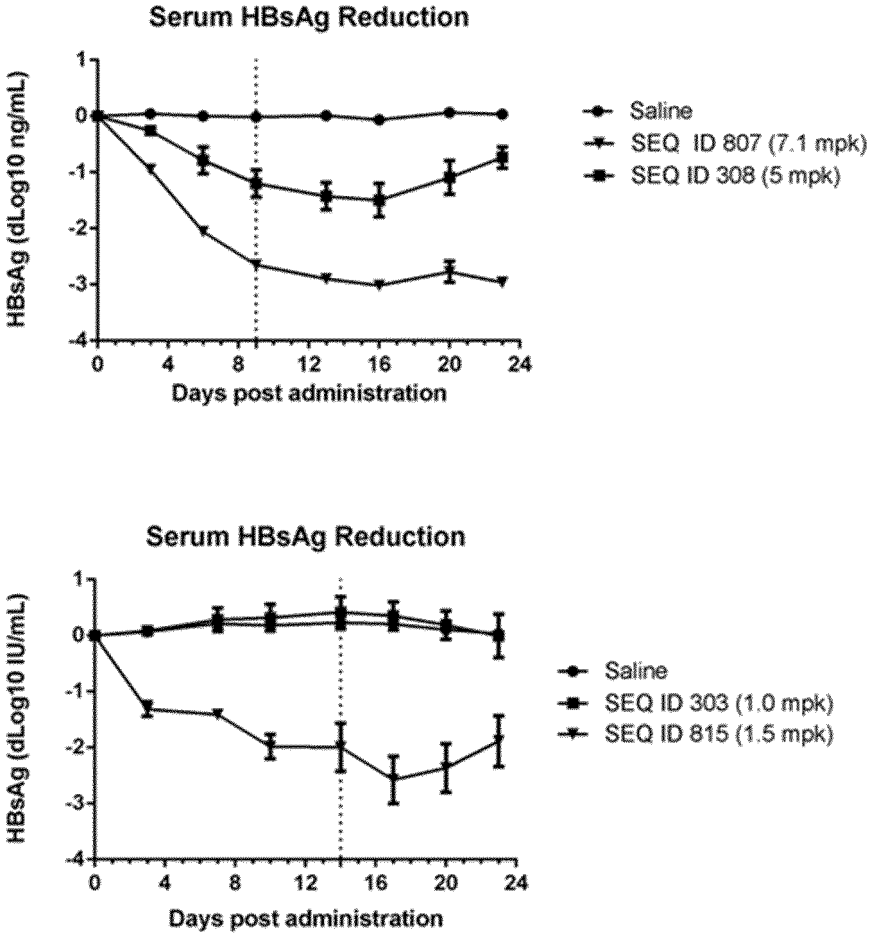


Figure 15

A)


Serum HBsAg Reduction
HBsAg (dLog10 ng/mL)
1
0
-1
-2
-3
-4
0
4
8
12
16
20
24
Days post administration
Saline
SEQ ID 807 (7.1 mpk)
SEQ ID 308 (5 mpk)
Serum HBsAg Reduction
HBsAg (dLog10 IU/mL)
1
0
-1
-2
-3
-4
0
4
8
12
16
20
24
Days post administration
Saline
SEQ ID 303 (1.0 mpk)
SEQ ID 815 (1.5 mpk)

B)

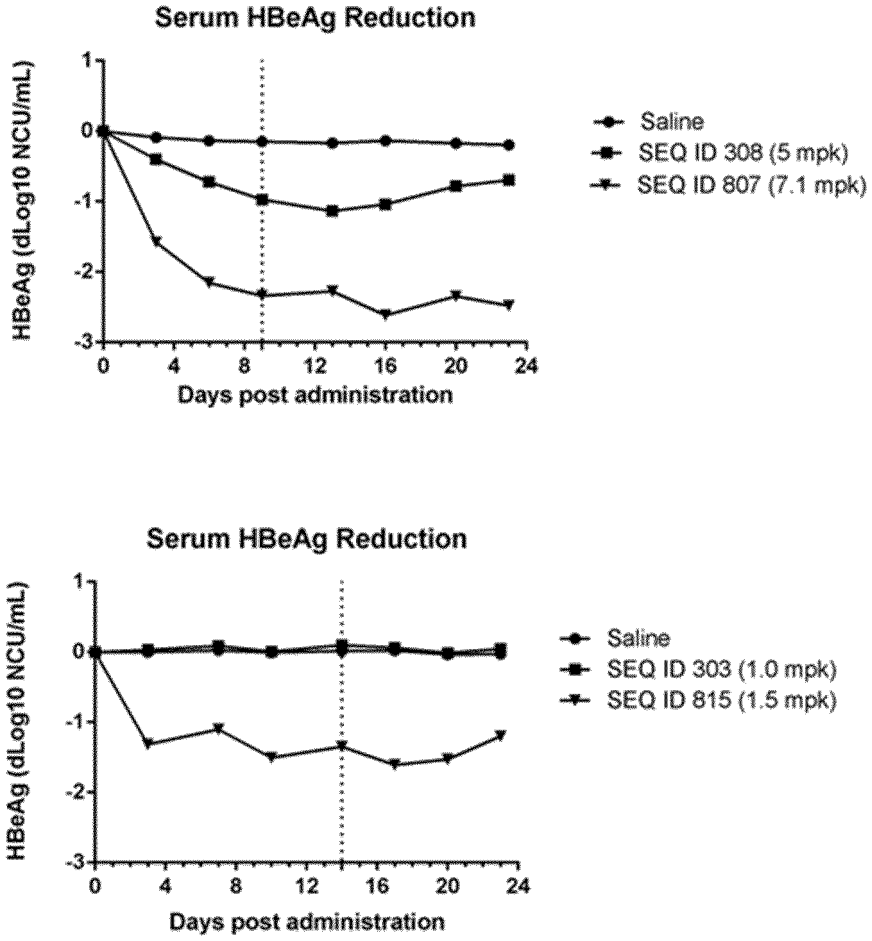

Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
1
0
-1
-2
-3
0
4
8
12
16
20
24
Days post administration
Saline
SEQ ID 308 (5 mpk)
SEQ ID 807 (7.1 mpk)
Serum HBeAg Reduction
HBeAg (dLog10 NCU/mL)
1
0
-1
-2
-3
0
4
8
12
16
20
24
Days post administration
Saline
SEQ ID 303 (1.0 mpk)
SEQ ID 815 (1.5 mpk)

Figure 15 cont'd

C)

