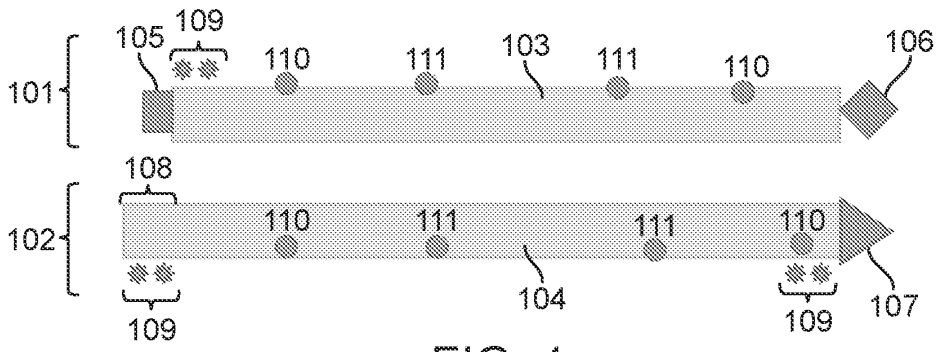
101
105
109
110
111
103
111
110
106
102
108
110
111
111
110
109
104
109
107

FIG. 1

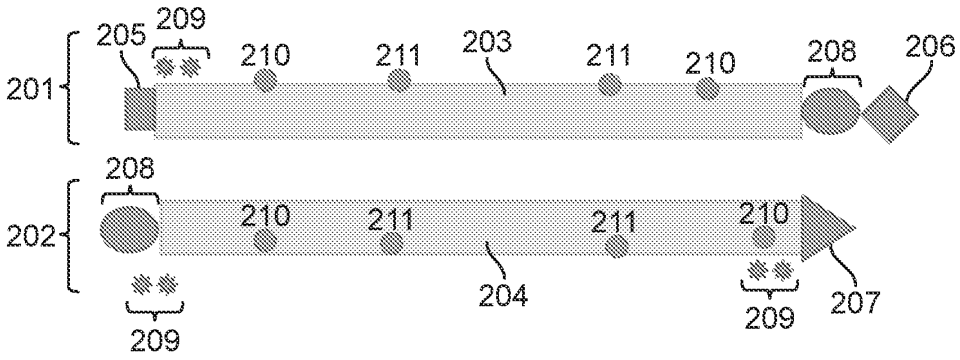
201
205
209
210
211
203
211
210
208
206
202
208
210
211
211
210
209
204
209
207

FIG. 2

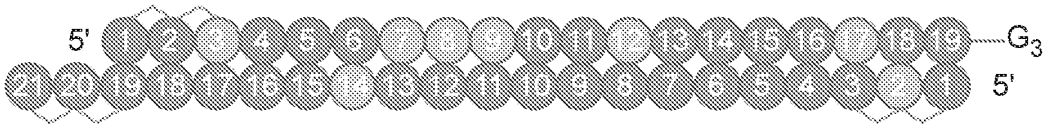

FIG. 3A

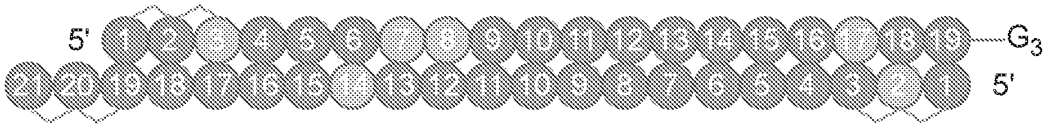

FIG. 3B

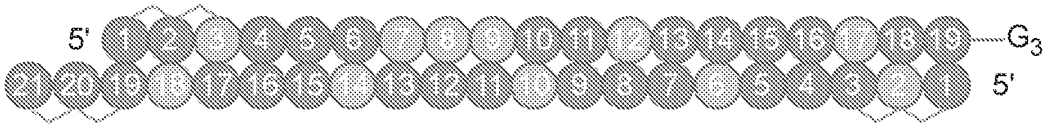

FIG. 3C

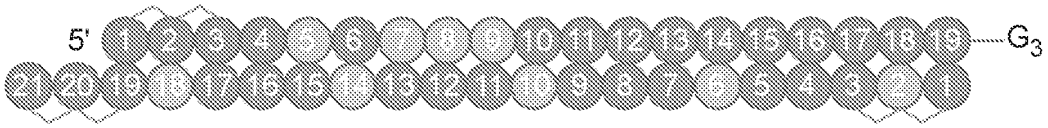

FIG. 3D

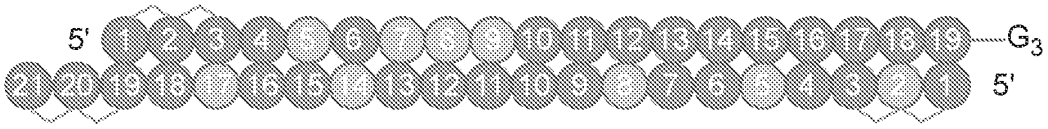

FIG. 3E

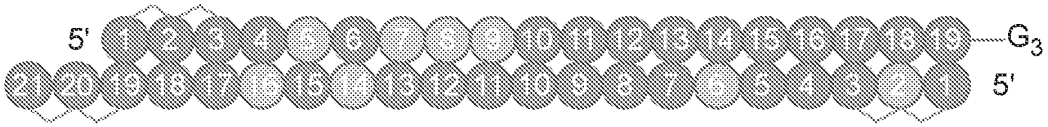

FIG. 3F

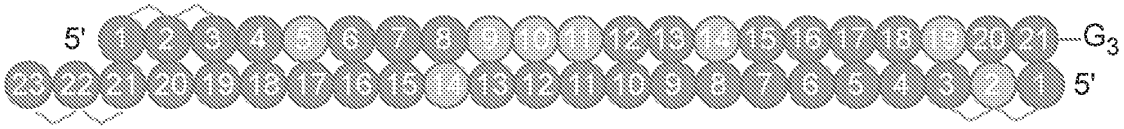

FIG. 3G

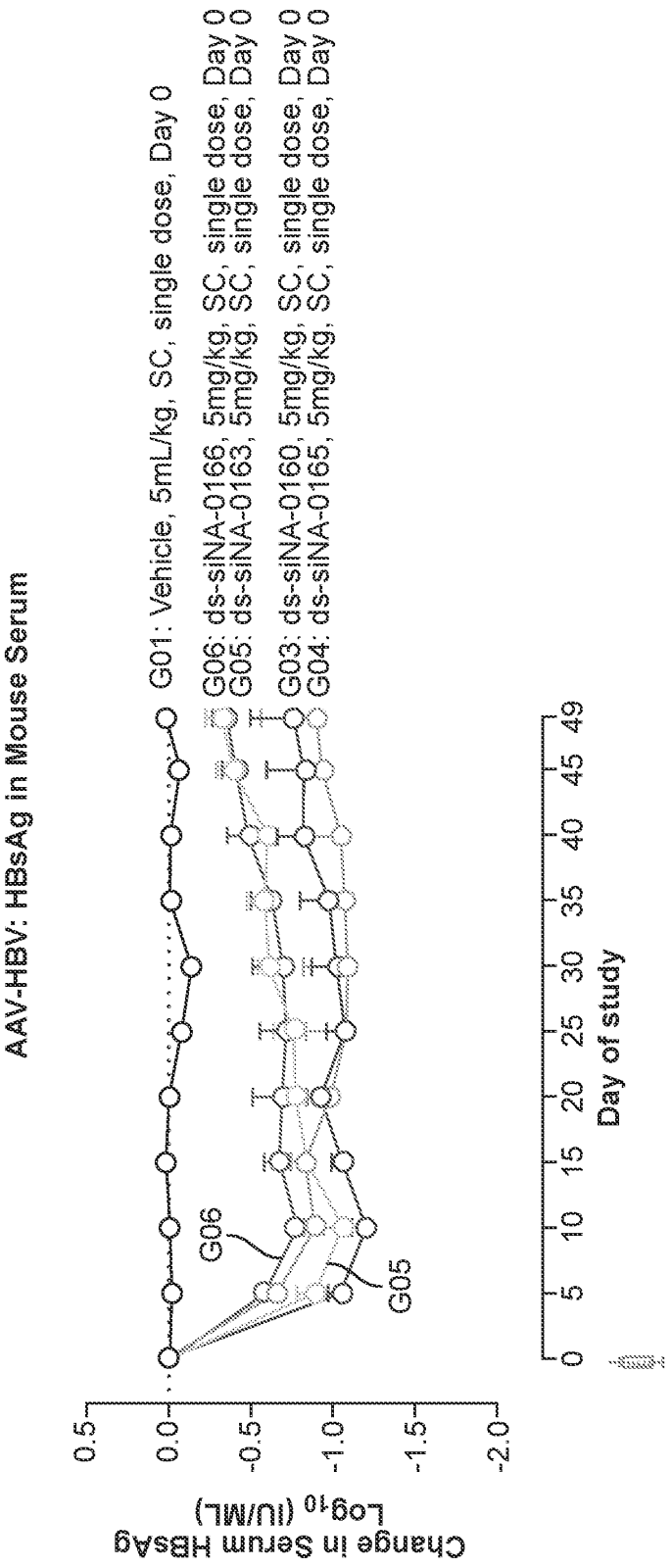
AAV-HBV: HBsAg in Mouse Serum
G01: Vehicle, 5mL/kg, SC, single dose, Day 0
G06: ds-siNA-0166, 5mg/kg, SC, single dose, Day 0
G05: ds-siNA-0163, 5mg/kg, SC, single dose, Day 0
G03: ds-siNA-0160, 5mg/kg, SC, single dose, Day 0
G04: ds-siNA-0165, 5mg/kg, SC, single dose, Day 0
G06
G05
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Change in Serum HBsAg
Log10 (IU/ML)
0
5
10
15
20
25
30
35
40
45
49
Day of study

FIG. 4

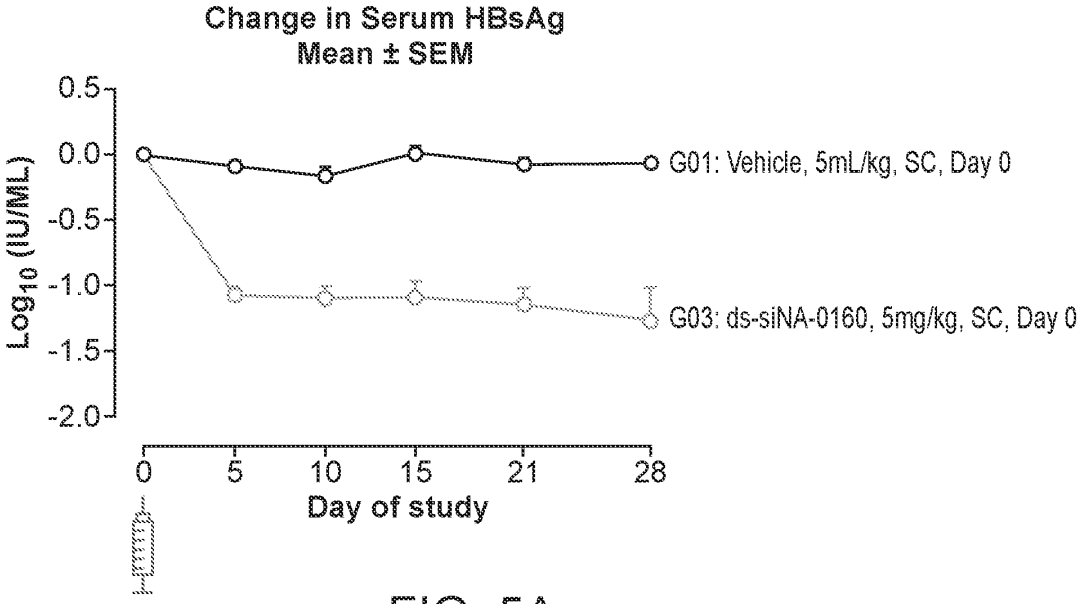
Change in Serum HBsAg
Mean ± SEM
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/ML)
G01: Vehicle, 5mL/kg, SC, Day 0
G03: ds-siNA-0160, 5mg/kg, SC, Day 0
0
5
10
15
21
28
Day of study

FIG. 5A

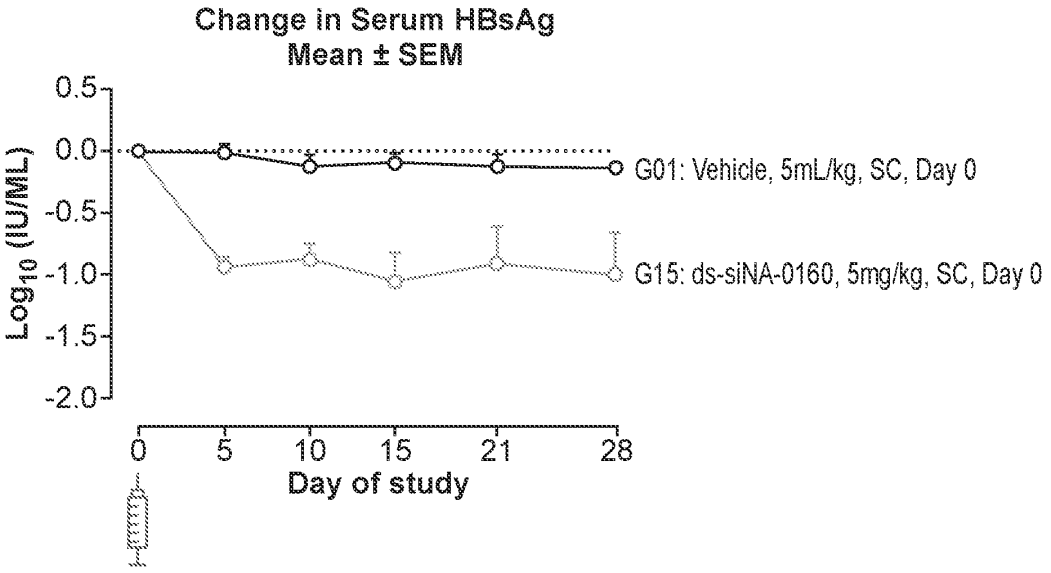
Change in Serum HBsAg
Mean ± SEM
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/ML)
G01: Vehicle, 5mL/kg, SC, Day 0
G15: ds-siNA-0160, 5mg/kg, SC, Day 0
0
5
10
15
21
28
Day of study

FIG. 5B

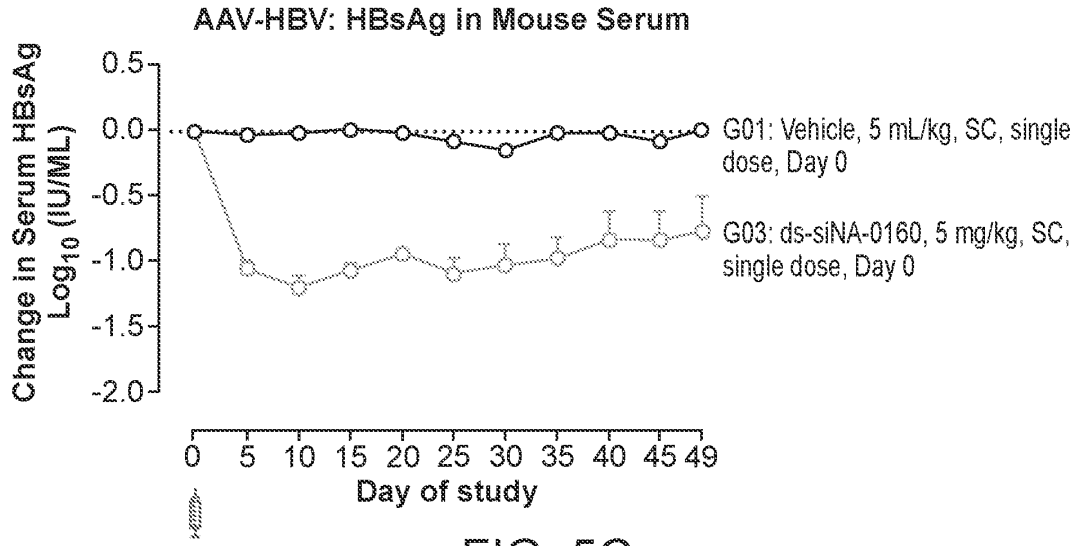
AAV-HBV: HBsAg in Mouse Serum
Change in Serum HBsAg Log10 (IU/ML)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0 5 10 15 20 25 30 35 40 45 49
Day of study
G01: Vehicle, 5 mL/kg, SC, single dose, Day 0
G03: ds-siNA-0160, 5 mg/kg, SC, single dose, Day 0

FIG. 5C

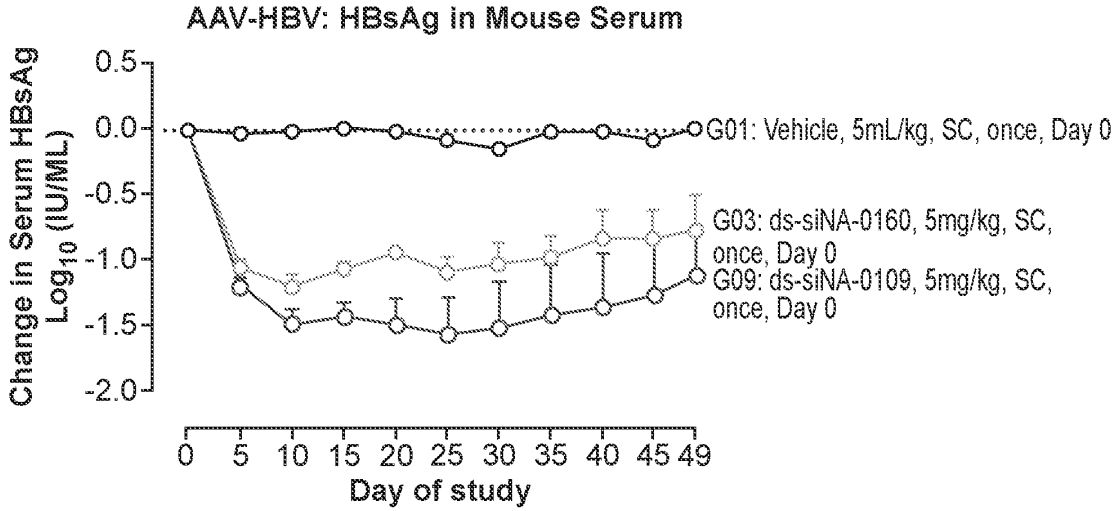
AAV-HBV: HBsAg in Mouse Serum
Change in Serum HBsAg Log10 (IU/ML)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0 5 10 15 20 25 30 35 40 45 49
Day of study
G01: Vehicle, 5mL/kg, SC, once, Day 0
G03: ds-siNA-0160, 5mg/kg, SC, once, Day 0
G09: ds-siNA-0109, 5mg/kg, SC, once, Day 0

FIG. 5D

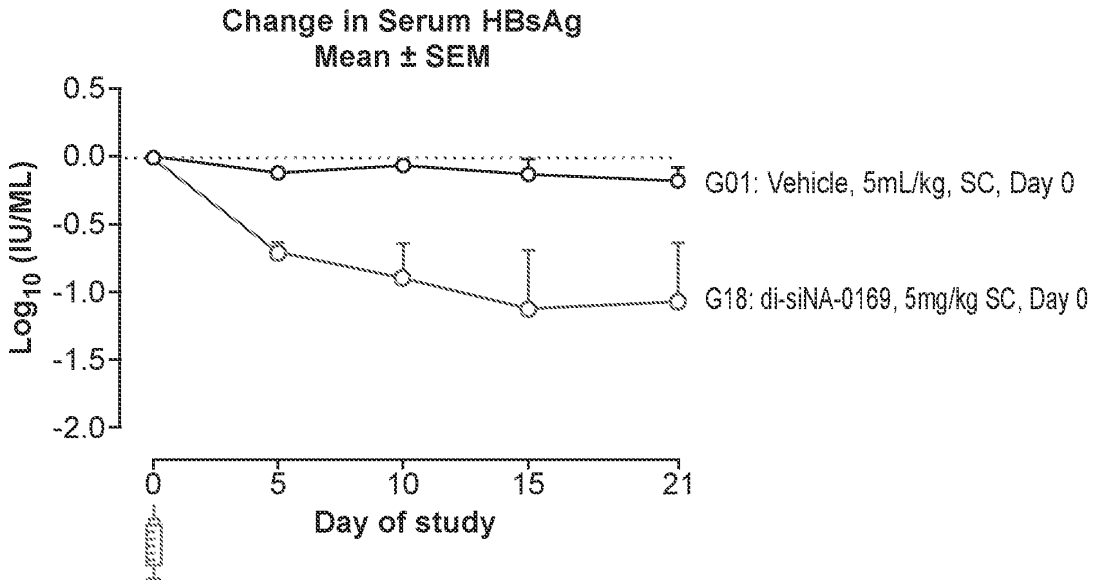
Change in Serum HBsAg
Mean ± SEM
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/ML)
0
5
10
15
21
Day of study
G01: Vehicle, 5mL/kg, SC, Day 0
G18: di-siNA-0169, 5mg/kg SC, Day 0

FIG. 5E

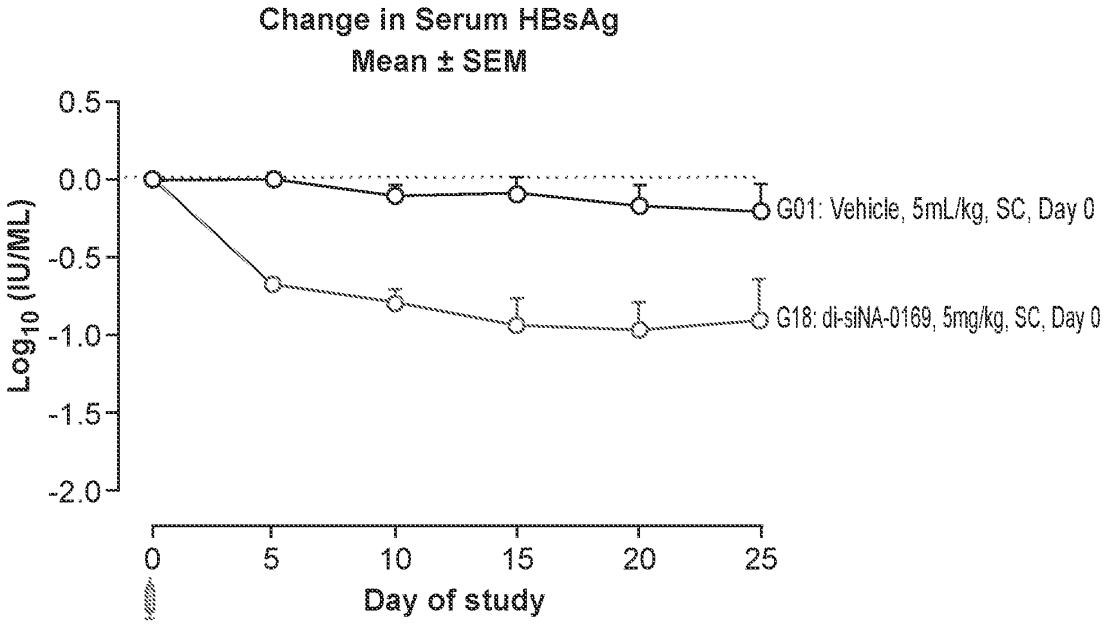
Change in Serum HBsAg
Mean ± SEM
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/ML)
0
5
10
15
20
25
Day of study
G01: Vehicle, 5mL/kg, SC, Day 0
G18: di-siNA-0169, 5mg/kg, SC, Day 0

FIG. 5F

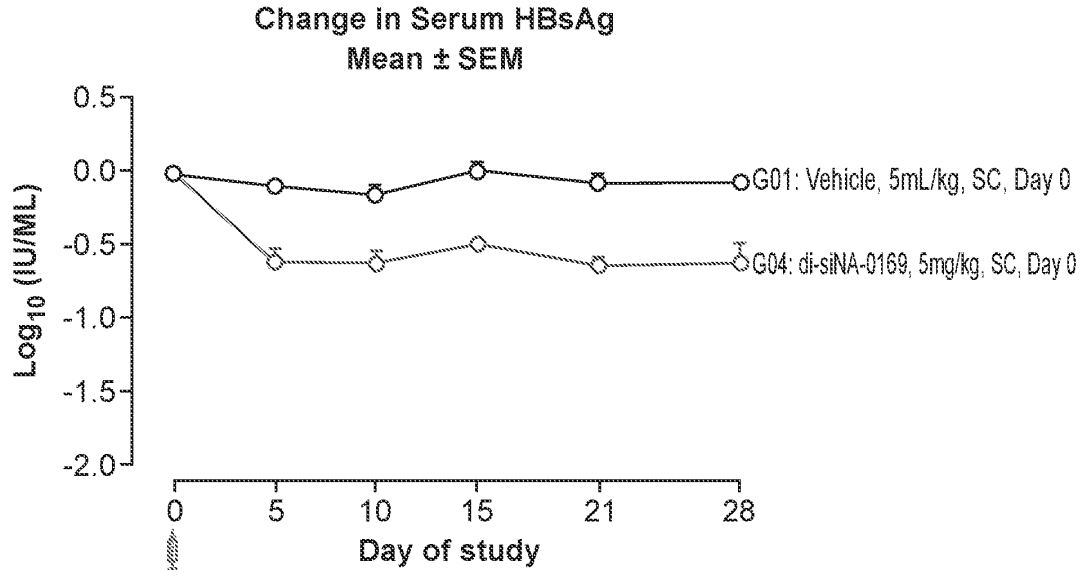
Change in Serum HBsAg
Mean ± SEM
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/ML)
0
5
10
15
21
28
Day of study
G01: Vehicle, 5mL/kg, SC, Day 0
G04: di-siNA-0169, 5mg/kg, SC, Day 0

FIG. 5G

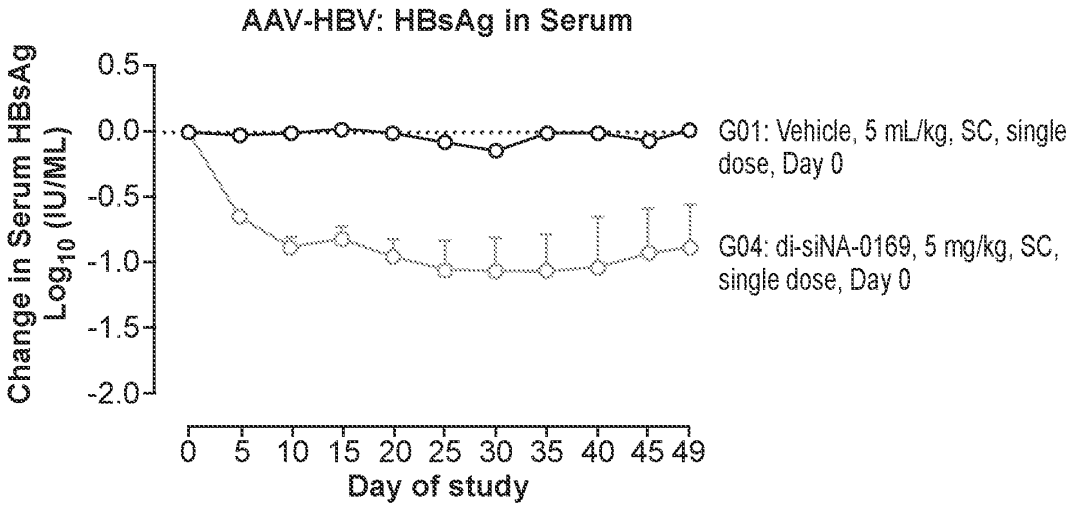
AAV-HBV: HBsAg in Serum
Change in Serum HBsAg Log10 (IU/ML)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0 5 10 15 20 25 30 35 40 45 49
Day of study
G01: Vehicle, 5 mL/kg, SC, single dose, Day 0
G04: di-siNA-0169, 5 mg/kg, SC, single dose, Day 0

FIG. 5H

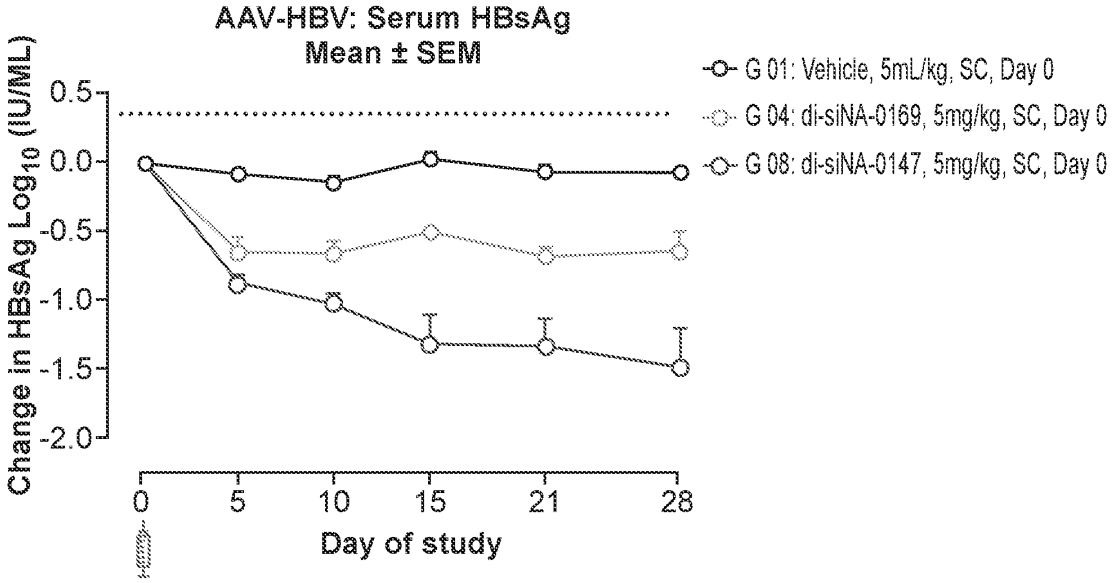
AAV-HBV: Serum HBsAg
Mean ± SEM
Change in HBsAg Log10 (IU/ML)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0 5 10 15 21 28
Day of study
G 01: Vehicle, 5mL/kg, SC, Day 0
G 04: di-siNA-0169, 5mg/kg, SC, Day 0
G 08: di-siNA-0147, 5mg/kg, SC, Day 0

FIG. 5I

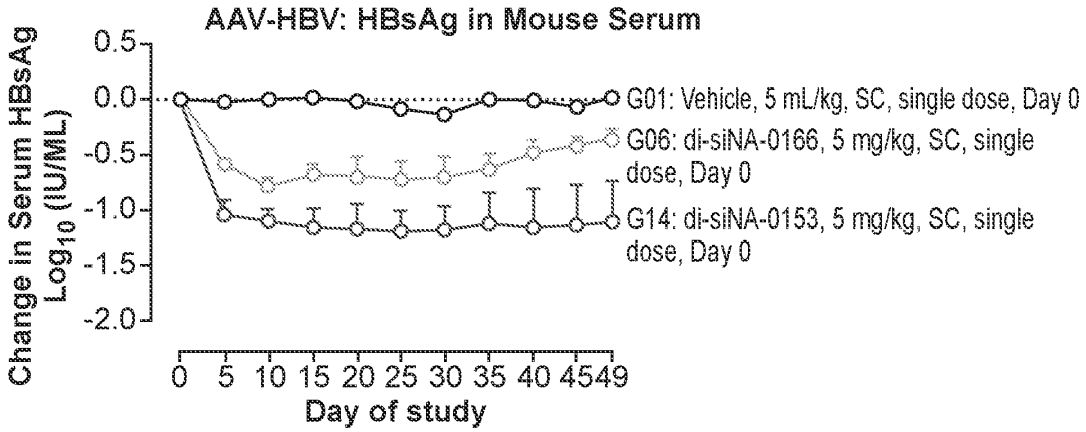
AAV-HBV: HBsAg in Mouse Serum
Change in Serum HBsAg Log10 (IU/ML)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0 5 10 15 20 25 30 35 40 4549
Day of study
G01: Vehicle, 5 mL/kg, SC, single dose, Day 0
G06: di-siNA-0166, 5 mg/kg, SC, single dose, Day 0
G14: di-siNA-0153, 5 mg/kg, SC, single dose, Day 0

FIG. 5J

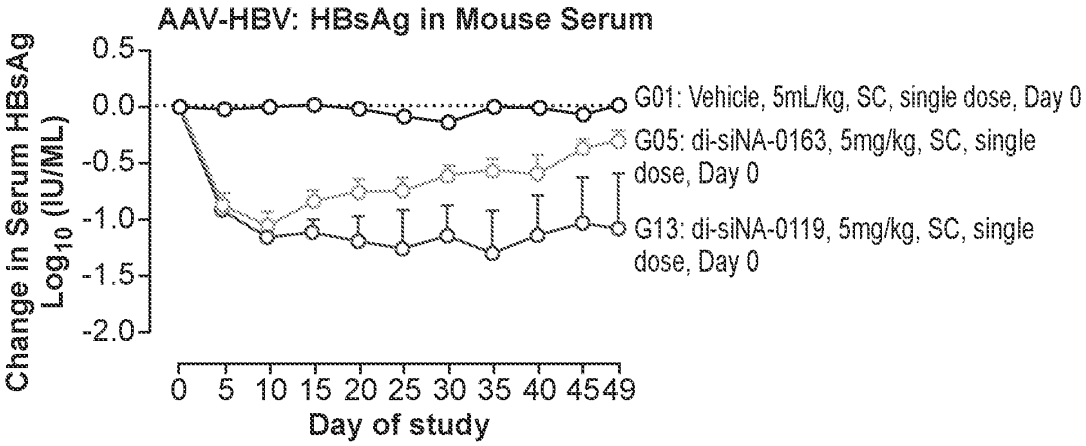
AAV-HBV: HBsAg in Mouse Serum
Change in Serum HBsAg Log10 (IU/ML)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0 5 10 15 20 25 30 35 40 4549
Day of study
G01: Vehicle, 5mL/kg, SC, single dose, Day 0
G05: di-siNA-0163, 5mg/kg, SC, single dose, Day 0
G13: di-siNA-0119, 5mg/kg, SC, single dose, Day 0

FIG. 5k

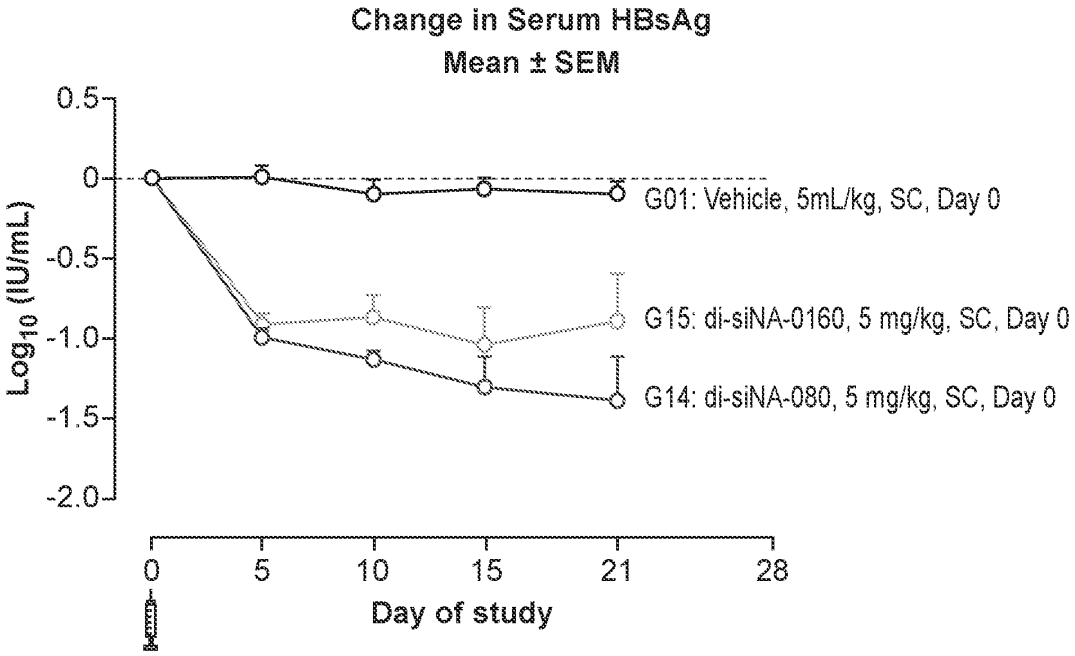
Change in Serum HBsAg
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/mL)
G01: Vehicle, 5mL/kg, SC, Day 0
G15: di-siNA-0160, 5 mg/kg, SC, Day 0
G14: di-siNA-080, 5 mg/kg, SC, Day 0
0
5
10
15
21
28
Day of study

FIG. 6A

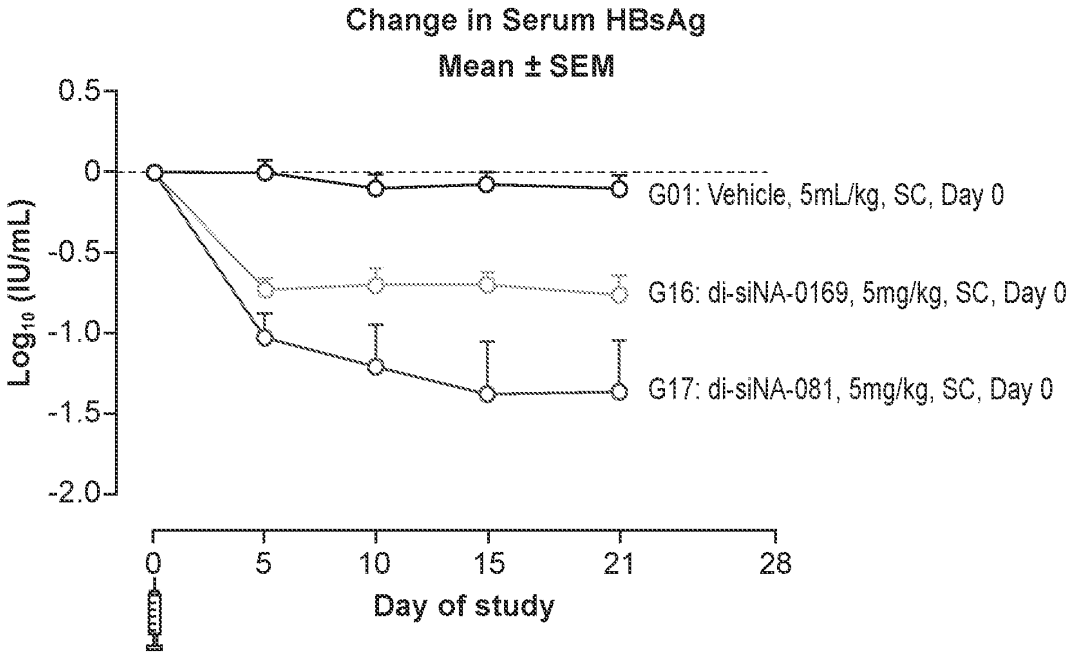
Change in Serum HBsAg
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/mL)
G01: Vehicle, 5mL/kg, SC, Day 0
G16: di-siNA-0169, 5mg/kg, SC, Day 0
G17: di-siNA-081, 5mg/kg, SC, Day 0
0
5
10
15
21
28
Day of study

FIG. 6B

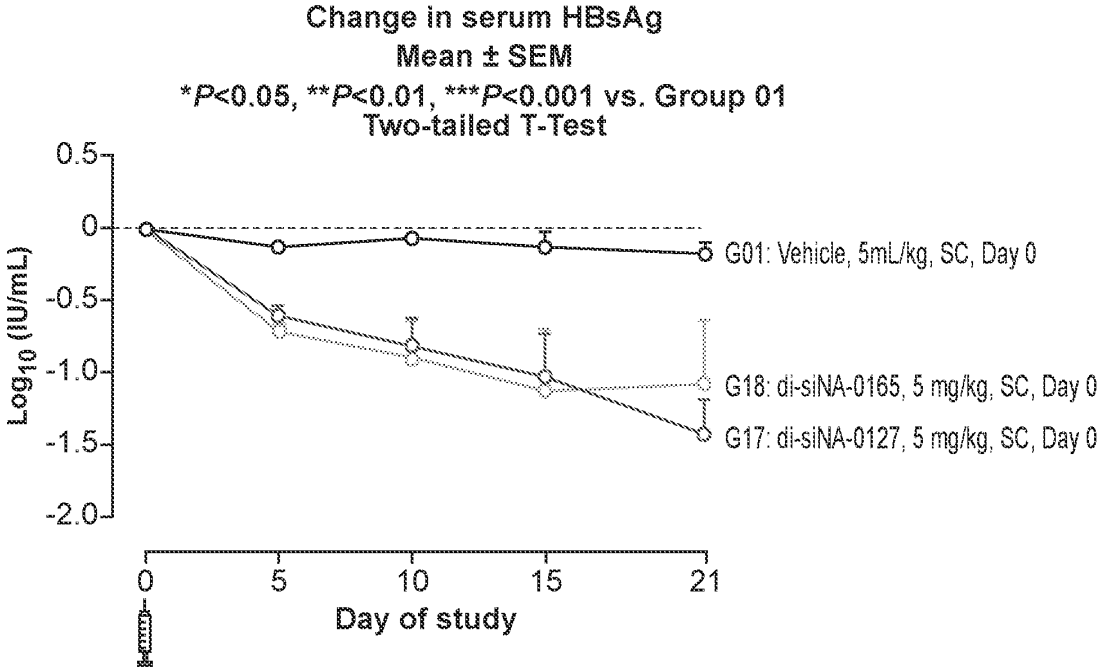
Change in serum HBsAg
Mean ± SEM
*P<0.05, **P<0.01, ***P<0.001 vs. Group 01
Two-tailed T-Test
0.5
0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/mL)
G01: Vehicle, 5mL/kg, SC, Day 0
G18: di-siNA-0165, 5 mg/kg, SC, Day 0
G17: di-siNA-0127, 5 mg/kg, SC, Day 0
0
5
10
15
21
Day of study

FIG. 7A

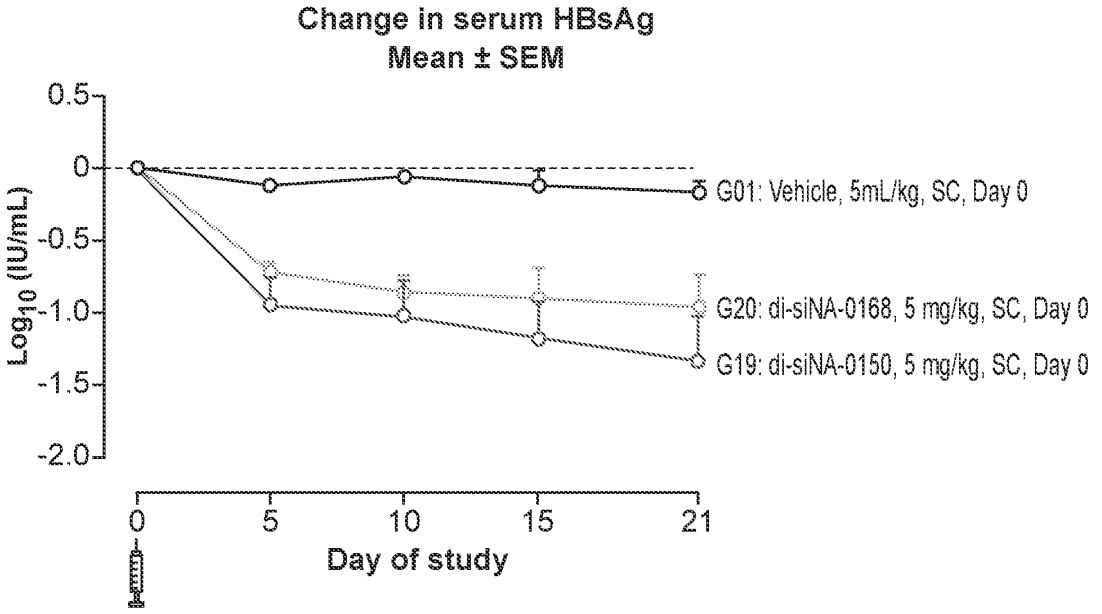
Change in serum HBsAg
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
-2.0
Log10 (IU/mL)
G01: Vehicle, 5mL/kg, SC, Day 0
G20: di-siNA-0168, 5 mg/kg, SC, Day 0
G19: di-siNA-0150, 5 mg/kg, SC, Day 0
0
5
10
15
21
Day of study

FIG. 7B

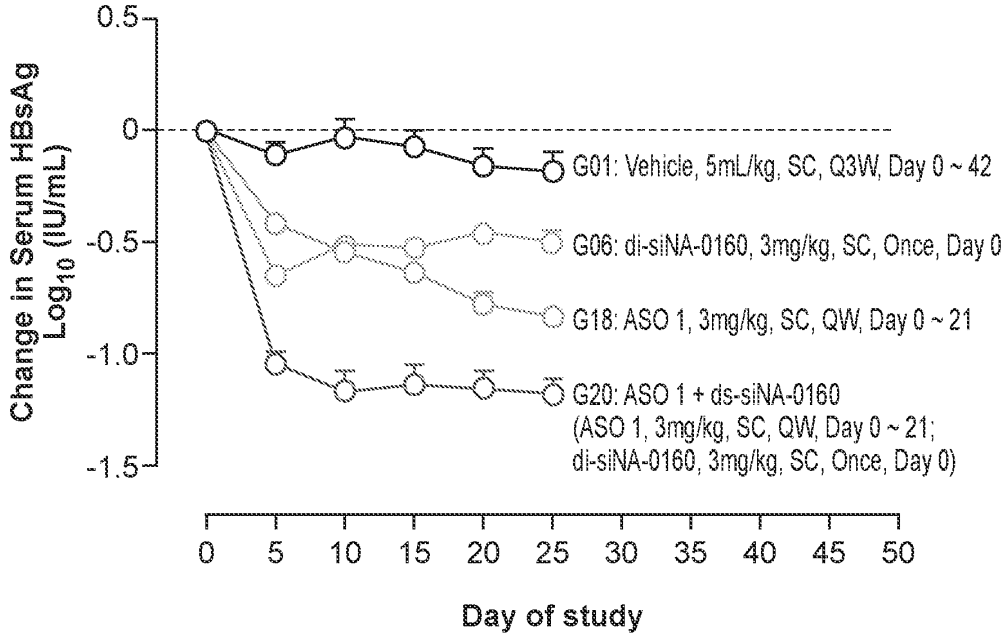
0.5
0
-0.5
-1.0
-1.5
Change in Serum HBsAg
Log10 (IU/mL)
G01: Vehicle, 5mL/kg, SC, Q3W, Day 0 ~ 42
G06: di-siNA-0160, 3mg/kg, SC, Once, Day 0
G18: ASO 1, 3mg/kg, SC, QW, Day 0 ~ 21
G20: ASO 1 + ds-siNA-0160
(ASO 1, 3mg/kg, SC, QW, Day 0 ~ 21;
di-siNA-0160, 3mg/kg, SC, Once, Day 0)
0 5 10 15 20 25 30 35 40 45 50
Day of study

FIG. 8A

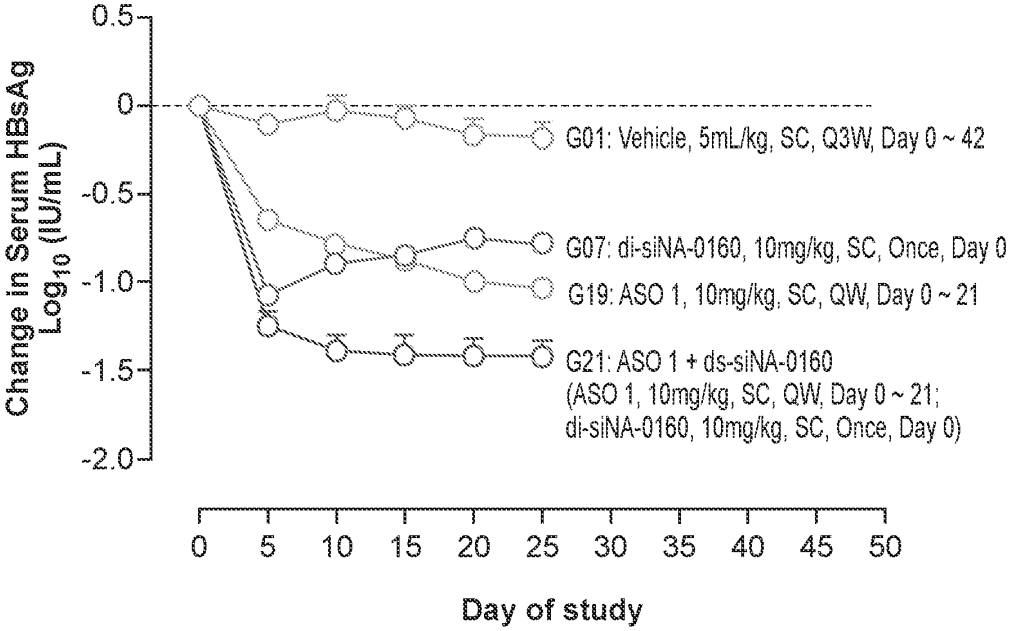
0.5
0
-0.5
-1.0
-1.5
-2.0
Change in Serum HBsAg
Log10 (IU/mL)
G01: Vehicle, 5mL/kg, SC, Q3W, Day 0 ~ 42
G07: di-siNA-0160, 10mg/kg, SC, Once, Day 0
G19: ASO 1, 10mg/kg, SC, QW, Day 0 ~ 21
G21: ASO 1 + ds-siNA-0160
(ASO 1, 10mg/kg, SC, QW, Day 0 ~ 21;
di-siNA-0160, 10mg/kg, SC, Once, Day 0)
0 5 10 15 20 25 30 35 40 45 50
Day of study

FIG. 8B

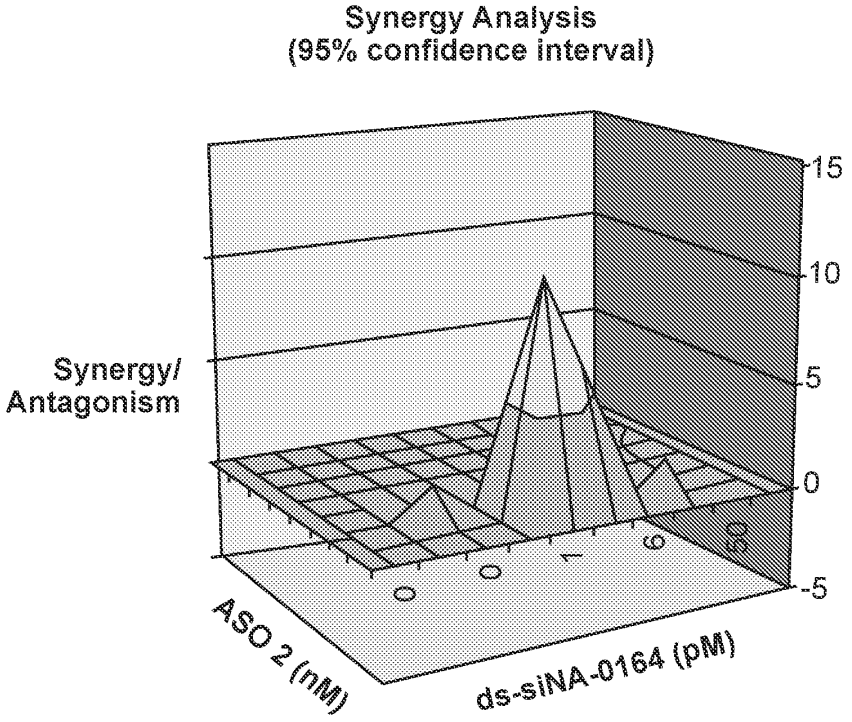
Synergy Analysis
(95% confidence interval)
Synergy/
Antagonism
15
10
5
0
-5
ASO 2 (nM)
ds-siNA-0164 (pM)

FIG. 8C

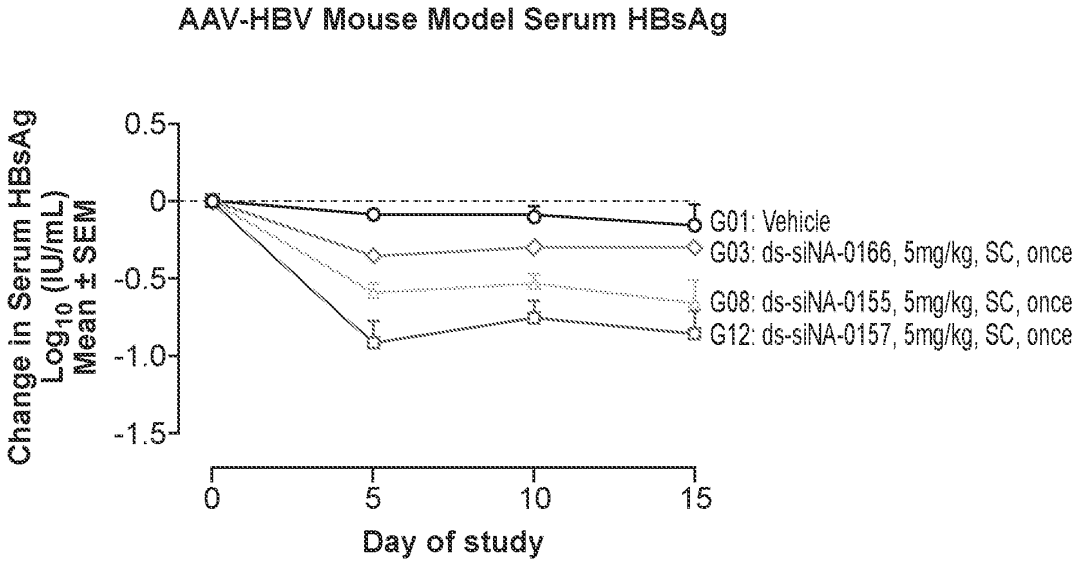
AAV-HBV Mouse Model Serum HBsAg
Change in Serum HBsAg
Log10 (IU/mL)
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0
5
10
15
Day of study
G01: Vehicle
G03: ds-siNA-0166, 5mg/kg, SC, once
G08: ds-siNA-0155, 5mg/kg, SC, once
G12: ds-siNA-0157, 5mg/kg, SC, once

FIG. 9

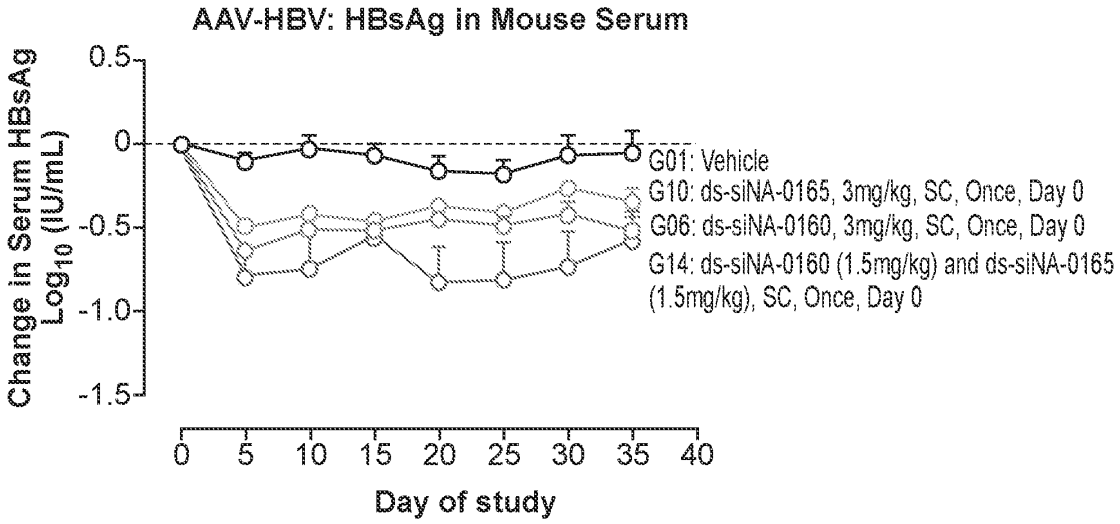
AAV-HBV: HBsAg in Mouse Serum
Change in Serum HBsAg Log10 (IU/mL)
0.5
0
-0.5
-1.0
-1.5
0 5 10 15 20 25 30 35 40
Day of study
G01: Vehicle
G10: ds-siNA-0165, 3mg/kg, SC, Once, Day 0
G06: ds-siNA-0160, 3mg/kg, SC, Once, Day 0
G14: ds-siNA-0160 (1.5mg/kg) and ds-siNA-0165 (1.5mg/kg), SC, Once, Day 0

FIG. 10

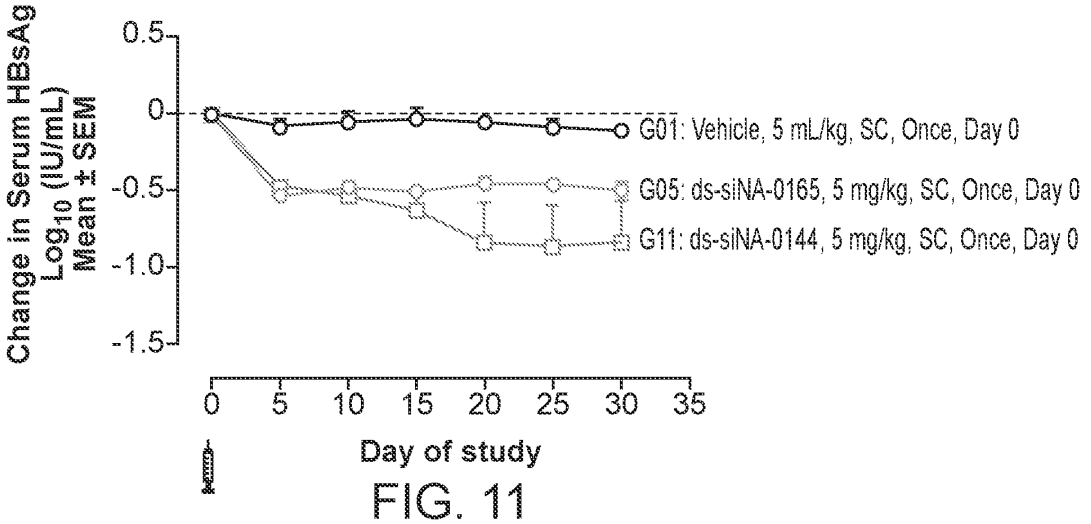
Change in Serum HBsAg Log10 (IU/mL) Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0 5 10 15 20 25 30 35
Day of study
G01: Vehicle, 5 mL/kg, SC, Once, Day 0
G05: ds-siNA-0165, 5 mg/kg, SC, Once, Day 0
G11: ds-siNA-0144, 5 mg/kg, SC, Once, Day 0

FIG. 11

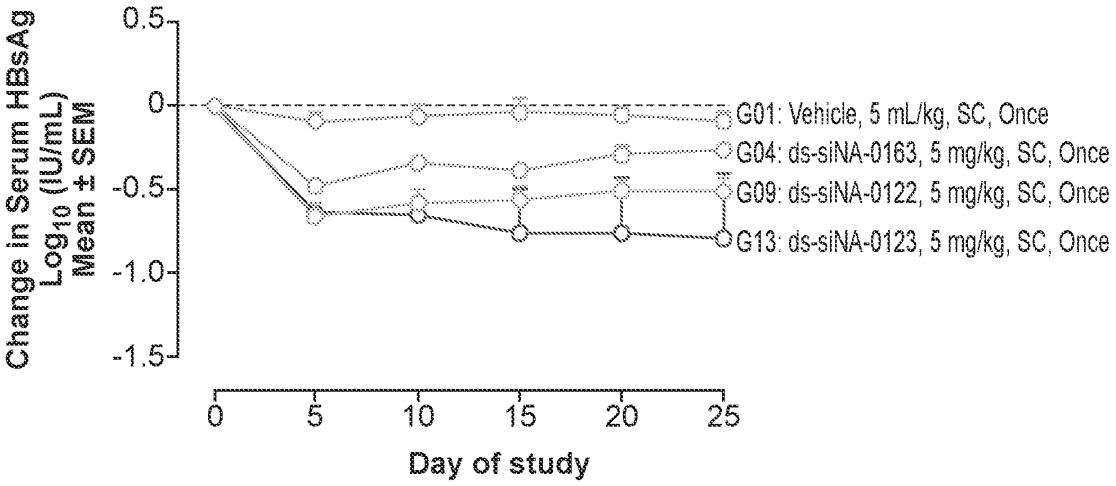
Change in Serum HBsAg
Log10 (IU/mL)
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0
5
10
15
20
25
Day of study
G01: Vehicle, 5 mL/kg, SC, Once
G04: ds-siNA-0163, 5 mg/kg, SC, Once
G09: ds-siNA-0122, 5 mg/kg, SC, Once
G13: ds-siNA-0123, 5 mg/kg, SC, Once

FIG. 12

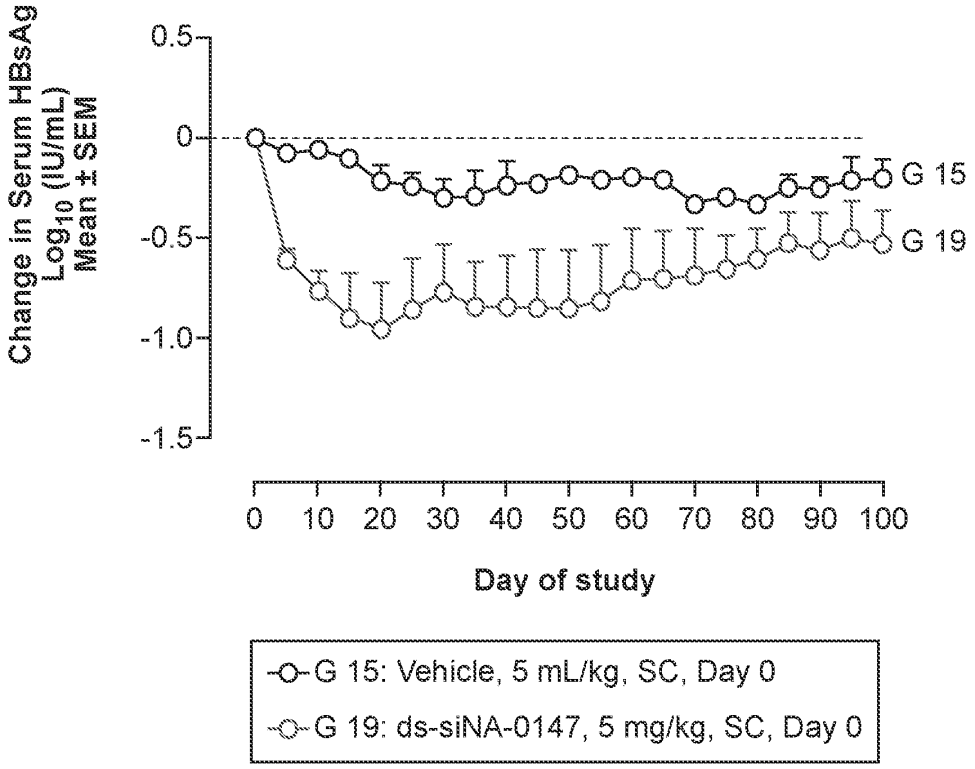
Change in Serum HBsAg
Log10 (IU/mL)
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0
10
20
30
40
50
60
70
80
90
100
Day of study
G 15
G 19
G 15: Vehicle, 5 mL/kg, SC, Day 0
G 19: ds-siNA-0147, 5 mg/kg, SC, Day 0

FIG. 13

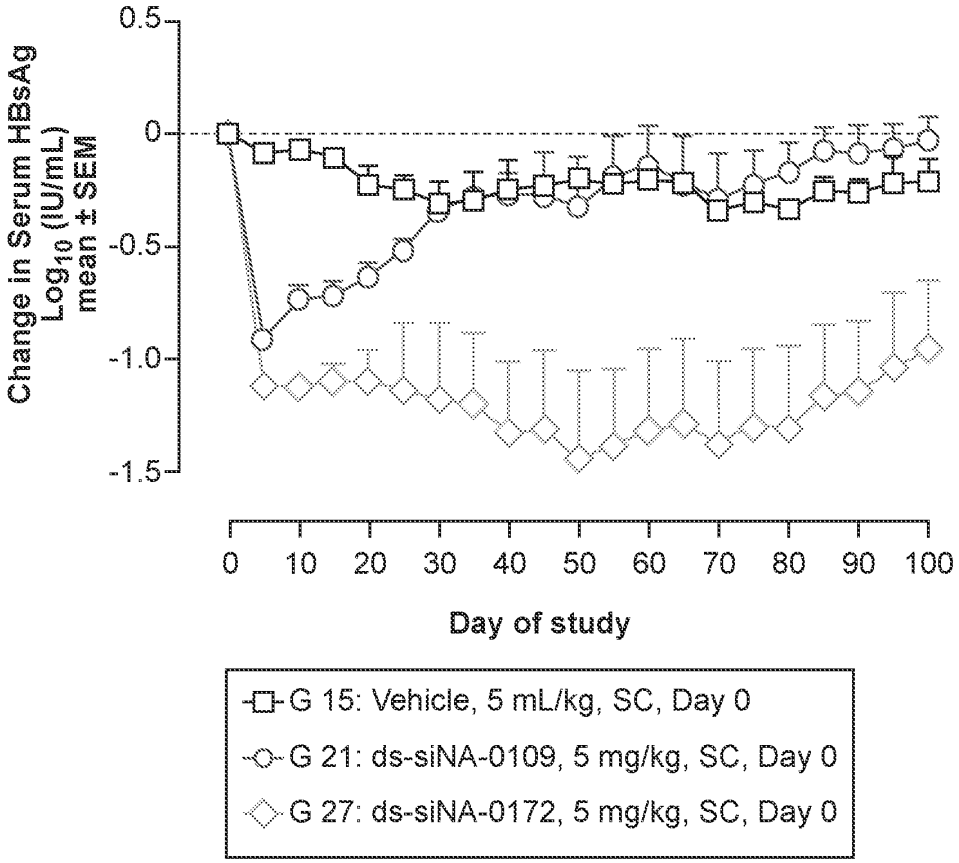
Change in Serum HBsAg
Log10 (IU/mL)
mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0
10
20
30
40
50
60
70
80
90
100
Day of study
G 15: Vehicle, 5 mL/kg, SC, Day 0
G 21: ds-siNA-0109, 5 mg/kg, SC, Day 0
G 27: ds-siNA-0172, 5 mg/kg, SC, Day 0

FIG. 14

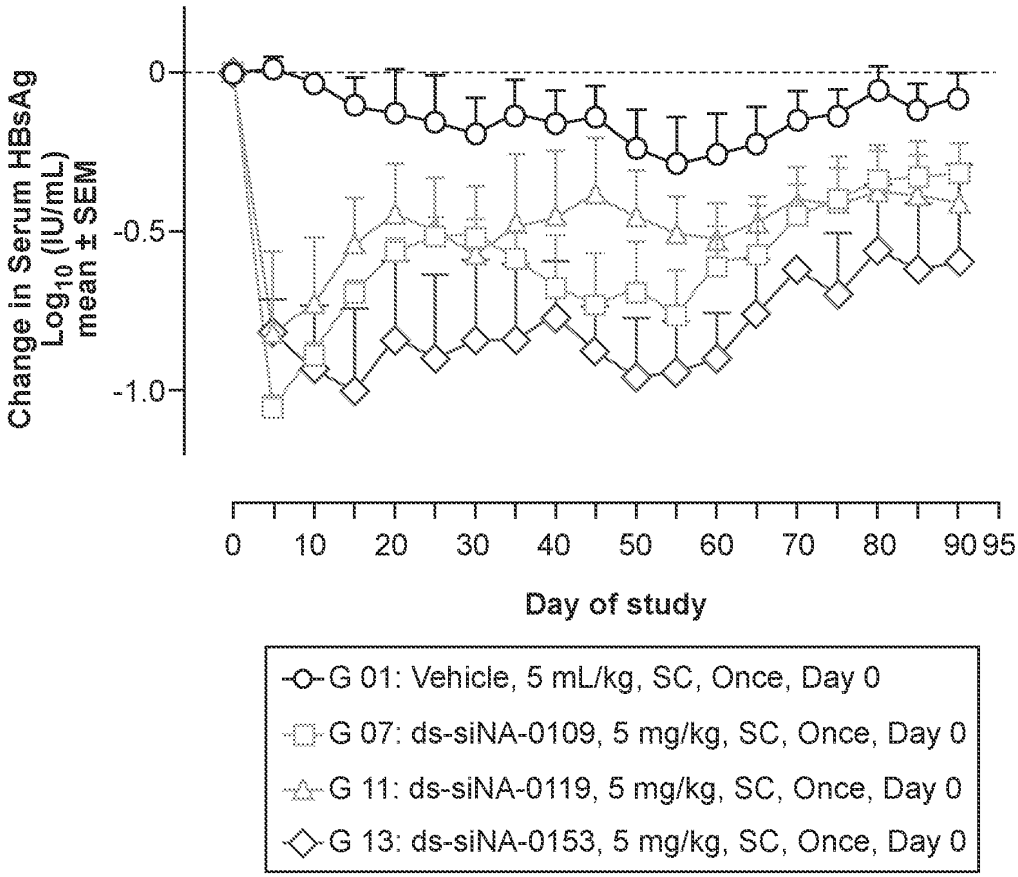
Change in Serum HBsAg
Log10 (IU/mL)
mean ± SEM
0
-0.5
-1.0
0
10
20
30
40
50
60
70
80
90
95
Day of study
G 01: Vehicle, 5 mL/kg, SC, Once, Day 0
G 07: ds-siNA-0109, 5 mg/kg, SC, Once, Day 0
G 11: ds-siNA-0119, 5 mg/kg, SC, Once, Day 0
G 13: ds-siNA-0153, 5 mg/kg, SC, Once, Day 0

FIG. 15

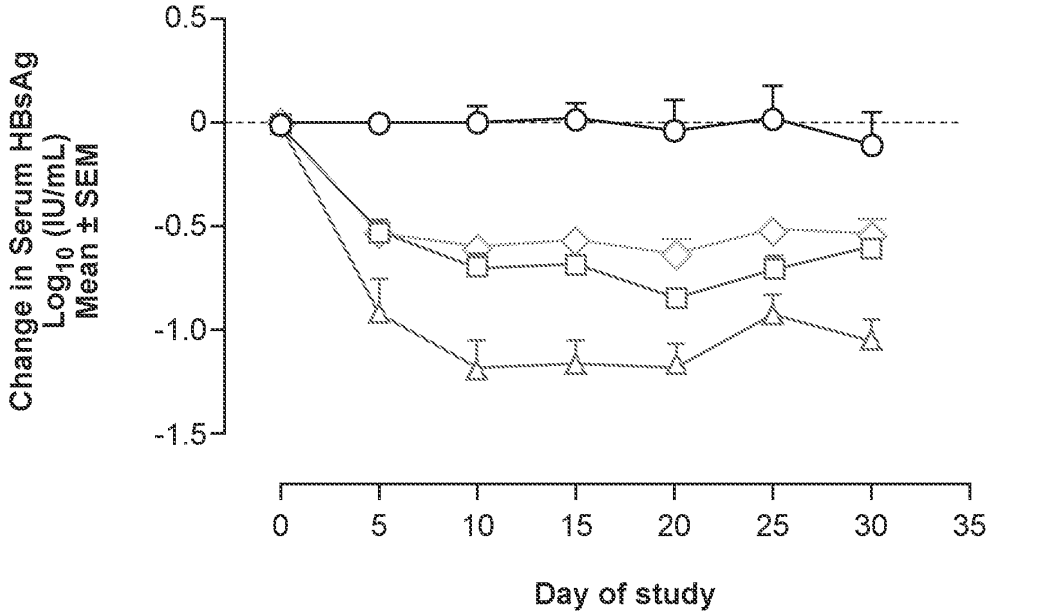
Change in Serum HBsAg
Log10 (IU/mL)
Mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0
5
10
15
20
25
30
35
Day of study
G 01: Vehicle, 5 mL/kg, SC, QW, Days 0, 7, 14
G 20: ASO 1, 5 mg/kg, SC, QW, Days 0, 7, 14
G 24: ds-siNA-0147, 5 mg/kg, SC, Once, Day 0
G 25: ds-siNA-0147 + ASO 1 (ds-siNA-0147: 5 mg/kg, SC, Once, Day 0; ASO 1:5 mg/kg, SC, QW, Days 0,7,14)

FIG. 16

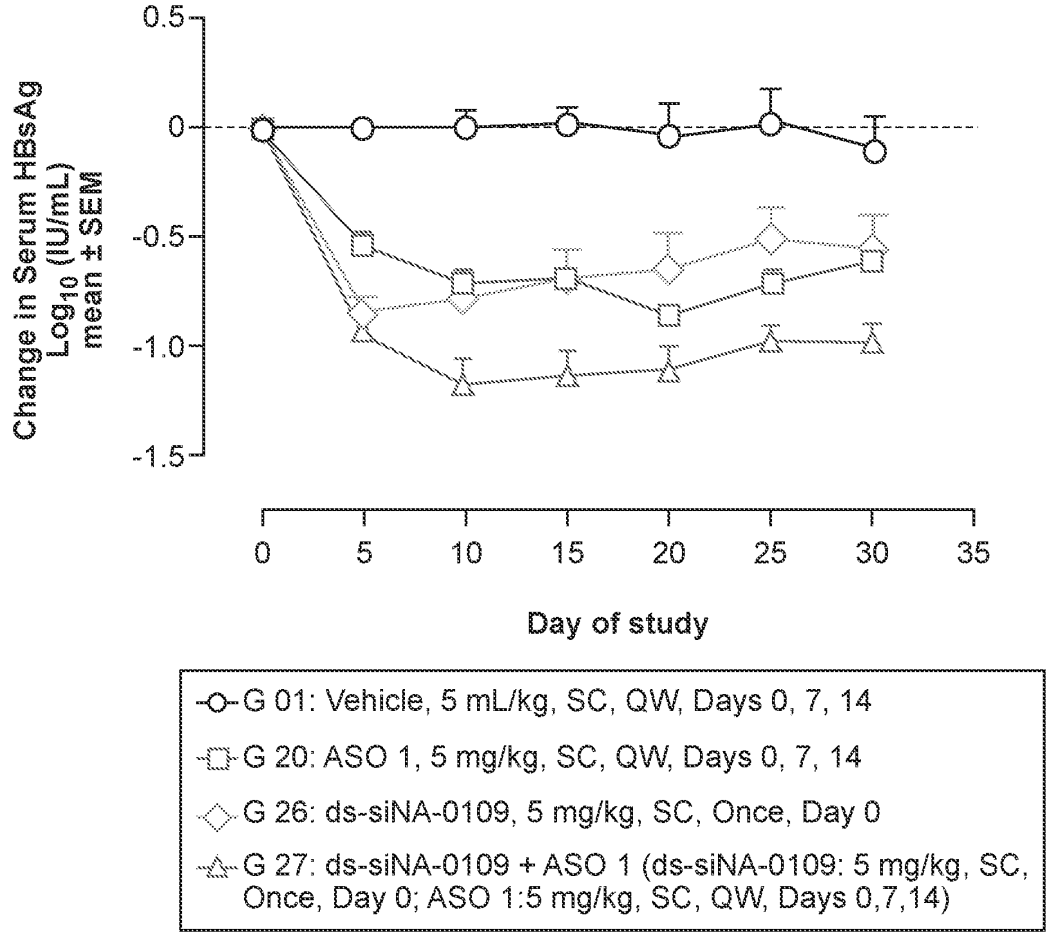
Change in Serum HBsAg
Log10 (IU/mL)
mean ± SEM
0.5
0
-0.5
-1.0
-1.5
0
5
10
15
20
25
30
35
Day of study
G 01: Vehicle, 5 mL/kg, SC, QW, Days 0, 7, 14
G 20: ASO 1, 5 mg/kg, SC, QW, Days 0, 7, 14
G 26: ds-siNA-0109, 5 mg/kg, SC, Once, Day 0
G 27: ds-siNA-0109 + ASO 1 (ds-siNA-0109: 5 mg/kg, SC, Once, Day 0; ASO 1:5 mg/kg, SC, QW, Days 0,7,14)

FIG. 17