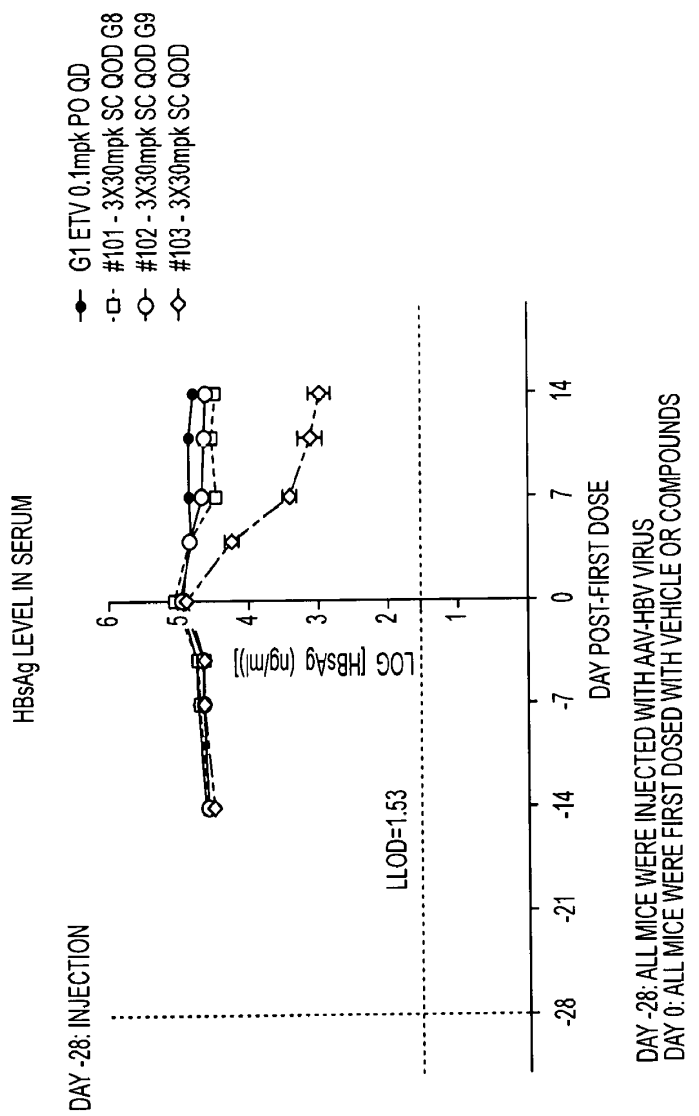

HBsAg LEVEL IN SERUM
G1 ETV 0.1mpk PO QD
#101 - 3X30mpk SC QOD G8
#102 - 3X30mpk SC QOD G9
#103 - 3X30mpk SC QOD
LOG [HBsAg (ng/ml)]
6
5
4
3
2
1
LLOD=1.53
DAY -28: INJECTION
-28
-21
-14
-7
0
7
14
DAY POST-FIRST DOSE
DAY -28: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 1A

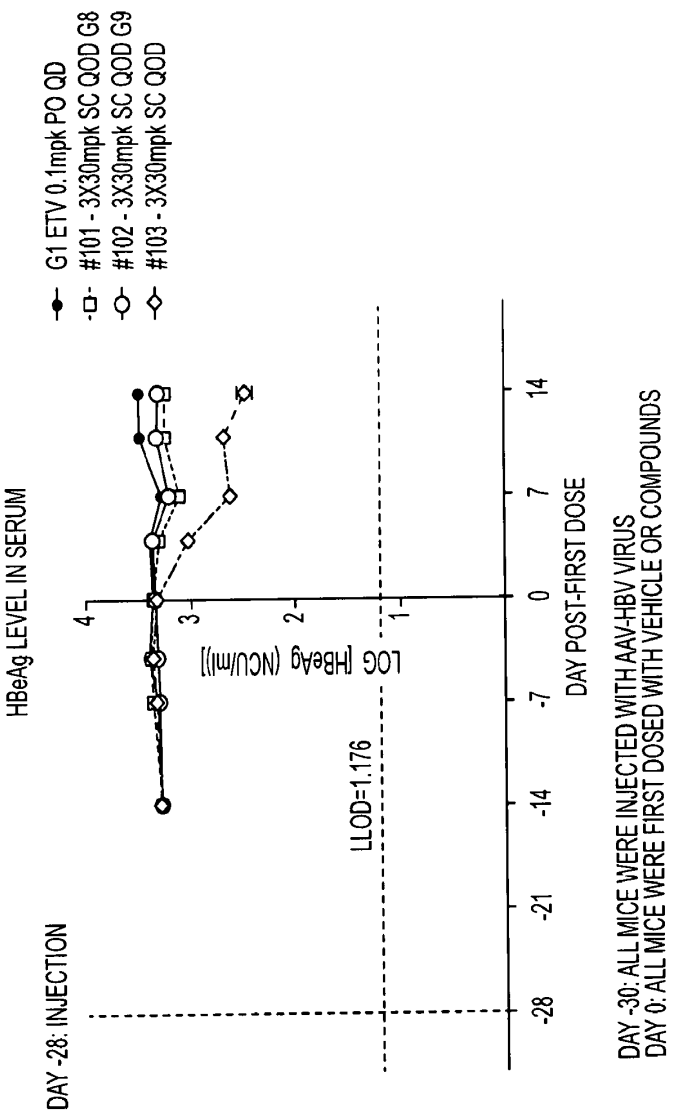

HBeAg LEVEL IN SERUM
G1 ETV 0.1mpk PO QD
#101 - 3X30mpk SC QOD G8
#102 - 3X30mpk SC QOD G9
#103 - 3X30mpk SC QOD
LOG [HBeAg (NCU/ml)]
LLOD=1.176
DAY -28: INJECTION
DAY POST-FIRST DOSE
DAY -30: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 1B

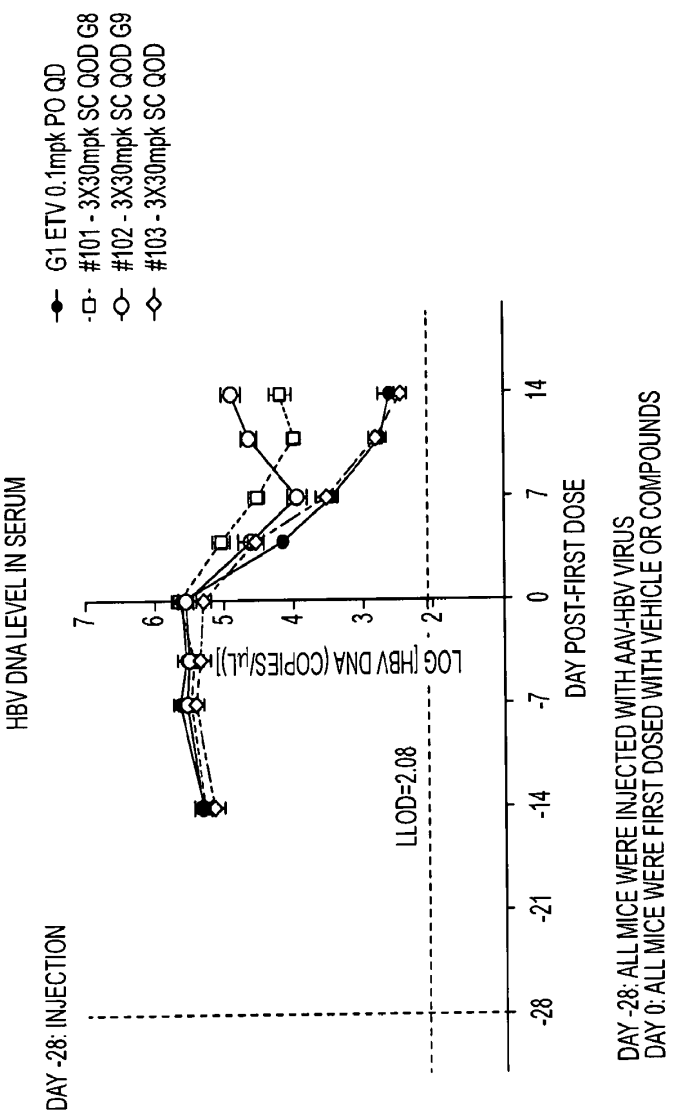

HBV DNA LEVEL IN SERUM
G1 ETV 0.1mpk PO QD
#101 - 3X30mpk SC QOD G8
#102 - 3X30mpk SC QOD G9
#103 - 3X30mpk SC QOD
LOG [HBV DNA (COPIES/μL)]
7
6
5
4
3
2
LLOD=2.08
DAY -28: INJECTION
-28
-21
-14
-7
0
7
14
DAY POST-FIRST DOSE
DAY -28: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 1C

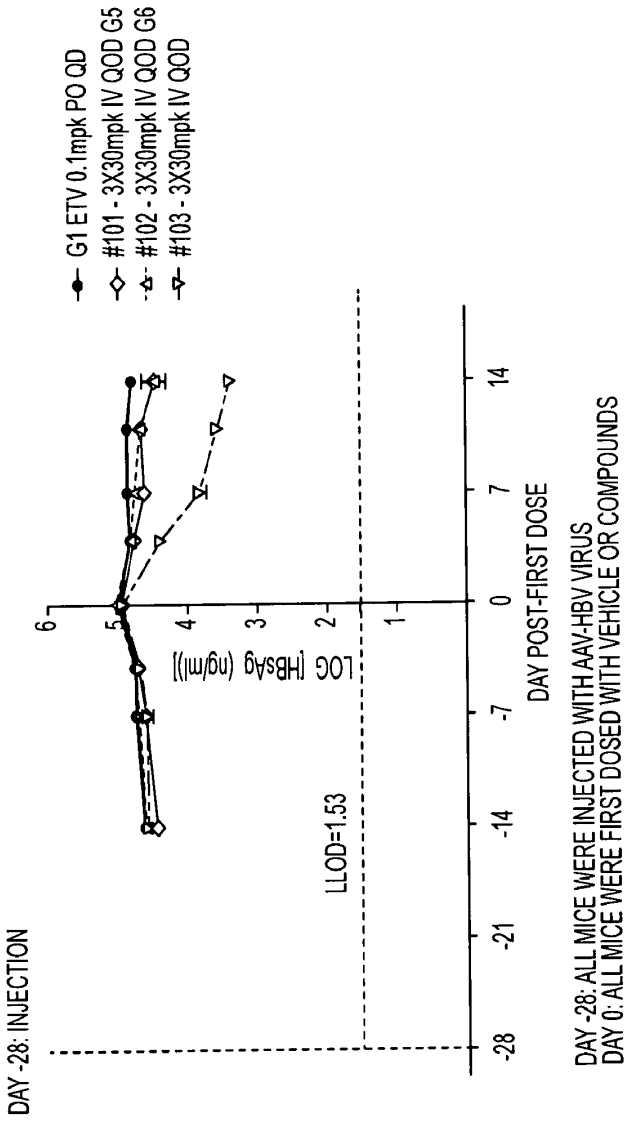

HBsAg LEVEL IN SERUM
G1 ETV 0.1mpk PO QD
#101 - 3X30mpk IV QOD G5
#102 - 3X30mpk IV QOD G6
#103 - 3X30mpk IV QOD
LOG [HBsAg (ng/ml)]
6
5
4
3
2
1
LLOD=1.53
DAY -28: INJECTION
-28
-21
-14
-7
0
7
14
DAY POST-FIRST DOSE
DAY -28: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 2A

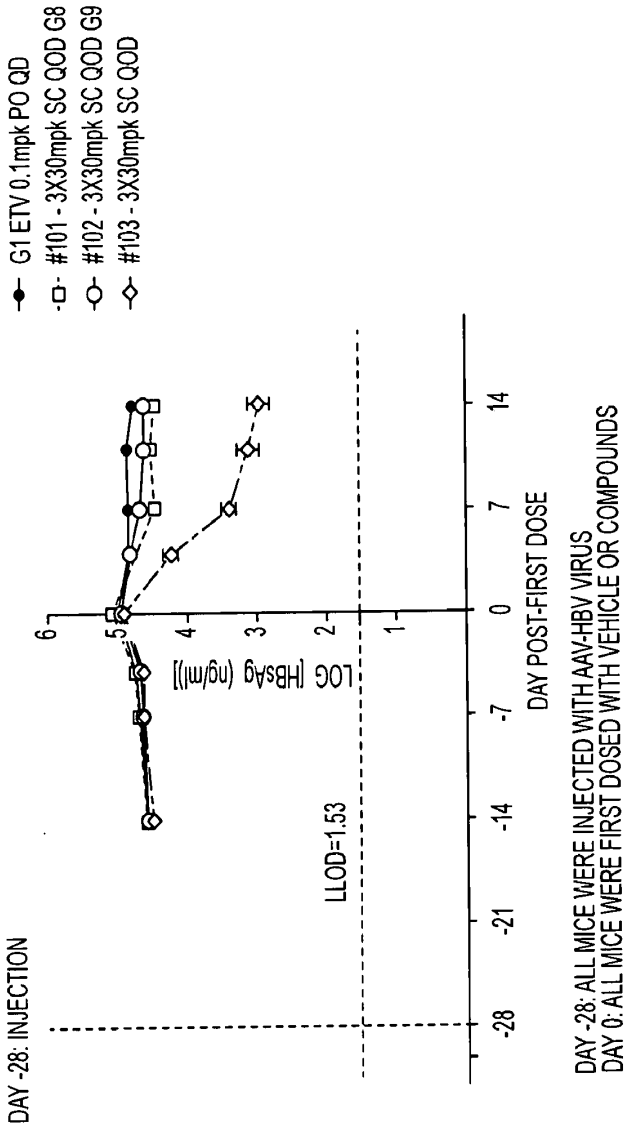
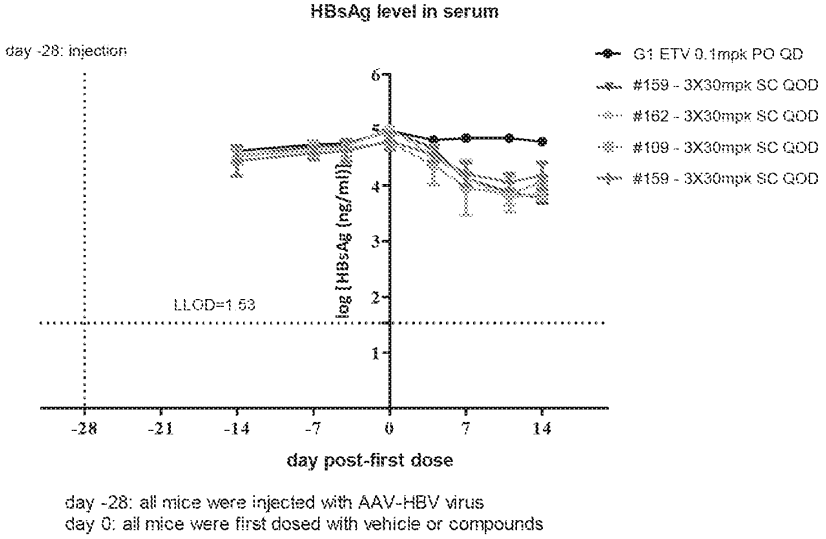

HBsAg LEVEL IN SERUM
G1 ETV 0.1mpk PO QD
#101 - 3X30mpk SC QOD G8
#102 - 3X30mpk SC QOD G9
#103 - 3X30mpk SC QOD
LOG [HBsAg (ng/ml)]
6
5
4
3
2
1
LLOD=1.53
DAY -28: INJECTION
-28
-21
-14
-7
0
7
14
DAY POST-FIRST DOSE
DAY -28: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 2B

FIG. 3



day -28: all mice were injected with AAV-HBV virus
day 0: all mice were first dosed with vehicle or compounds

	5'-mGpsmApsmUpsmUpsmApsmGpsGpsCpsApsGpsApsGpsGpsTpsmGpsmApsmApsmApsmApsmApsmG-GalNAc-3'
	5'-mGpsmApsmUpsmUpsmApsGpsGpsCpsApsGpsApsGpsGpsTpsmGpsmApsmApsmApsmApsmApsmG-GalNAc-3'
	5'mApsmApsmGpsmApsmGpsApsGpsGpsTpsGps5meCpsGps5meCps5meCps5meCps5memCpsmGpsmUpsmGpsmG –GalNac 3'
	5'5memCpsmUpsmApsmGmGpsApsGpsTpsTps5meCps5meCpsGps5meCpsApsGpsmUpsmApsmUpsmGpsmG–GalNac 3'

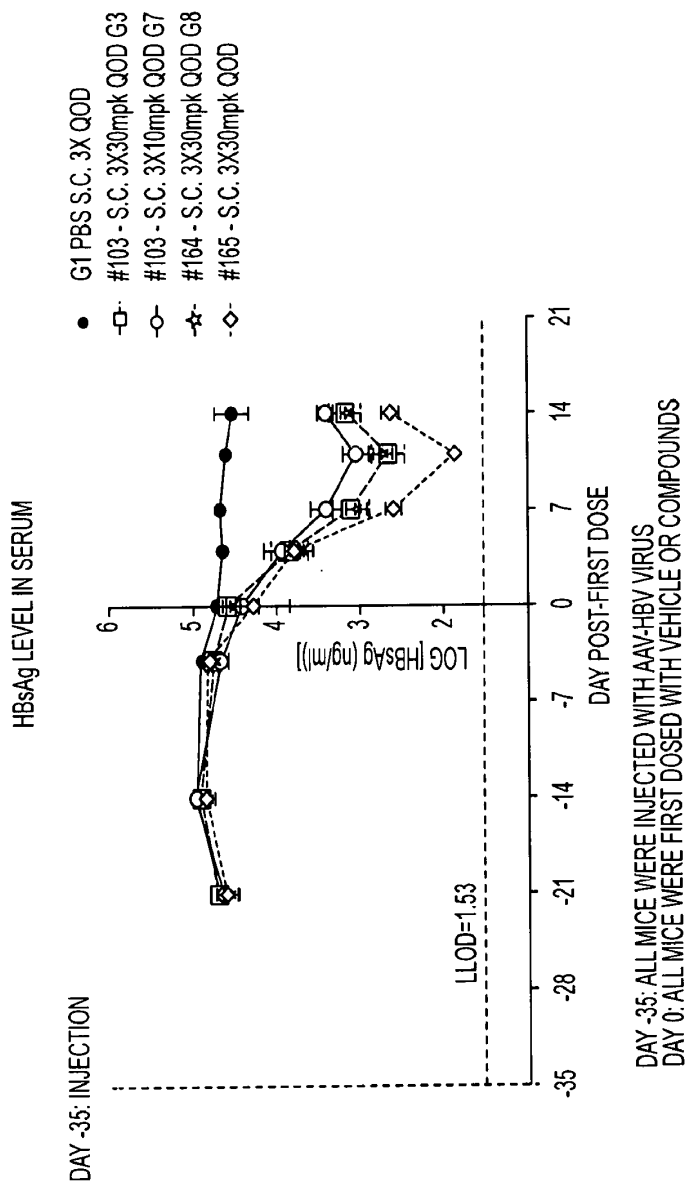

HBsAg LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#103 - S.C. 3X30mpk QOD G3
#103 - S.C. 3X10mpk QOD G7
#164 - S.C. 3X30mpk QOD G8
#165 - S.C. 3X30mpk QOD
LOG [HBsAg (ng/ml)]
6
5
4
3
2
LLOD=1.53
DAY -35: INJECTION
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -35: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 4A

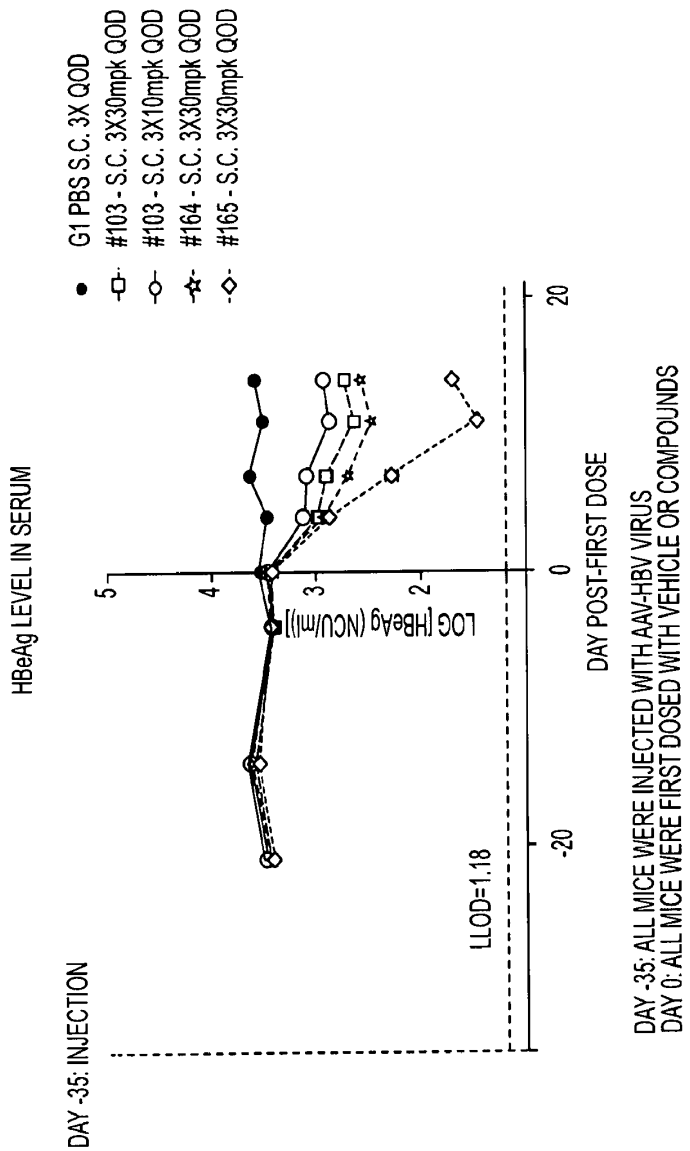

HBeAg LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#103 - S.C. 3X30mpk QOD
#103 - S.C. 3X10mpk QOD
#164 - S.C. 3X30mpk QOD
#165 - S.C. 3X30mpk QOD
LOG [HBeAg (NCU/ml)]
5
4
3
2
LLOD=1.18
DAY -35: INJECTION
-20
0
20
DAY POST-FIRST DOSE
DAY -35: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 4B

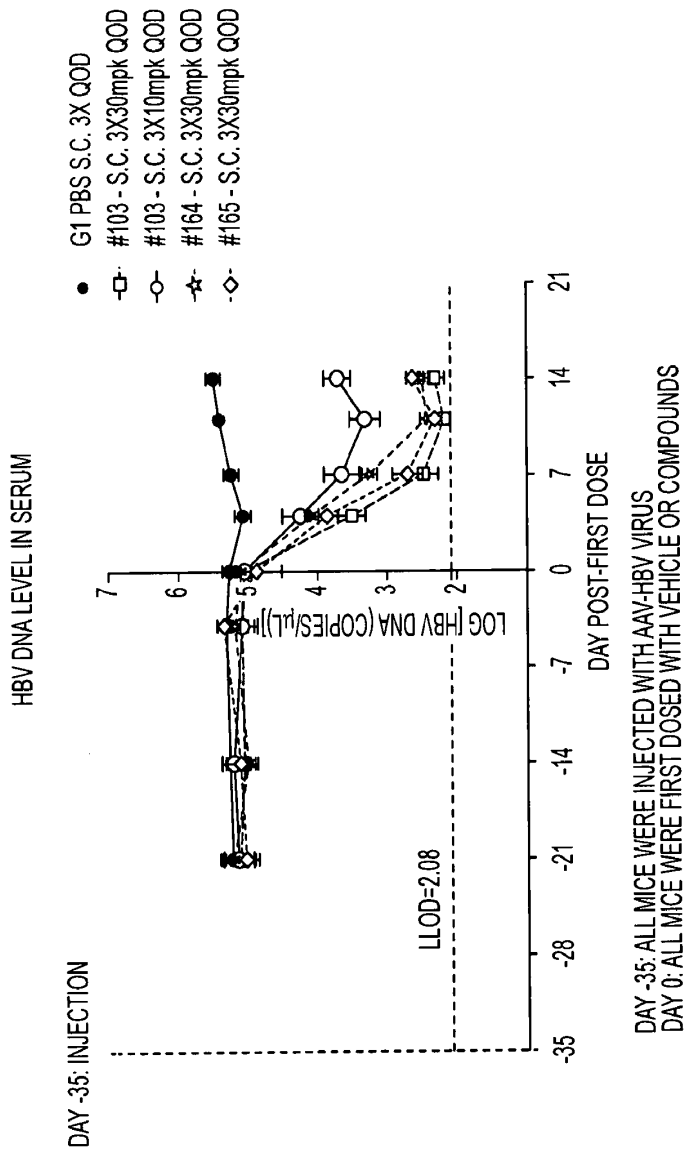

HBV DNA LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#103 - S.C. 3X30mpk QOD
#103 - S.C. 3X10mpk QOD
#164 - S.C. 3X30mpk QOD
#165 - S.C. 3X30mpk QOD
LOG [HBV DNA (COPIES/μL)]
7
6
5
4
3
2
LLOD=2.08
DAY -35: INJECTION
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -35: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 4C

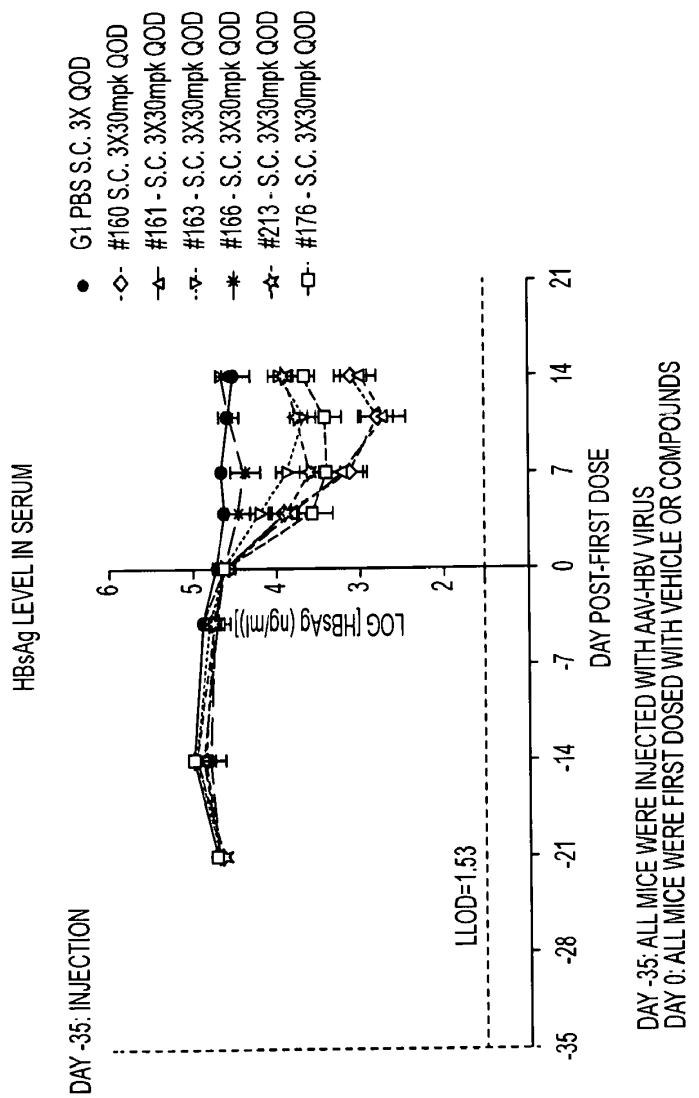

HBsAg LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#160 S.C. 3X30mpk QOD
#161 - S.C. 3X30mpk QOD
#163 - S.C. 3X30mpk QOD
#166 - S.C. 3X30mpk QOD
#213 - S.C. 3X30mpk QOD
#176 - S.C. 3X30mpk QOD
LOG [HBsAg (ng/ml)]
6
5
4
3
2
LLOD=1.53
DAY -35: INJECTION
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -35: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 5A

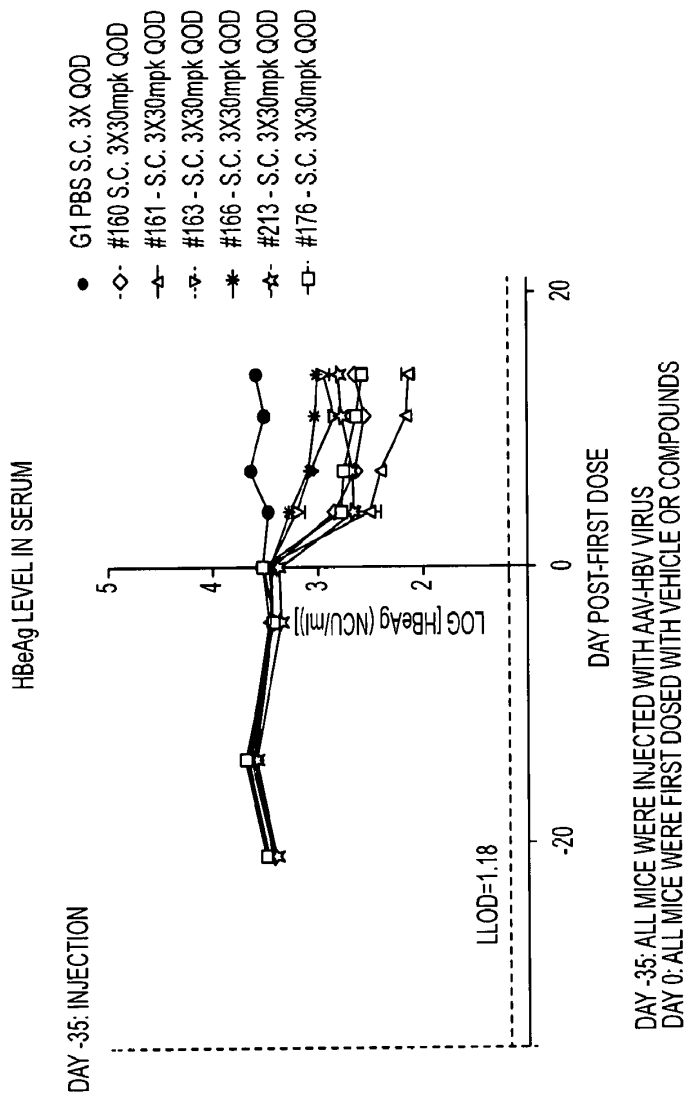

HBeAg LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#160 S.C. 3X30mpk QOD
#161 - S.C. 3X30mpk QOD
#163 - S.C. 3X30mpk QOD
#166 - S.C. 3X30mpk QOD
#213 - S.C. 3X30mpk QOD
#176 - S.C. 3X30mpk QOD
LOG [HBeAg (NCU/ml)]
5
4
3
2
LLOD=1.18
DAY -35: INJECTION
-20
0
20
DAY POST-FIRST DOSE
DAY -35: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 5B

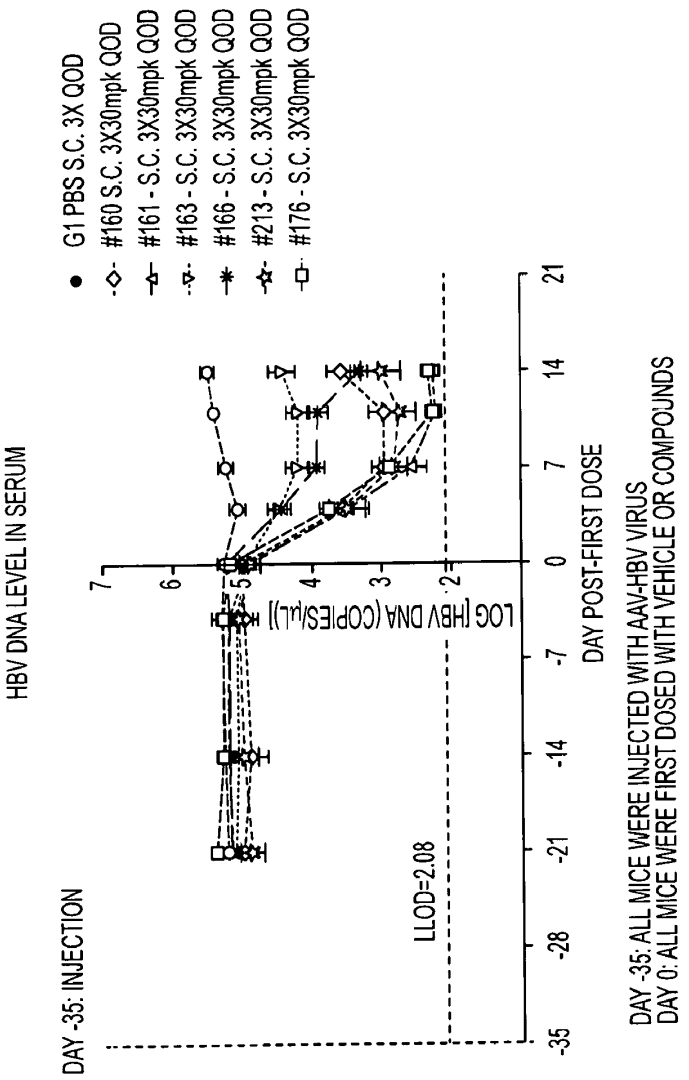

HBV DNA LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#160 S.C. 3X30mpk QOD
#161 - S.C. 3X30mpk QOD
#163 - S.C. 3X30mpk QOD
#166 - S.C. 3X30mpk QOD
#213 - S.C. 3X30mpk QOD
#176 - S.C. 3X30mpk QOD
LOG [HBV DNA (COPIES/μL)]
7
6
5
4
3
2
LLOD=2.08
DAY -35: INJECTION
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -35: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 5C

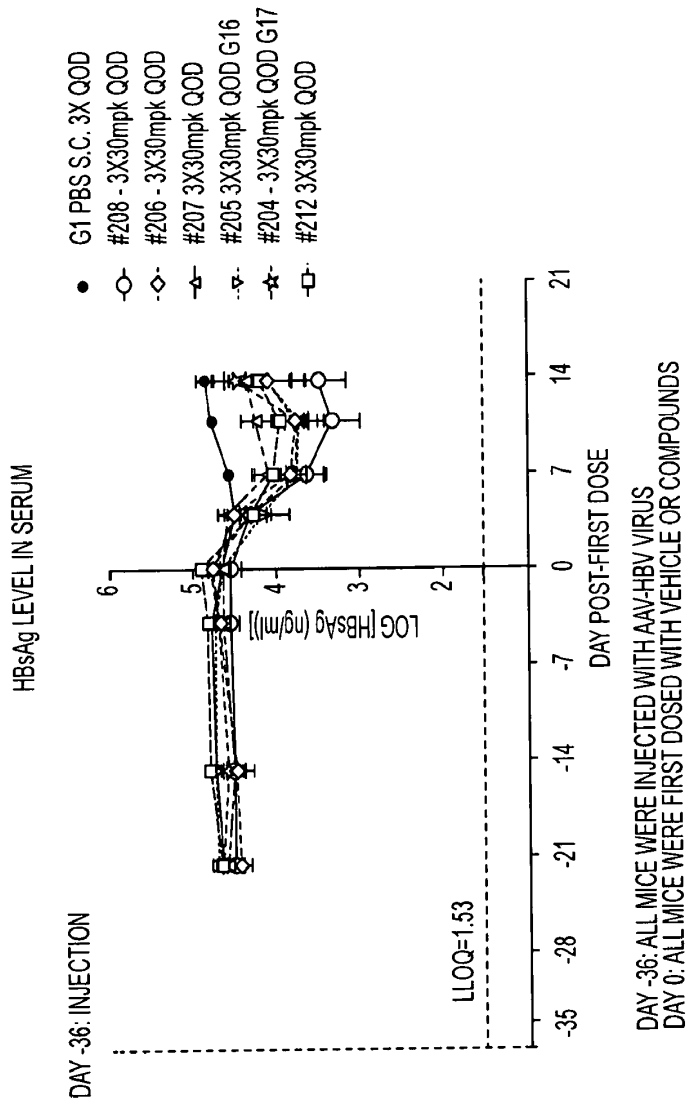

HBsAg LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#208 - 3X30mpk QOD
#206 - 3X30mpk QOD
#207 3X30mpk QOD
#205 3X30mpk QOD G16
#204 - 3X30mpk QOD G17
#212 3X30mpk QOD
LOG [HBsAg (ng/ml)]
6
5
4
3
2
LLOQ=1.53
DAY -36: INJECTION
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -36: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 6A

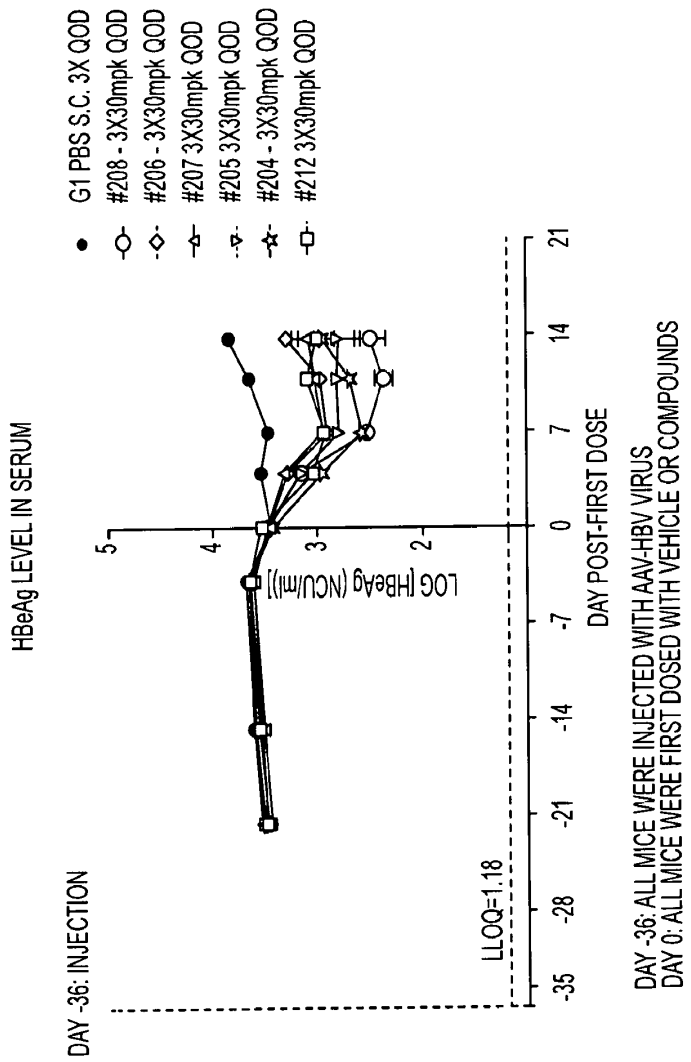

HBeAg LEVEL IN SERUM
G1 PBS S.C. 3X QOD
#208 - 3X30mpk QOD
#206 - 3X30mpk QOD
#207 3X30mpk QOD
#205 3X30mpk QOD
#204 - 3X30mpk QOD
#212 3X30mpk QOD
LOG [HBeAg (NCU/ml)]
5
4
3
2
DAY -36: INJECTION
LLOQ=1.18
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -36: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 6B

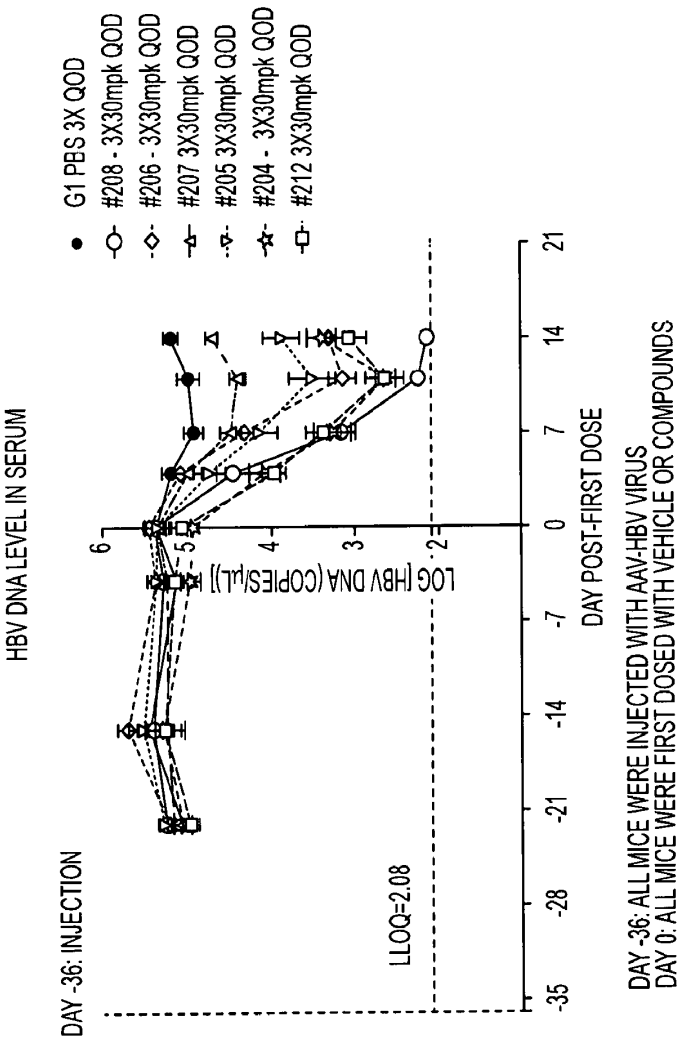

HBV DNA LEVEL IN SERUM
G1 PBS 3X QOD
#208 - 3X30mpk QOD
#206 - 3X30mpk QOD
#207 3X30mpk QOD
#205 3X30mpk QOD
#204 - 3X30mpk QOD
#212 3X30mpk QOD
LOG [HBV DNA (COPIES/µL)]
6
5
4
3
2
LLOQ=2.08
DAY -36: INJECTION
-35
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
DAY -36: ALL MICE WERE INJECTED WITH AAV-HBV VIRUS
DAY 0: ALL MICE WERE FIRST DOSED WITH VEHICLE OR COMPOUNDS

FIG. 6C

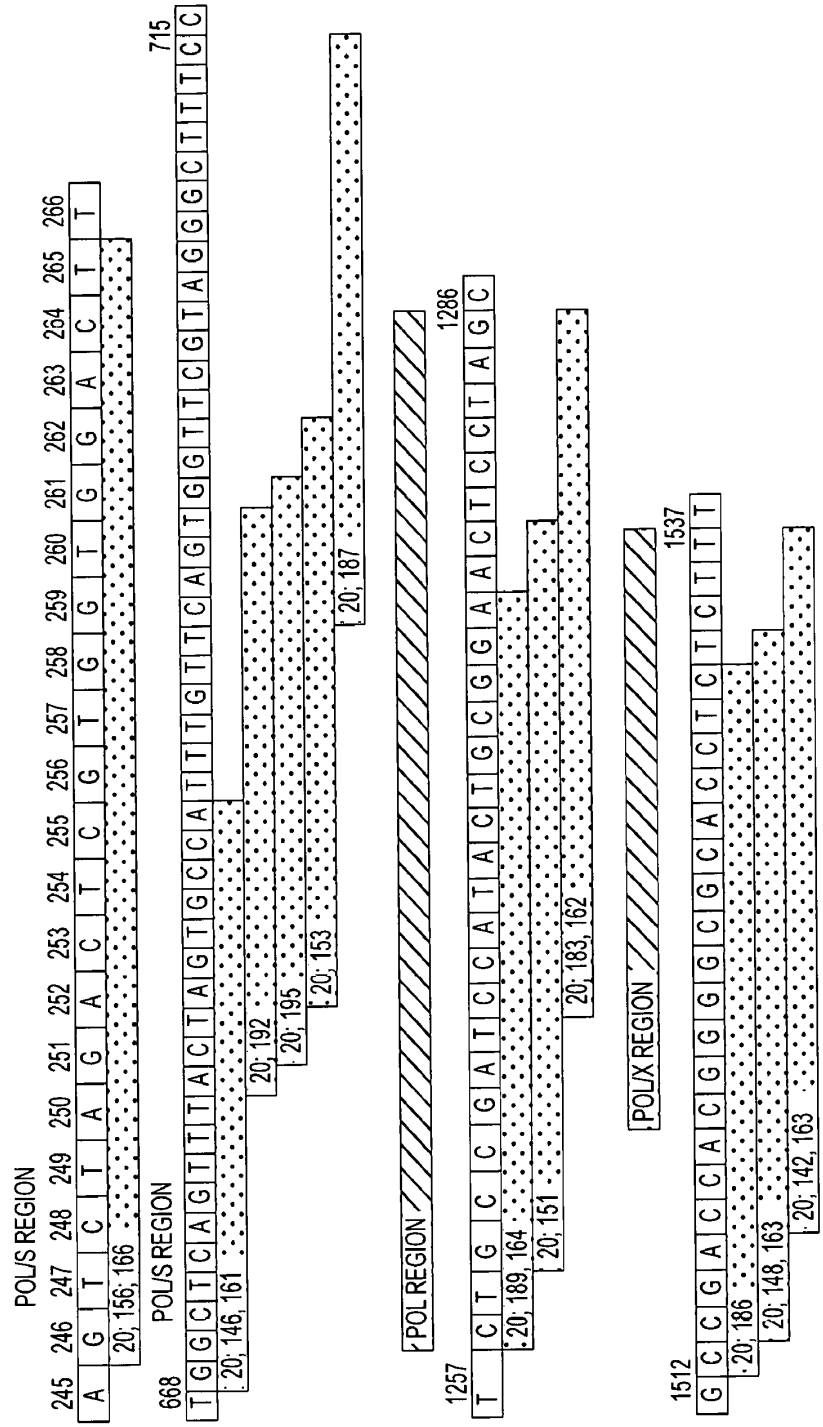
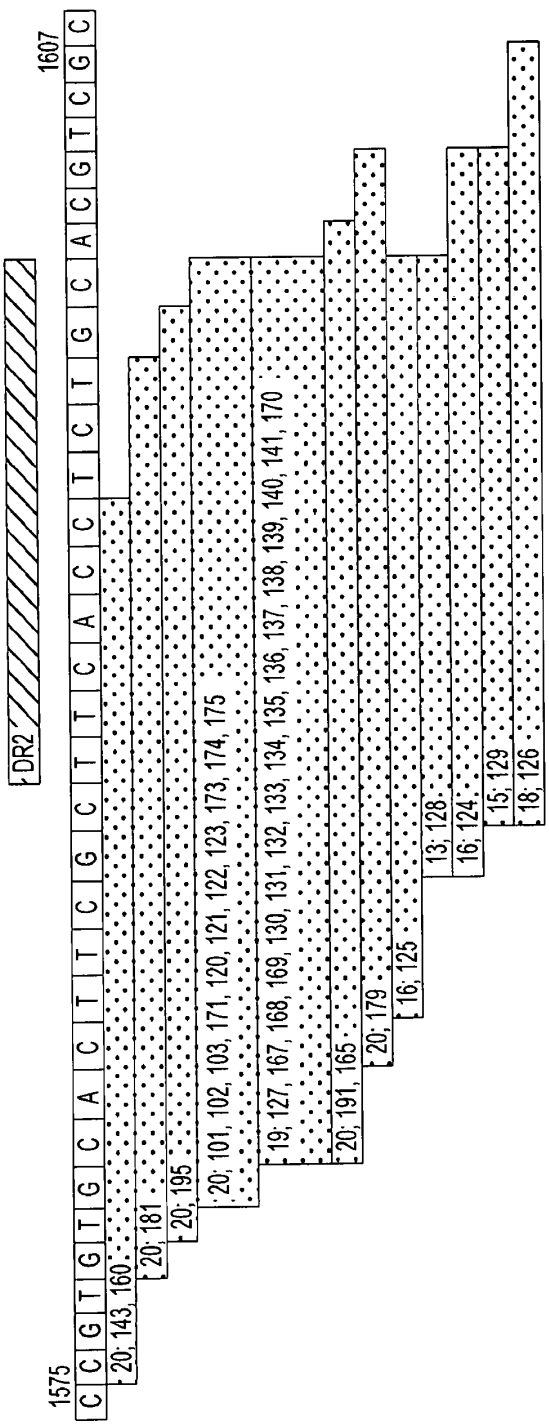

POL/S REGION
245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266
A G T C T A G A C T C G T G G G T G G A C T T
20; 156; 166
POL/S REGION
668 715
T G G C T C A G T T A C T A G T G C C A T T T G T T C A G T G G T T C G T A G G G C T T T C C
20; 146, 161
20; 192
20; 195
20; 153
20; 187
POL REGION
1257 1286
T C T G C C G A T C C A T A C T G C G G A A C T C C T A G C
20; 189, 164
20; 151
20; 183, 162
POL/X REGION
1512 1537
G C C G A C C A C G G G G C G C A C C T C T T T
20; 186
20; 148, 163
20; 142, 163

FIG. 7



Continuation of FIG. 7

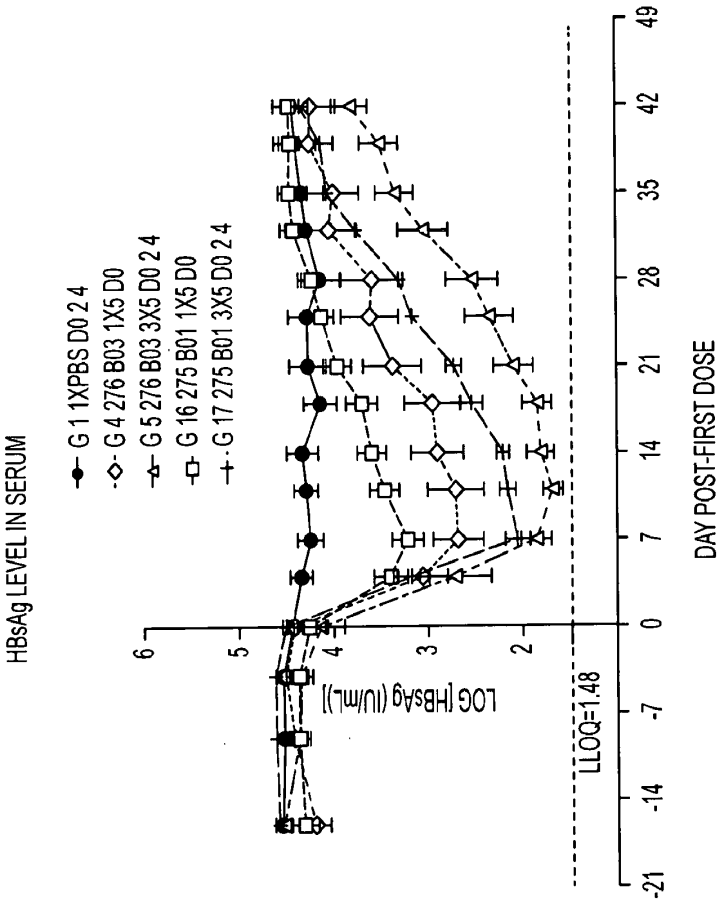

HBsAg LEVEL IN SERUM
G 1 1XPBS D0 2 4
G 4 276 B03 1X5 D0
G 5 276 B03 3X5 D0 2 4
G 16 275 B01 1X5 D0
G 17 275 B01 3X5 D0 2 4
LOG [HBsAg (IU/mL)]
6
5
4
3
2
LLOQ=1.48
-21
-14
-7
0
7
14
21
28
35
42
49
DAY POST-FIRST DOSE

FIG. 8

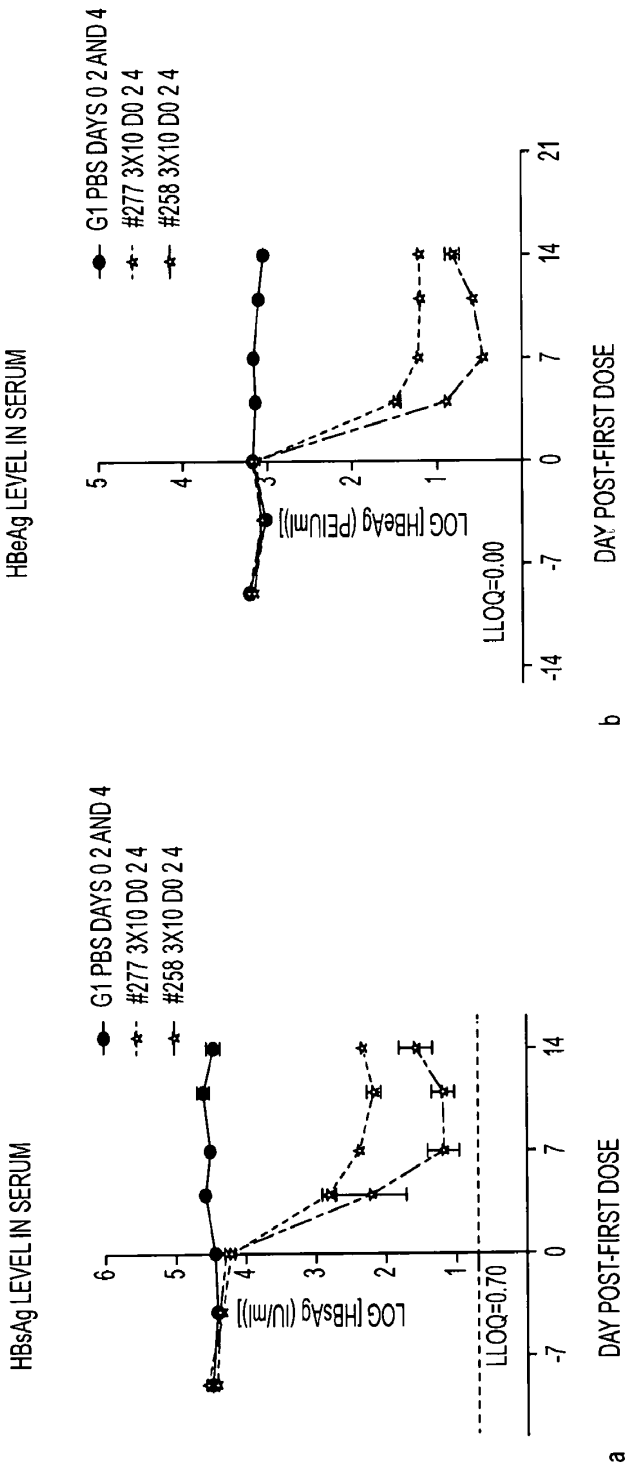

HBsAg LEVEL IN SERUM
G1 PBS DAYS 0 2 AND 4
#277 3X10 D0 2 4
#258 3X10 D0 2 4
LOG [HBsAg (IU/ml)]
LLOQ=0.70
DAY POST-FIRST DOSE
a
HBeAg LEVEL IN SERUM
G1 PBS DAYS 0 2 AND 4
#277 3X10 D0 2 4
#258 3X10 D0 2 4
LOG [HBeAg (PEIU/ml)]
LLOQ=0.00
DAY POST-FIRST DOSE
b

FIG. 9A

FIG. 9B

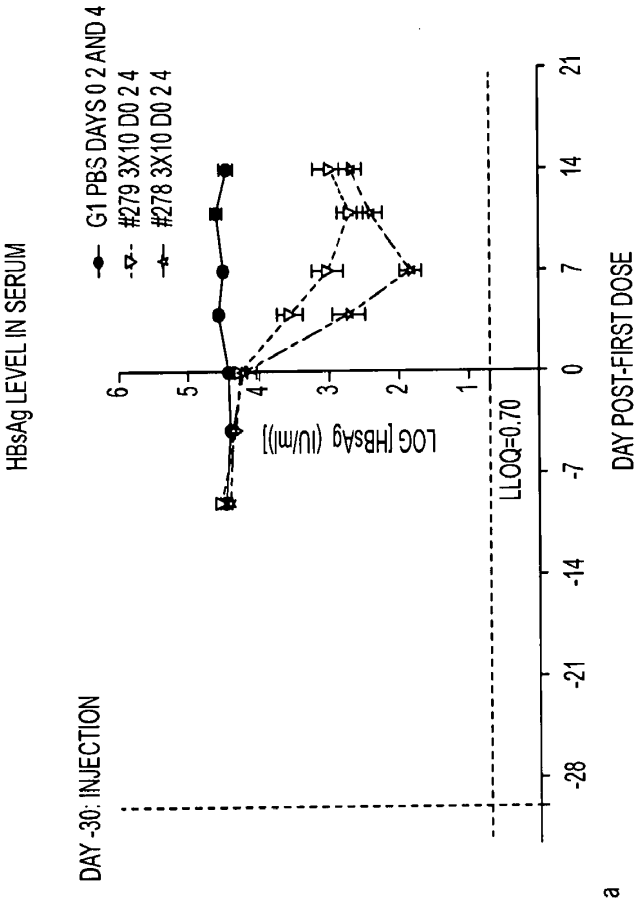

HBsAg LEVEL IN SERUM
G1 PBS DAYS 0 2 AND 4
#279 3X10 D0 2 4
#278 3X10 D0 2 4
LOG [HBsAg (IU/ml)]
6
5
4
3
2
1
LLOQ=0.70
DAY -30: INJECTION
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
a

FIG. 10A

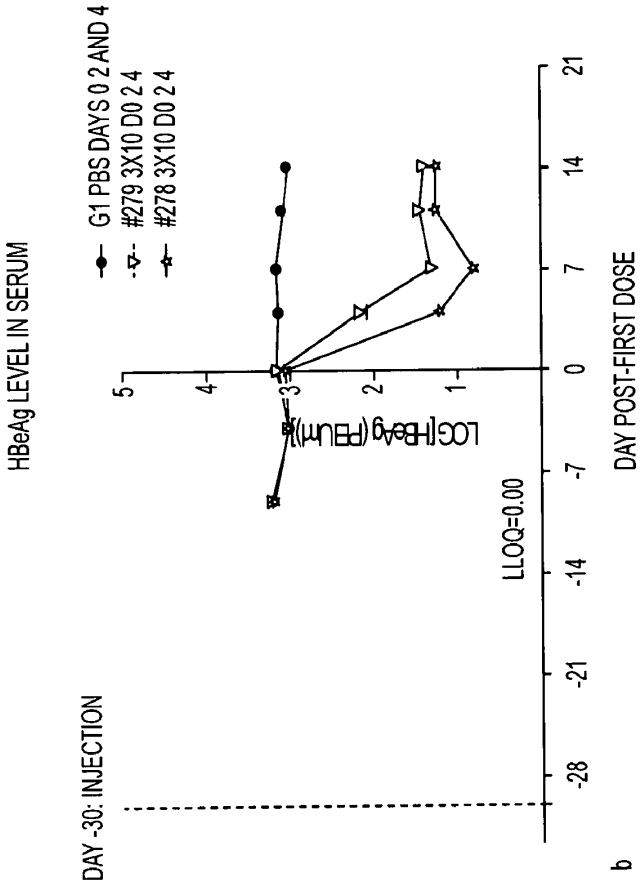

HBeAg LEVEL IN SERUM
G1 PBS DAYS 0 2 AND 4
#279 3X10 D0 2 4
#278 3X10 D0 2 4
LOG(HBeAg (PEU/ml))
5
4
3
2
1
0
DAY -30: INJECTION
LLOQ=0.00
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
b

FIG. 10B

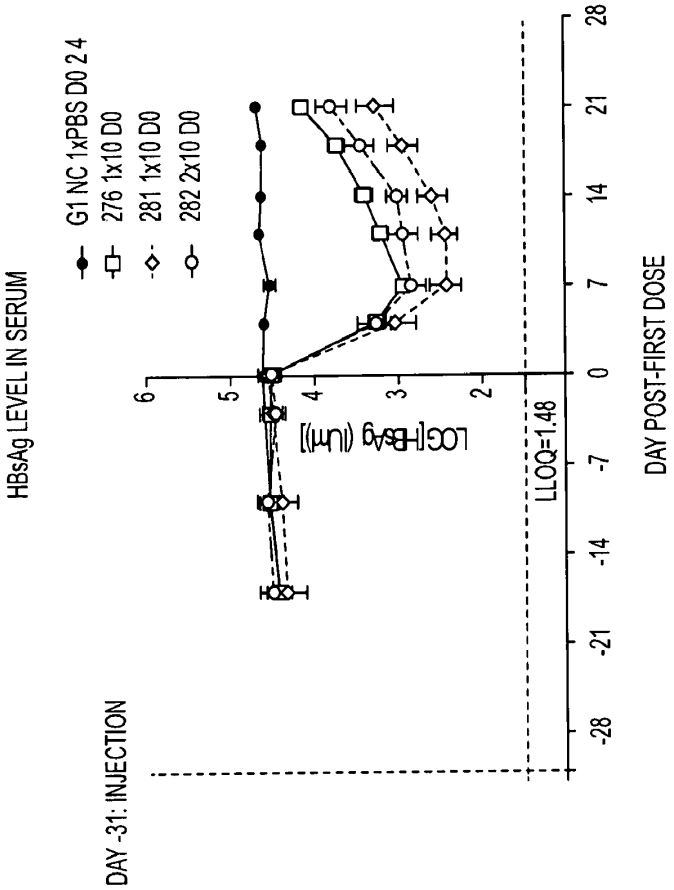

HBsAg LEVEL IN SERUM
G1 NC 1xPBS D0 2 4
276 1x10 D0
281 1x10 D0
282 2x10 D0
Log[HBsAg (IU/mL)]
6
5
4
3
2
LLOQ=1.48
DAY -31: INJECTION
-28
-21
-14
-7
0
7
14
21
28
DAY POST-FIRST DOSE

FIG. 11A

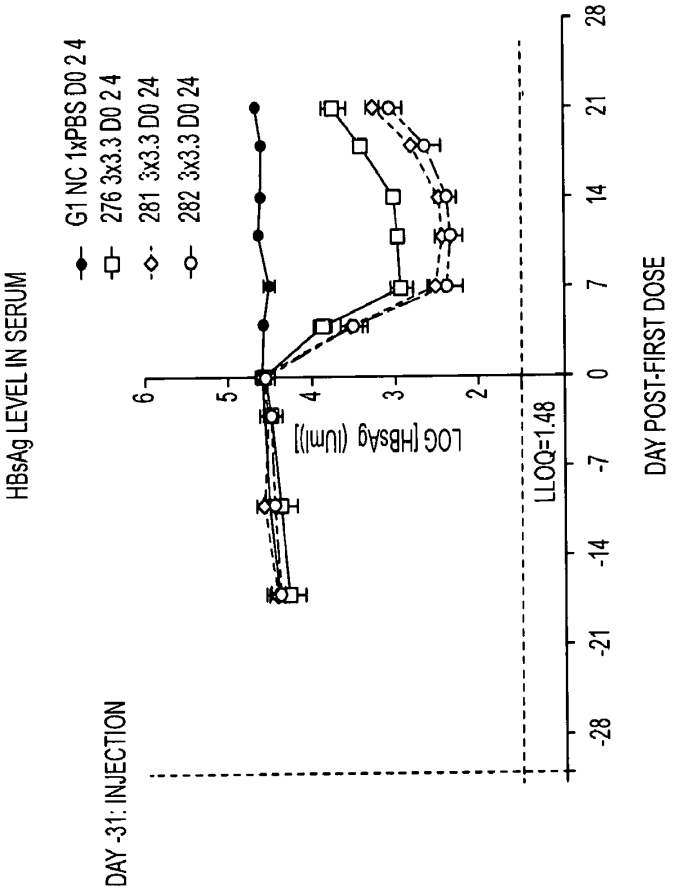

HBsAg LEVEL IN SERUM
G1 NC 1xPBS D0 2 4
276 3x3.3 D0 2 4
281 3x3.3 D0 24
282 3x3.3 D0 24
LOG [HBsAg (IU/ml)]
6
5
4
3
2
LLOQ=1.48
DAY -31: INJECTION
-28
-21
-14
-7
0
7
14
21
28
DAY POST-FIRST DOSE

FIG. 11B

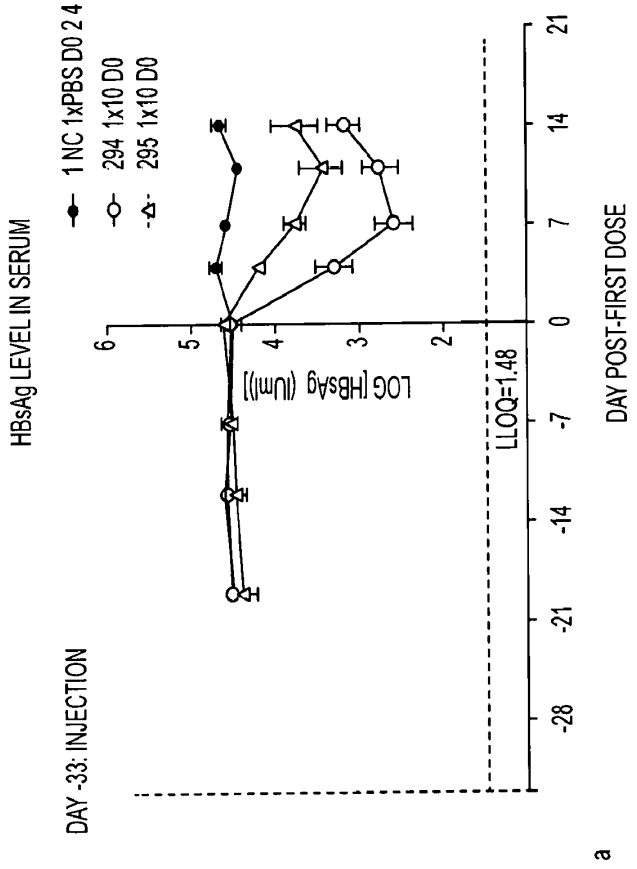

HBsAg LEVEL IN SERUM
1 NC 1xPBS D0 2 4
294 1x10 D0
295 1x10 D0
LOG [HBsAg (IU/ml)]
6
5
4
3
2
LLOQ=1.48
DAY -33: INJECTION
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
a

FIG. 12A

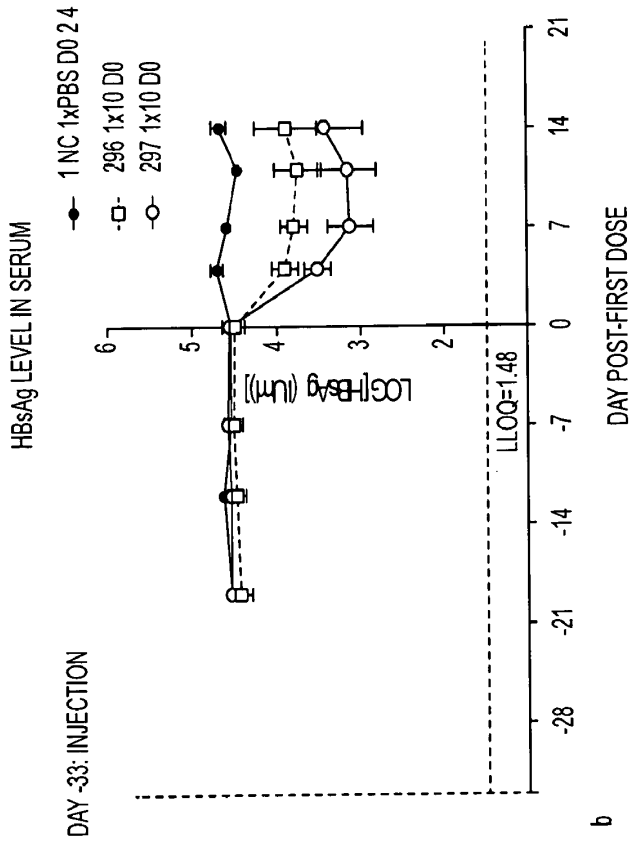

HBsAg LEVEL IN SERUM
1 NC 1xPBS D0 2 4
296 1x10 D0
297 1x10 D0
DAY -33: INJECTION
LOG[HBsAg (IU/mL)]
6
5
4
3
2
LLOQ=1.48
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
b

FIG. 12B

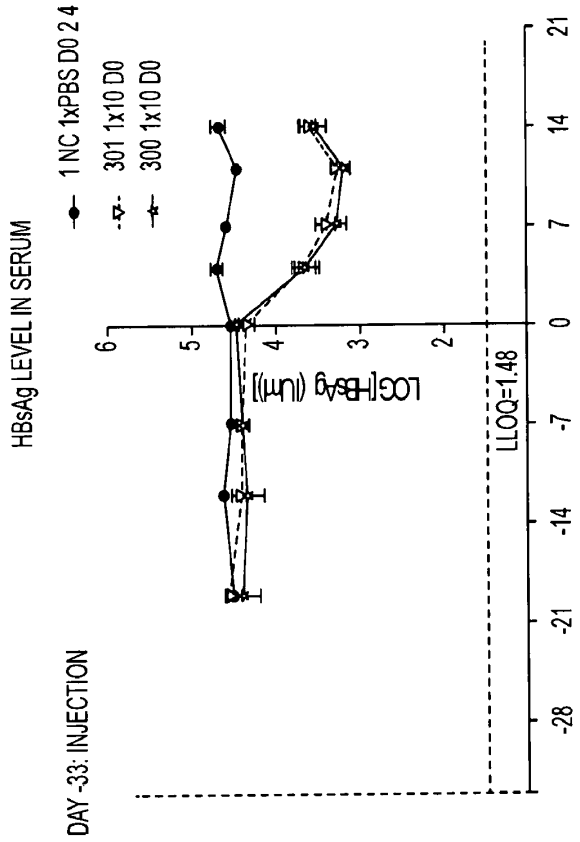

HBsAg LEVEL IN SERUM
1 NC 1xPBS D0 2 4
301 1x10 D0
300 1x10 D0
LOG[HBsAg (IUnit)]
6
5
4
3
2
LLOQ=1.48
DAY -33: INJECTION
-28
-21
-14
-7
0
7
14
21
DAY POST-FIRST DOSE
C

FIG. 12C