
enhancer
promoter
intron
signal peptide
GLA coding region
3' UTR
polyA
name
APOE
hAAT
HBB-IGG
GLA
GLAco
bGH
Variant #4 (Fabry 1.0)

FIG.1A


APOE
hAAT
HBB-IGG
GLA
GLAco
WPREmut6 v1
bGH
Variant #21 (Fabry 2.0)

FIG.1B

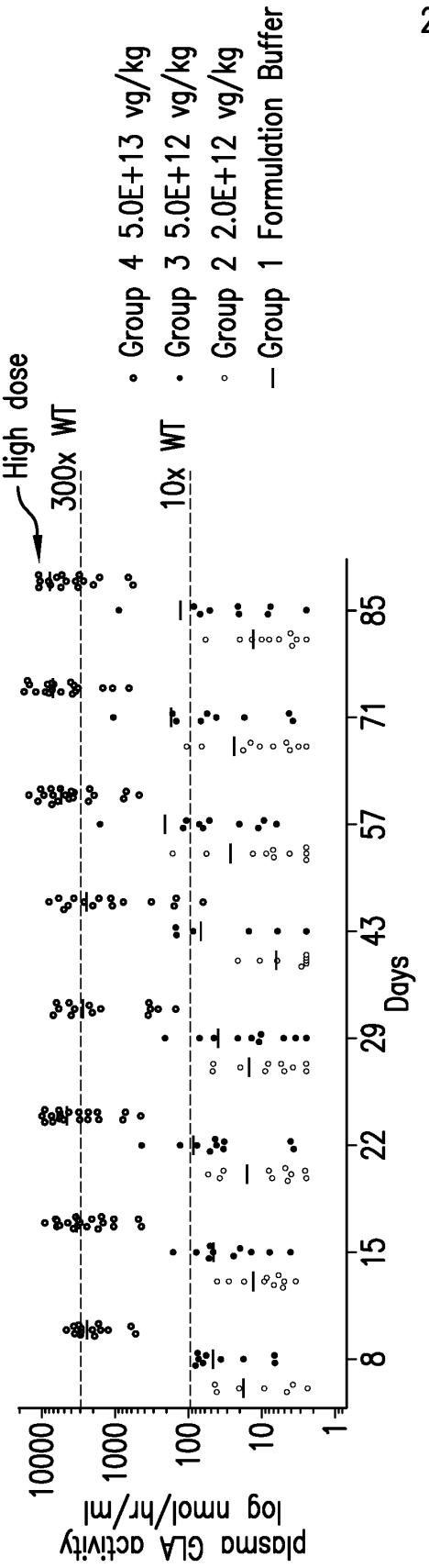

plasma GLA activity
log nmol/hr/ml
10000
1000
100
10
1
8
15
22
29
43
57
71
85
Days
High dose
300x WT
10x WT
Group 4 5.0E+13 vg/kg
Group 3 5.0E+12 vg/kg
Group 2 2.0E+12 vg/kg
Group 1 Formulation Buffer

FIG.2

Variant 4
plasma α-Gal A activity
log nmol/hr/ml
10000
1000
100
10
1
15
29
43
57
71
85
Days
Group 4 5.0E+13 vg/kg
Group 3 5.0E+12 vg/kg
Group 2 2.0E+12 vg/kg
Group 1 Formulation Buffer
5e13 vg/kg
5e12 vg/kg
2e12 vg/kg
formulation
Plasma activity per group at Day 85
nmol/hr/ml
Fold of WT
Formulation
2e12
5e12
5e13 vg/kg
below LOQ
n/a
13
1x
34*
3x
7750
775x

FIG.3

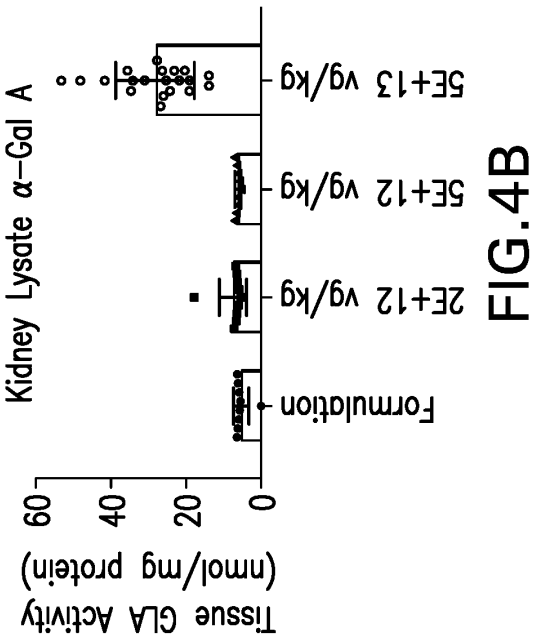


FIG.4B

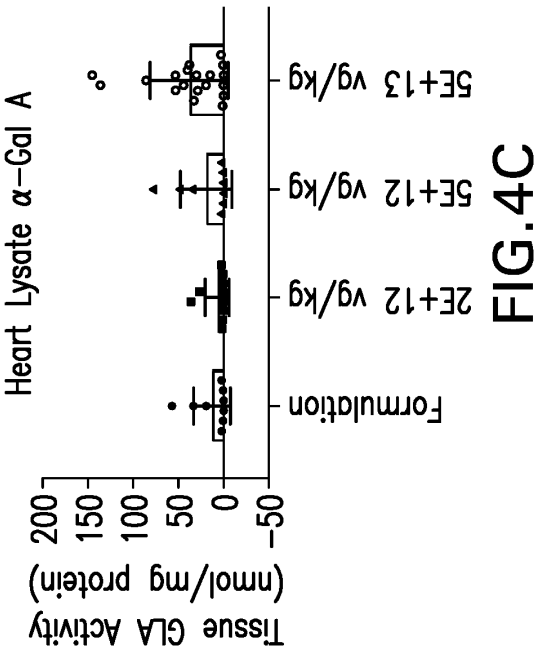


FIG.4C

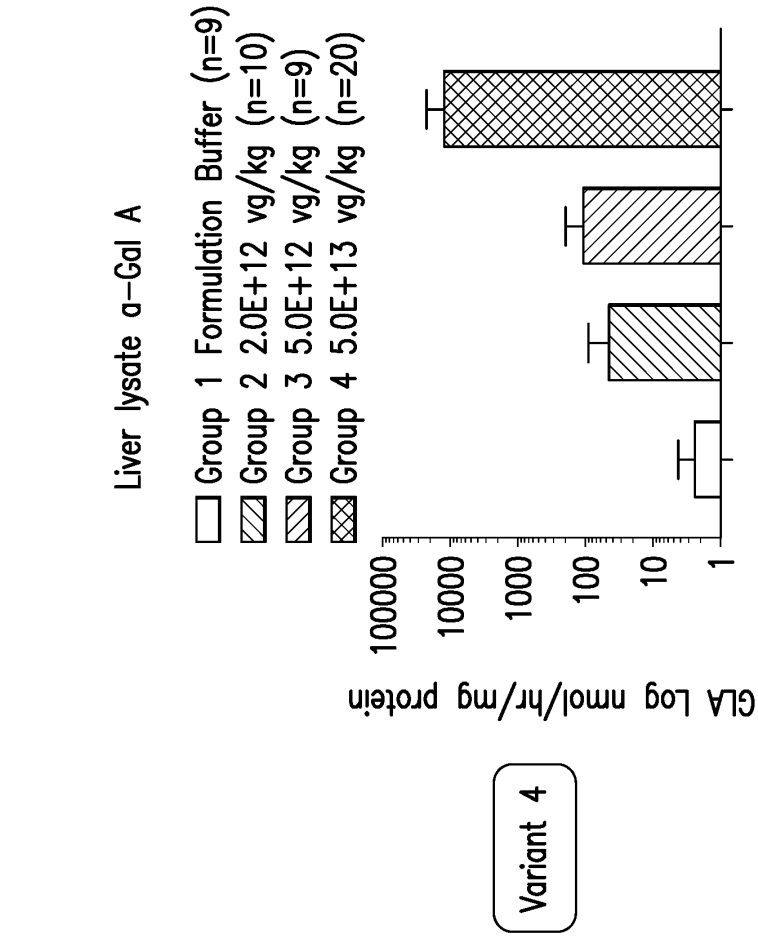


FIG.4A

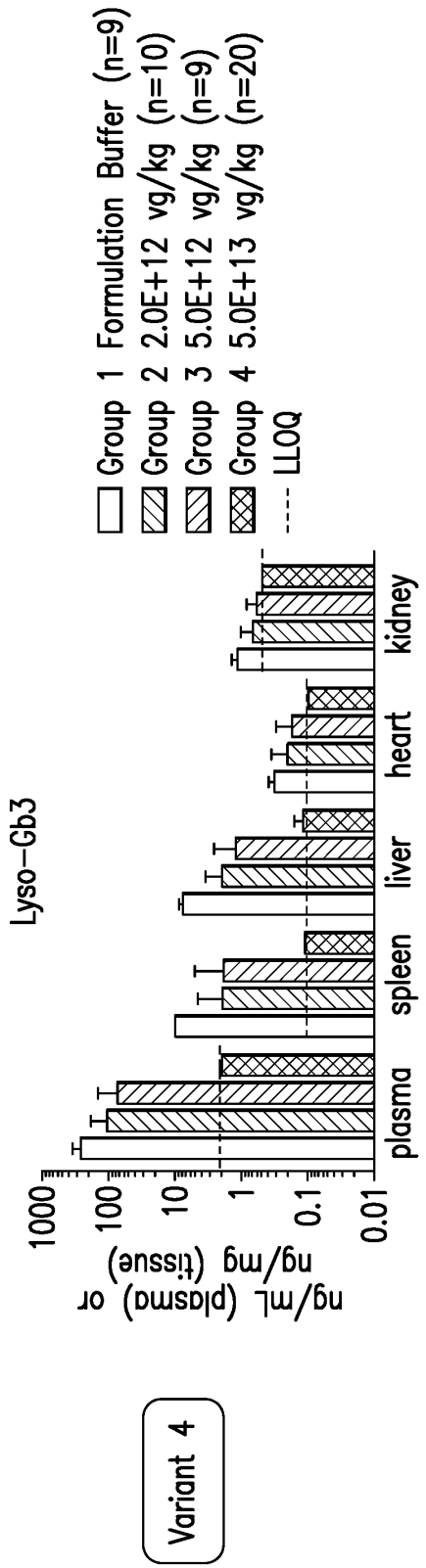

Lyso-Gb3
ng/mL (plasma) or
ng/mg (tissue)
1000
100
10
1
0.1
0.01
plasma
spleen
liver
heart
kidney
Group 1 Formulation Buffer (n=9)
Group 2 2.0E+12 vg/kg (n=10)
Group 3 5.0E+12 vg/kg (n=9)
Group 4 5.0E+13 vg/kg (n=20)
LLOQ
Variant 4

FIG.5A

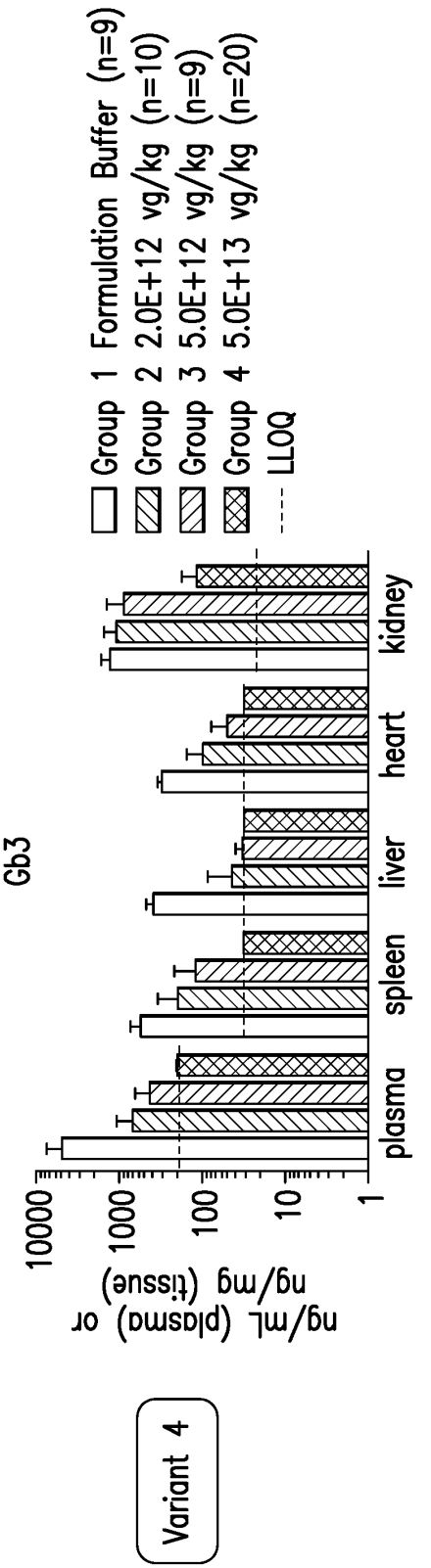

Gb3
ng/mL (plasma) or
ng/mg (tissue)
10000
1000
100
10
1
plasma
spleen
liver
heart
kidney
Group 1 Formulation Buffer (n=9)
Group 2 2.0E+12 vg/kg (n=10)
Group 3 5.0E+12 vg/kg (n=9)
Group 4 5.0E+13 vg/kg (n=20)
LLOQ
Variant 4

FIG.5B

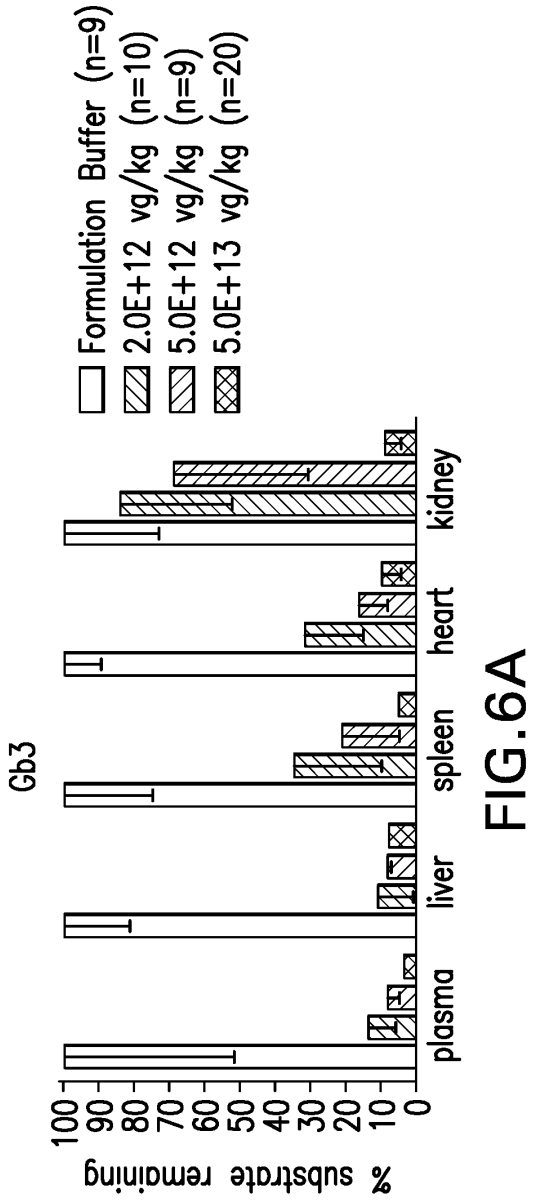

Gb3
Formulation Buffer (n=9)
2.0E+12 vg/kg (n=10)
5.0E+12 vg/kg (n=9)
5.0E+13 vg/kg (n=20)
% substrate remaining
100
90
80
70
60
50
40
30
20
10
0
plasma
liver
spleen
heart
kidney
Variant 4

FIG.6A

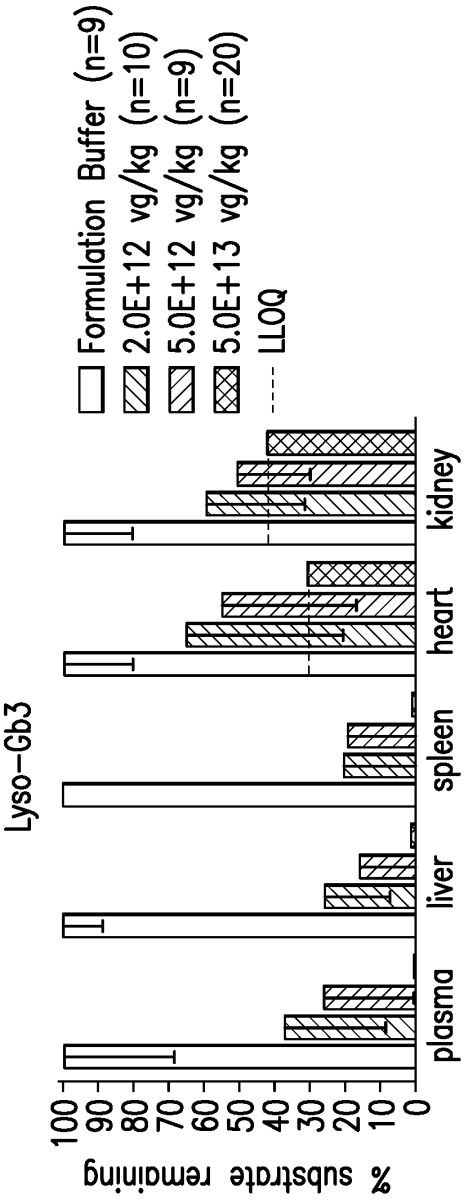

Lyso-Gb3
Formulation Buffer (n=9)
2.0E+12 vg/kg (n=10)
5.0E+12 vg/kg (n=9)
5.0E+13 vg/kg (n=20)
LLOQ
% substrate remaining
100
90
80
70
60
50
40
30
20
10
0
plasma
liver
spleen
heart
kidney
Variant 4

FIG.6B

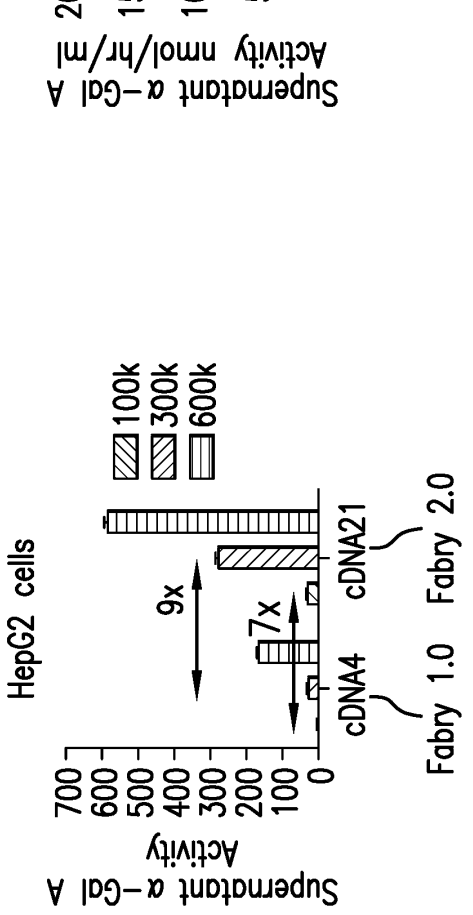


FIG.7A

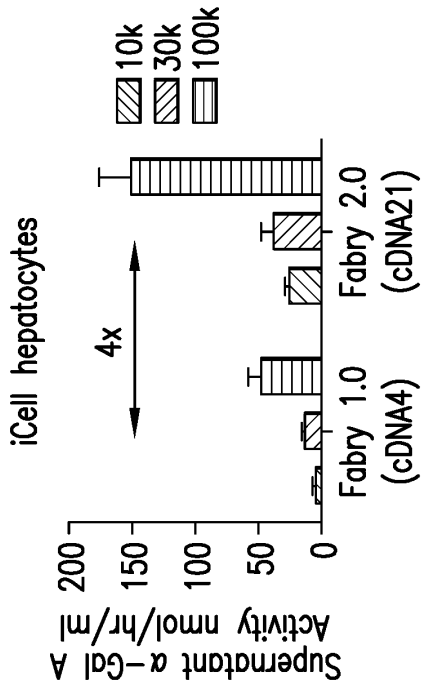


FIG.7B

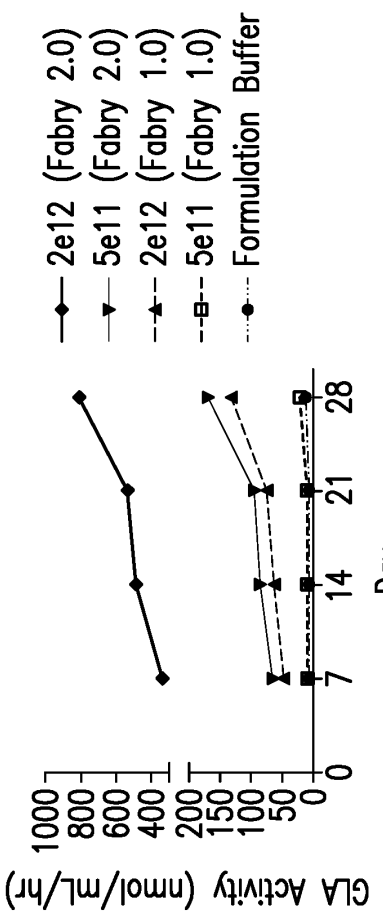


FIG.8

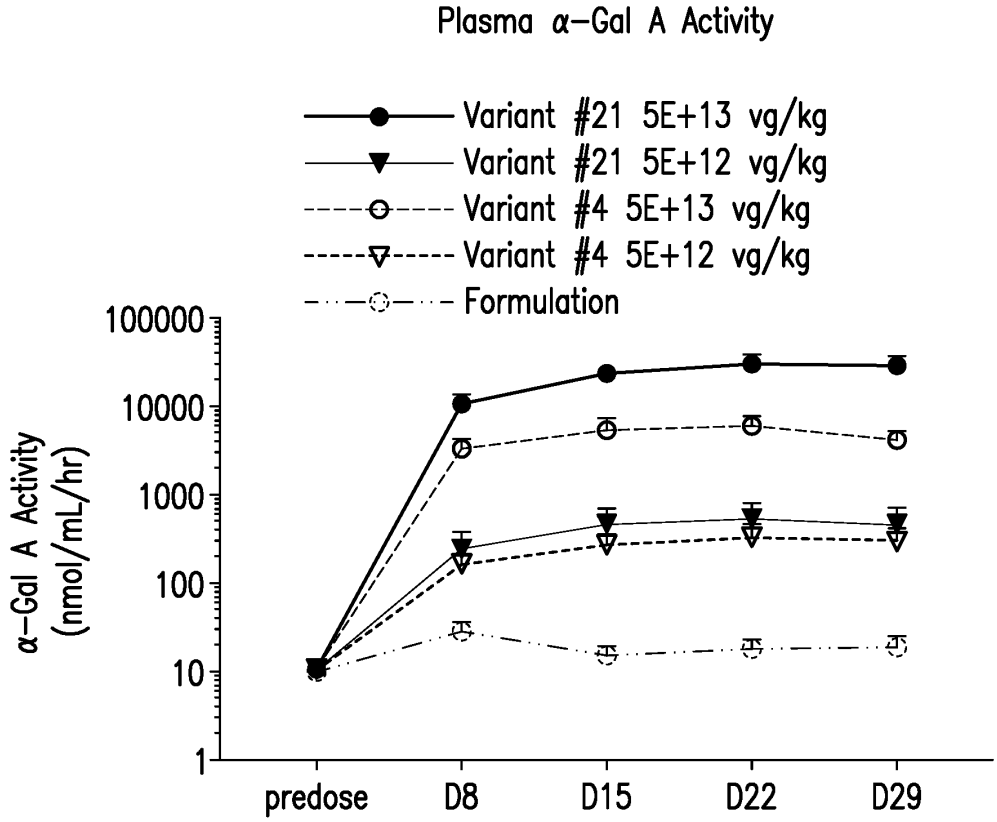
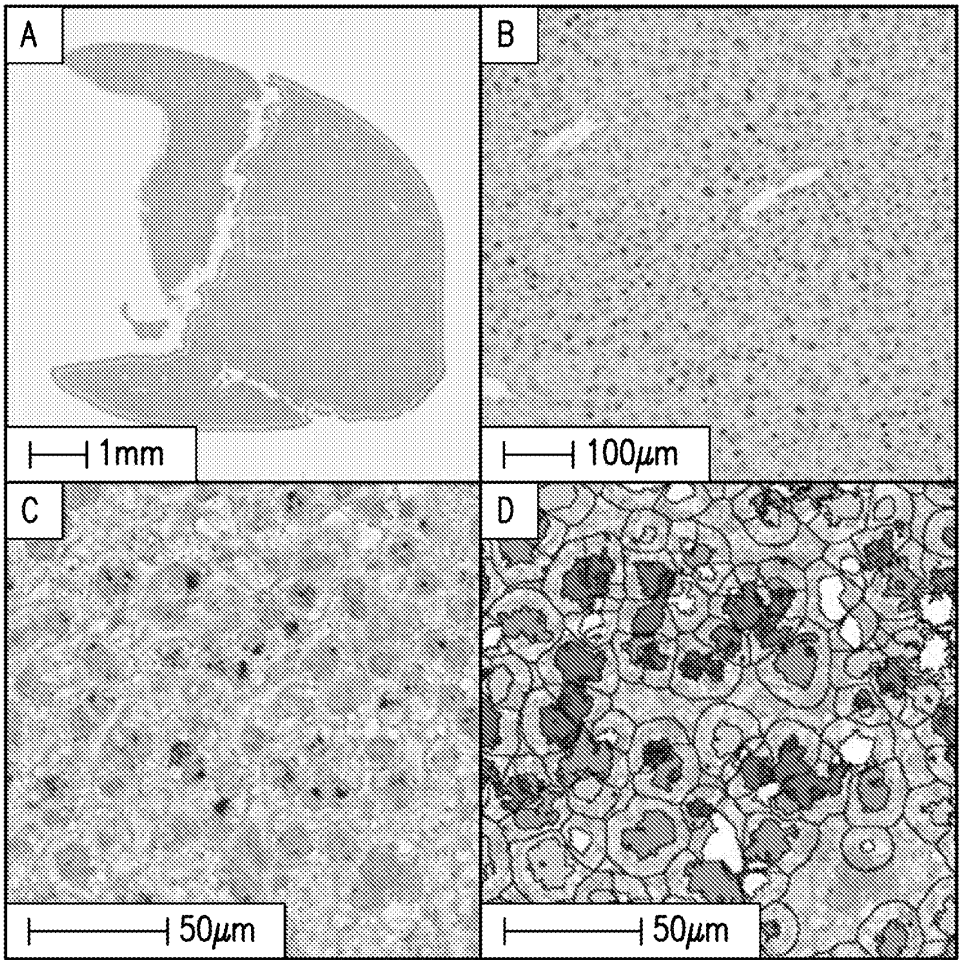
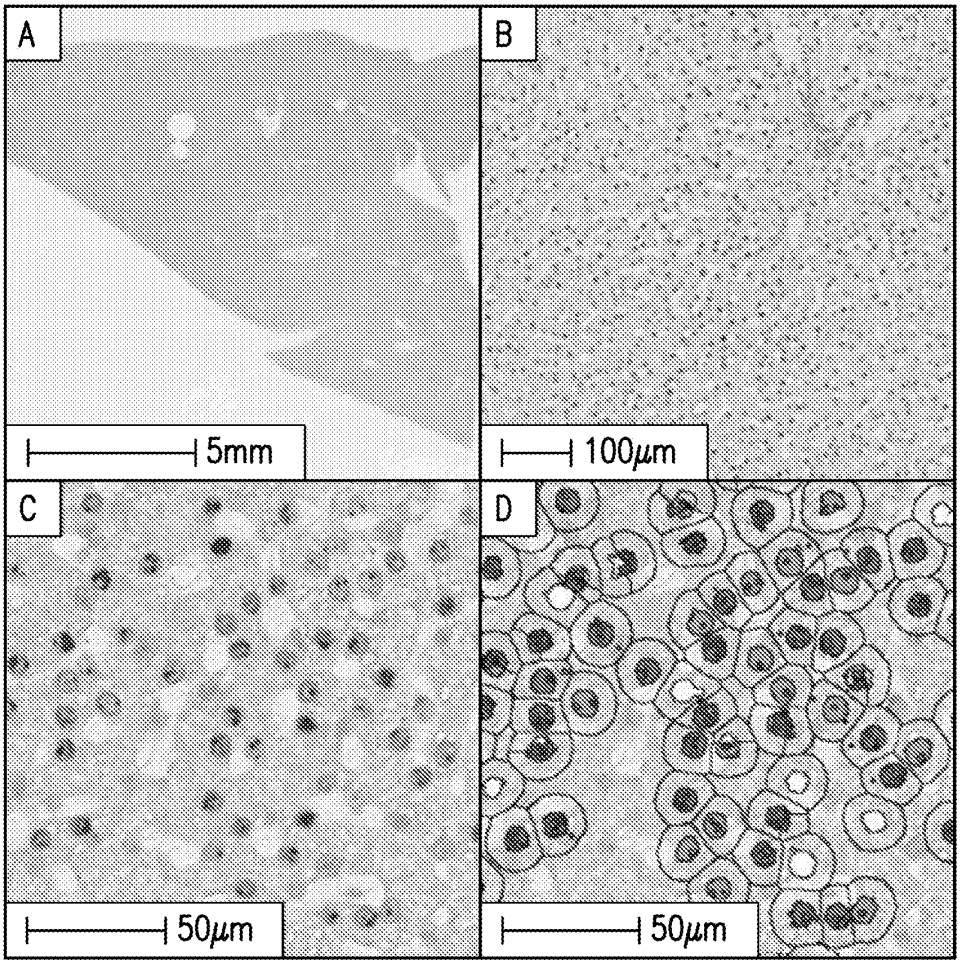

Plasma α–Gal A Activity
Variant #21 5E+13 vg/kg
Variant #21 5E+12 vg/kg
Variant #4 5E+13 vg/kg
Variant #4 5E+12 vg/kg
Formulation
α–Gal A Activity (nmol/mL/hr)
100000
10000
1000
100
10
1
predose
D8
D15
D22
D29

FIG.9



Variant 4

FIG.10



Variant 4

FIG.11

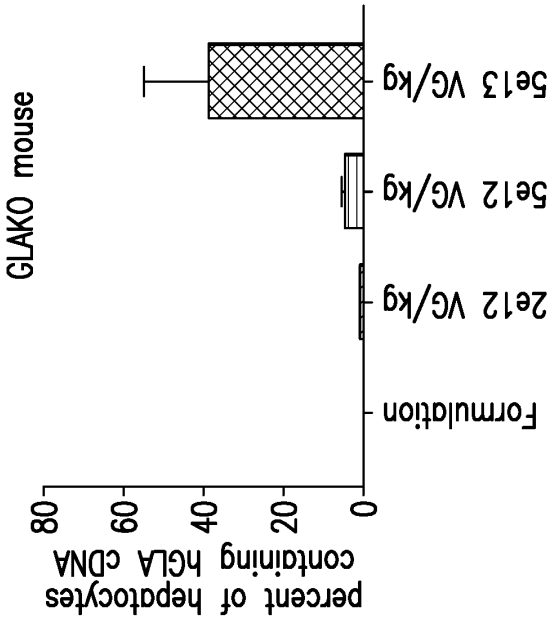


FIG.12A

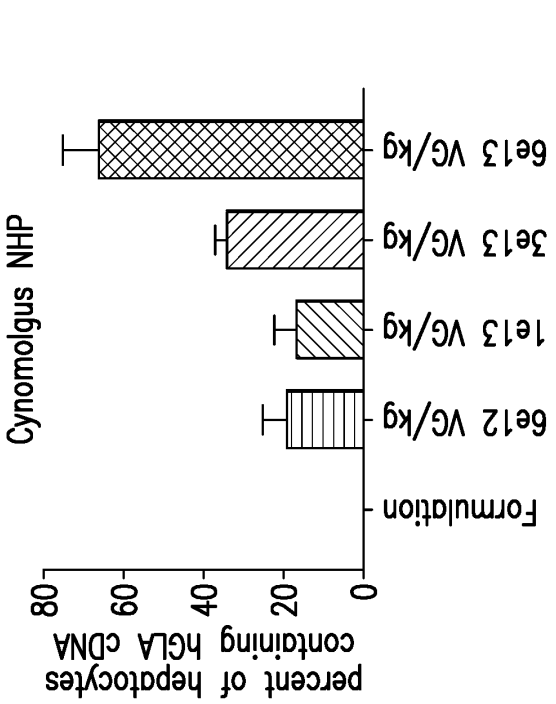


FIG.12B

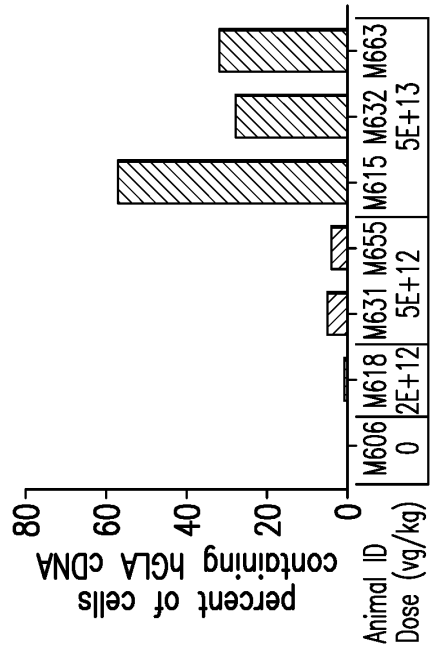


FIG.12C

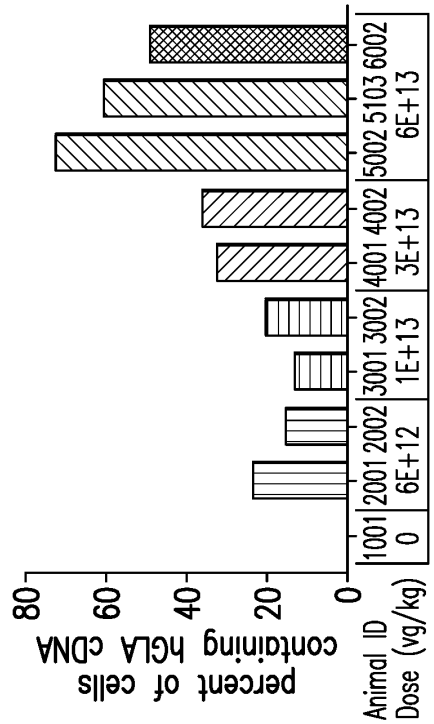


FIG.12D

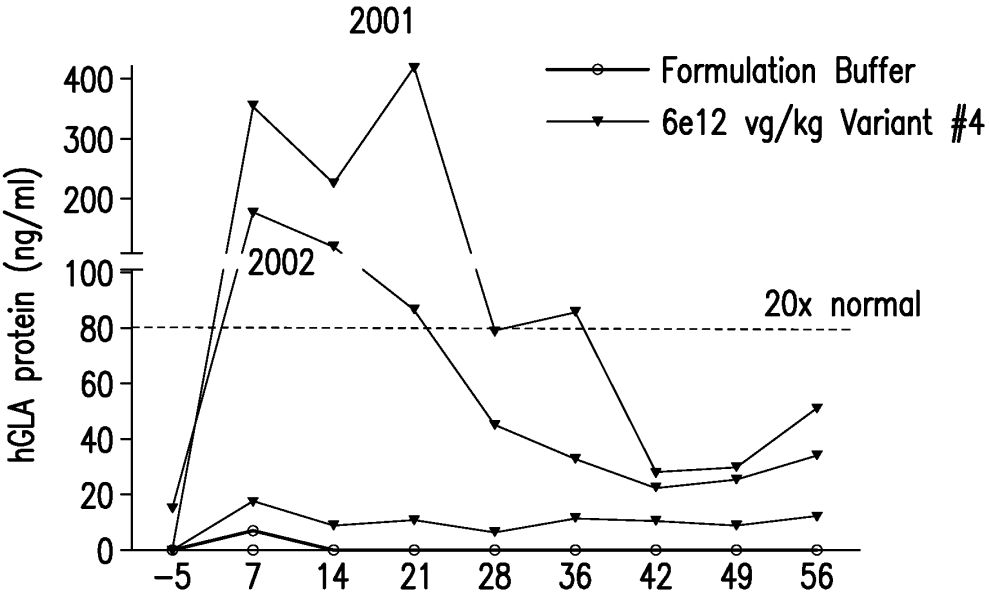


FIG.13A

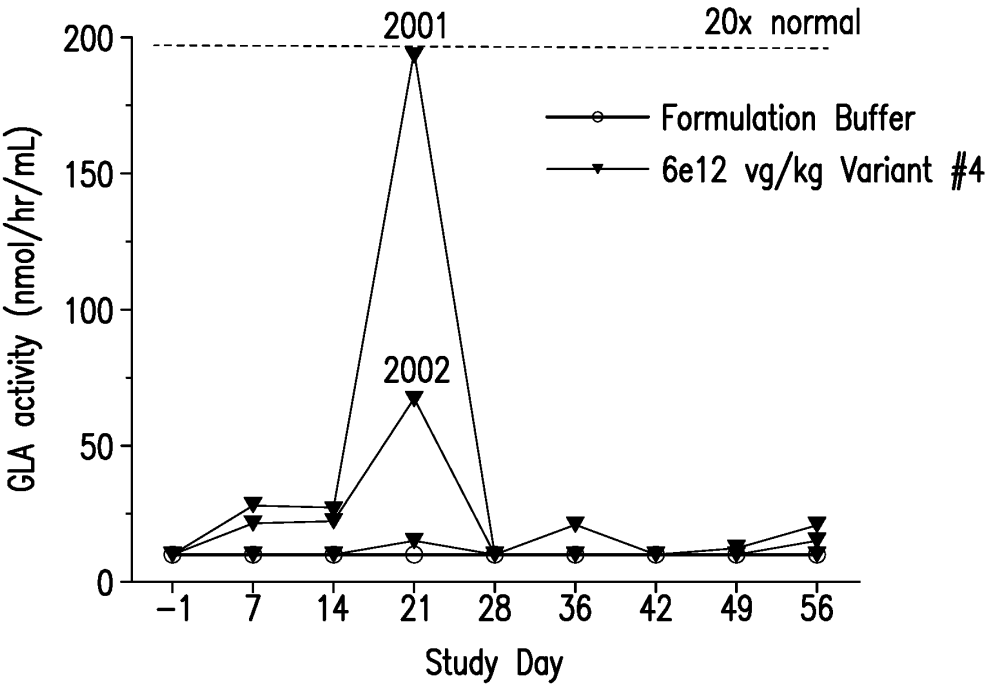


FIG.13B

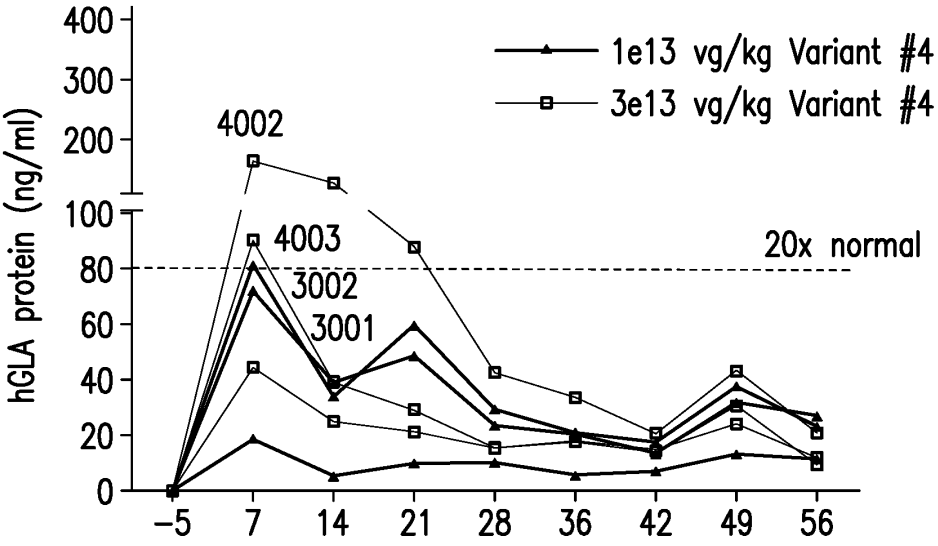


FIG.13C

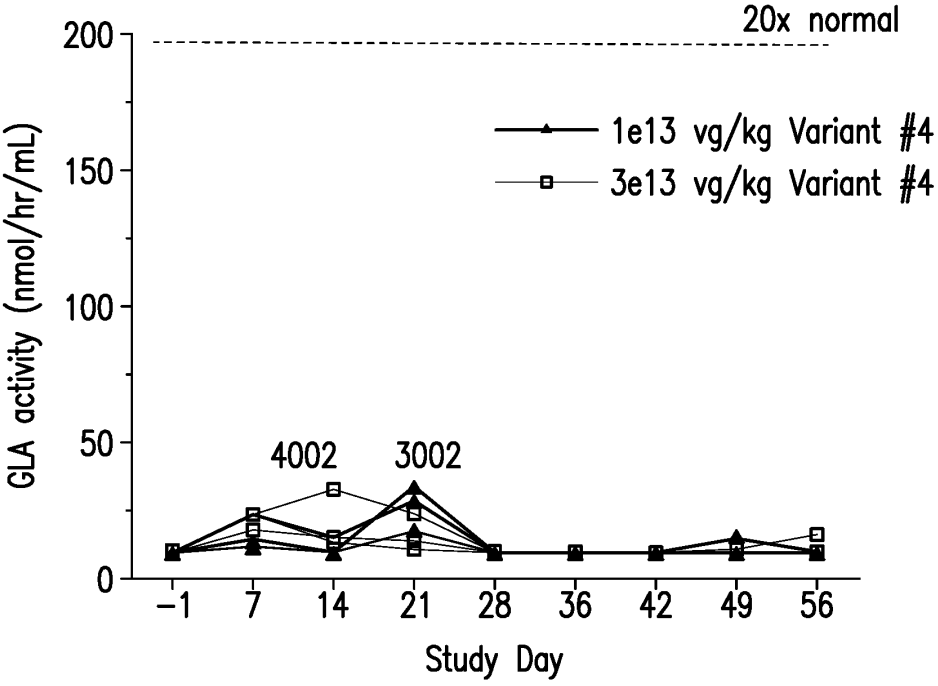


FIG.13D

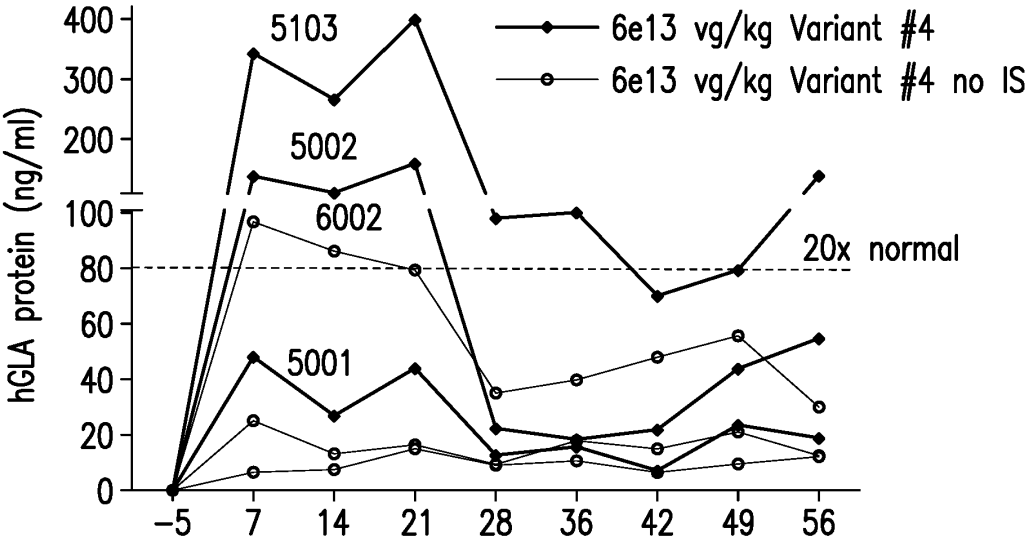


FIG.13E

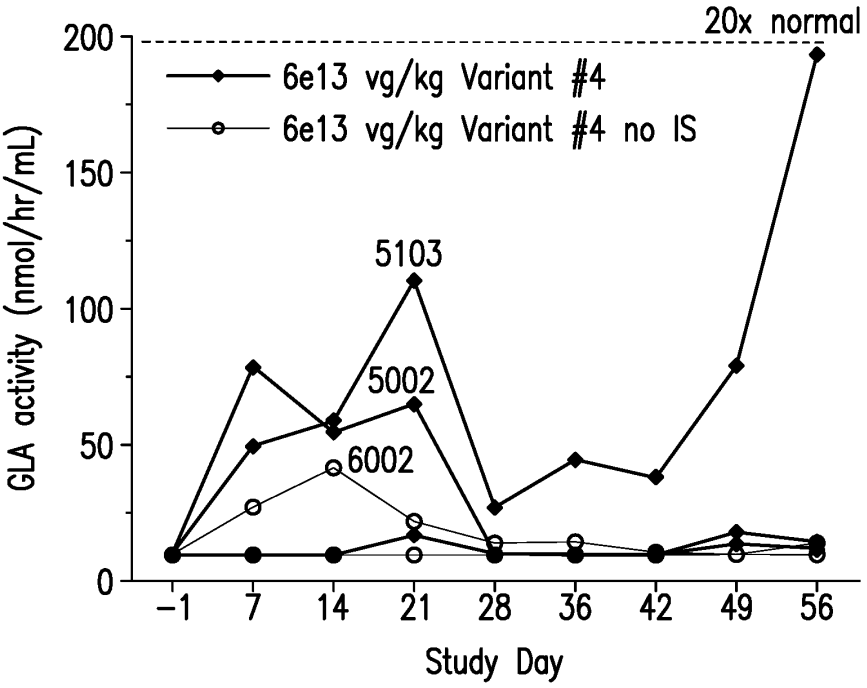


FIG.13F

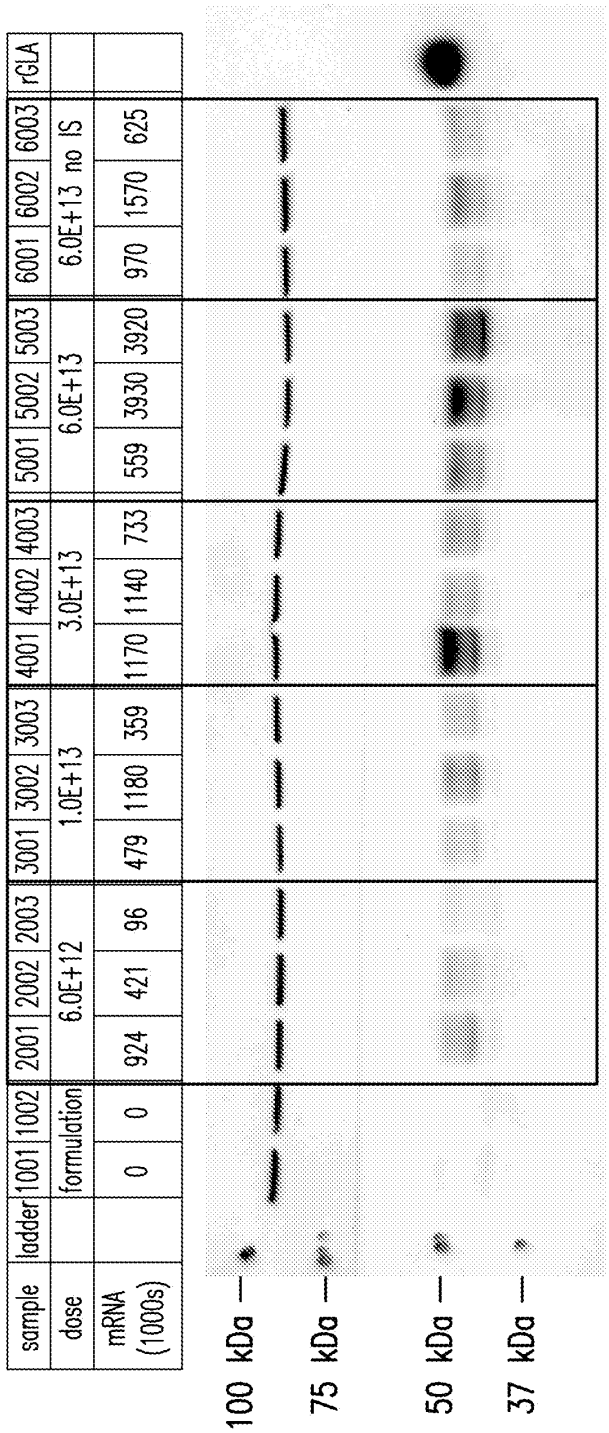

sample
ladder
1001
1002
2001
2002
2003
3001
3002
3003
4001
4002
4003
5001
5002
5003
6001
6002
6003
rGLA
dose
formulation
0
0
6.0E+12
1.0E+13
3.0E+13
6.0E+13
6.0E+13 no IS
mRNA (1000s)
924
421
96
479
1180
359
1170
1140
733
559
3930
3920
970
1570
625
100 kDa
75 kDa
50 kDa
37 kDa
α-HSP-90 (loading control)
Human GLA
Variant 4

FIG.14