

Figure 1A

Figure 1B

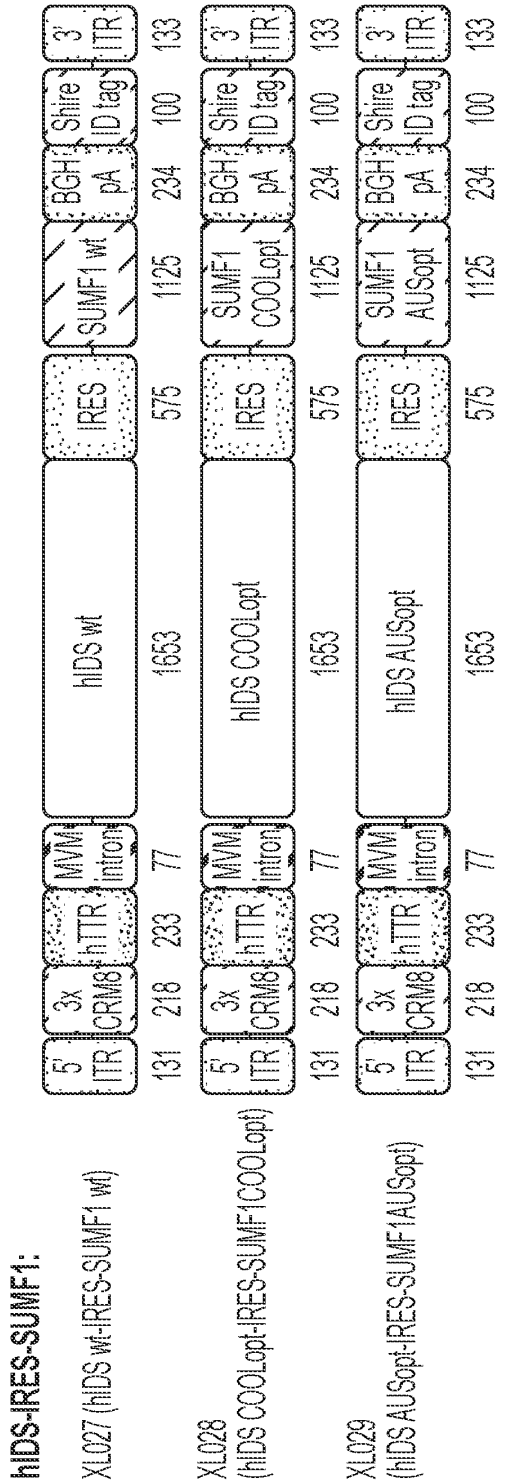

hIDS-IRES-SUMF1:
XL027 (hIDS wt-IRES-SUMF1 wt)
5' ITR
131
3x CRM8
218
hTTR
233
MVM intron
77
hIDS wt
1653
IRES
575
SUMF1 wt
1125
BGH pA
234
Shire ID tag
100
3' ITR
133
XL028 (hIDS COOLopt-IRES-SUMF1COOLopt)
5' ITR
131
3x CRM8
218
hTTR
233
MVM intron
77
hIDS COOLopt
1653
IRES
575
SUMF1 COOLopt
1125
BGH pA
234
Shire ID tag
100
3' ITR
133
XL029 (hIDS AUSopt-IRES-SUMF1AUSopt)
5' ITR
131
3x CRM8
218
hTTR
233
MVM intron
77
hIDS AUSopt
1653
IRES
575
SUMF1 AUSopt
1125
BGH pA
234
Shire ID tag
100
3' ITR
133
Control:
XL030 (SUMF1 wt)
5' ITR
131
3x CRM8
218
hTTR
233
MVM intron
77
SUMF1 wt
1125
BGH pA
234
Shire ID tag
100
3' ITR
133

Figure 2

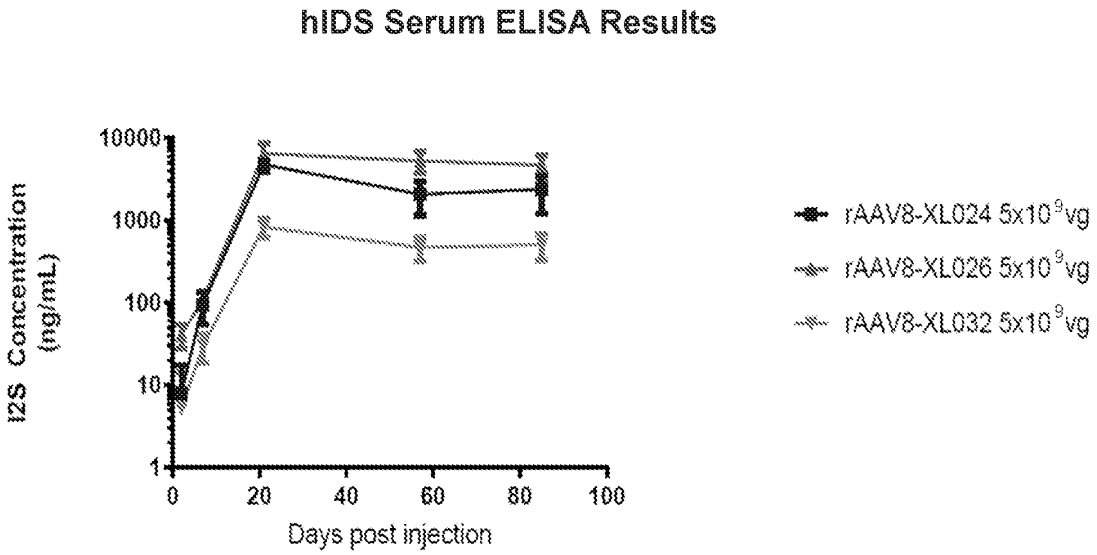

hIDS Serum ELISA Results
I2S Concentration (ng/mL)
10000
1000
100
10
1
0
20
40
60
80
100
Days post injection
rAAV8-XL024 5x10^9vg
rAAV8-XL026 5x10^9vg
rAAV8-XL032 5x10^9vg

Figure 3

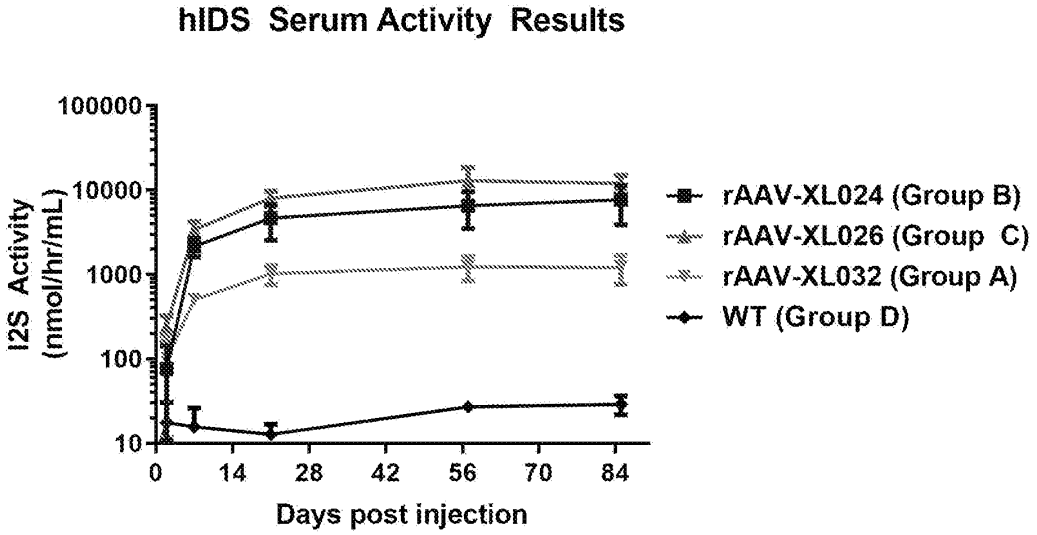

hIDS Serum Activity Results
I2S Activity (nmol/hr/mL)
100000
10000
1000
100
10
0
14
28
42
56
70
84
Days post injection
rAAV-XL024 (Group B)
rAAV-XL026 (Group C)
rAAV-XL032 (Group A)
WT (Group D)

Figure 4A

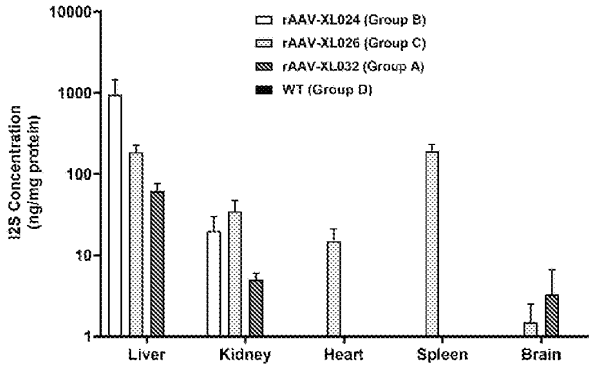


Figure 4B

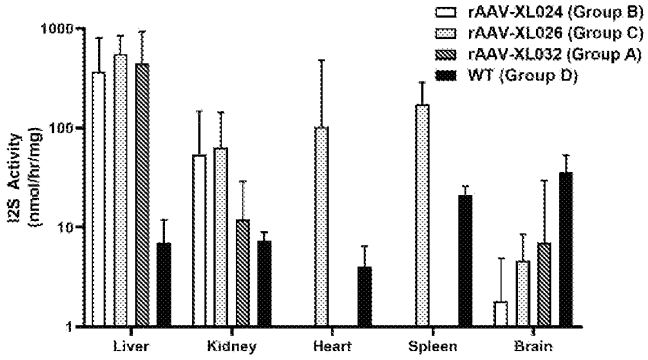


Figure 4C

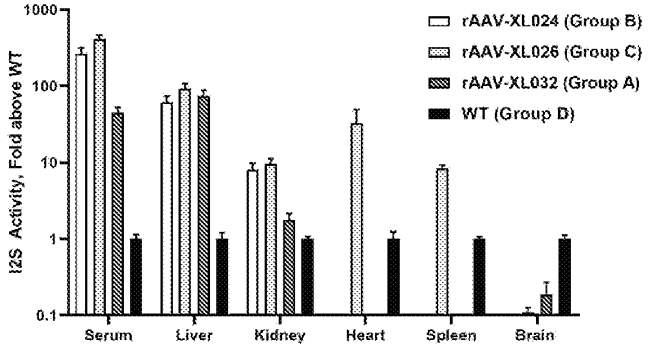


Figure 4D

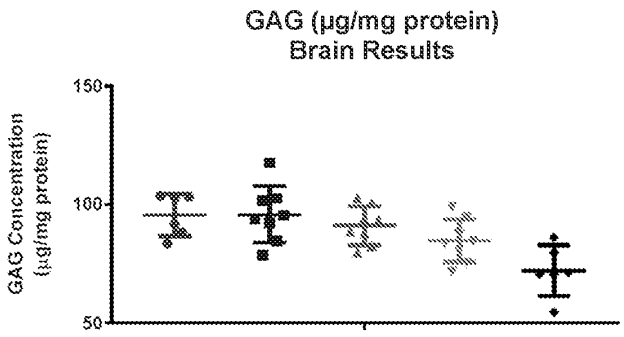


Figure 5A

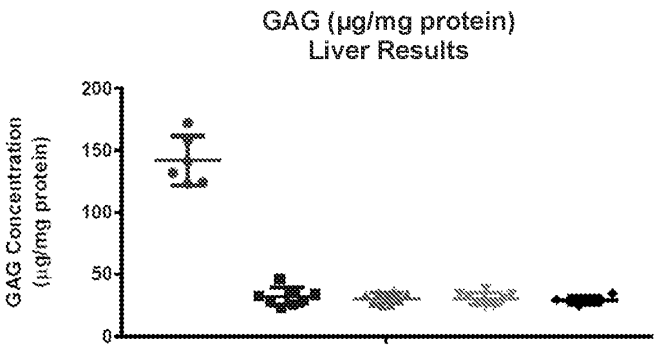


Figure 5B

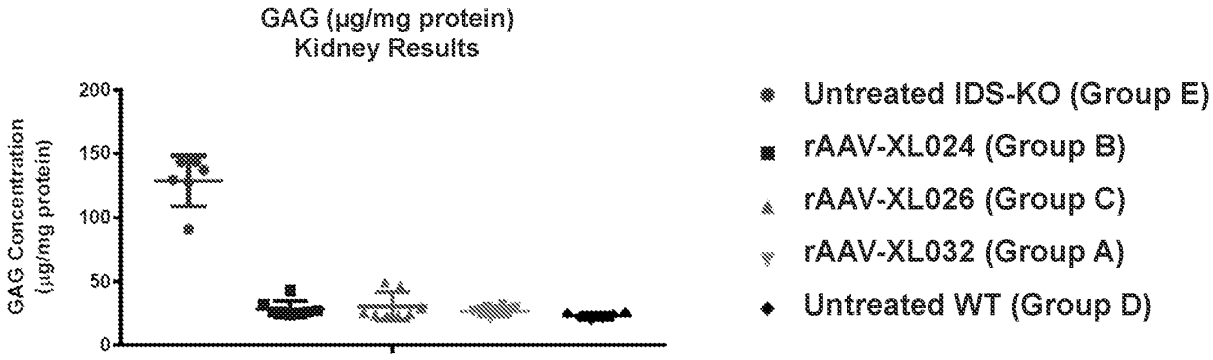


Figure 5C

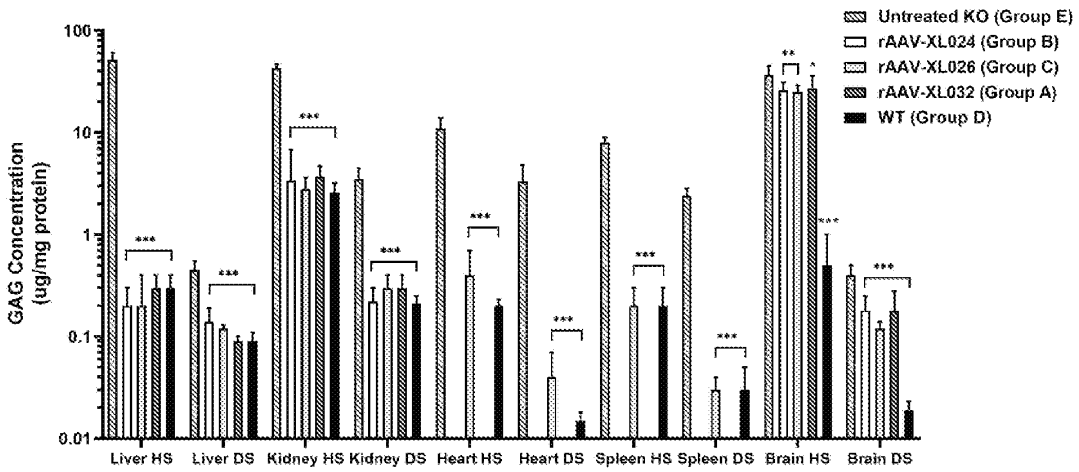


Figure 6A

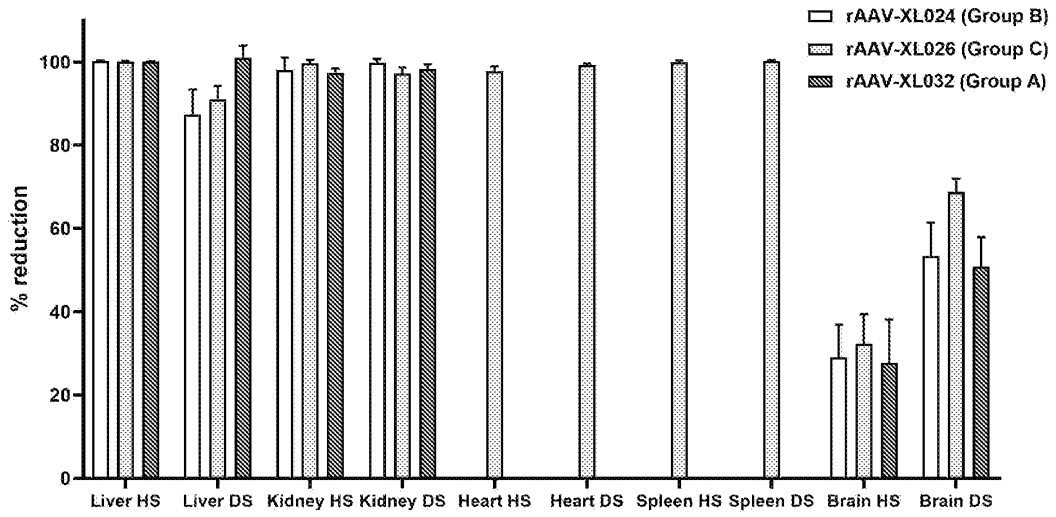


Figure 6B

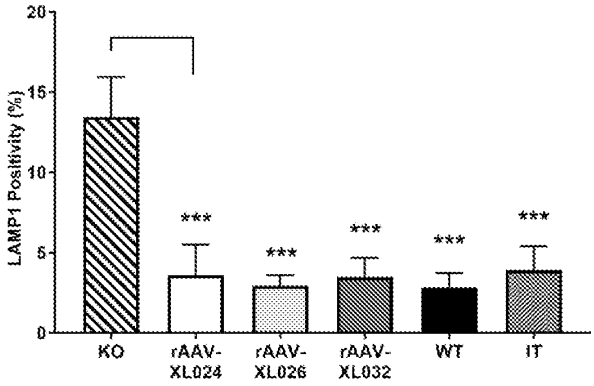


Figure 7A

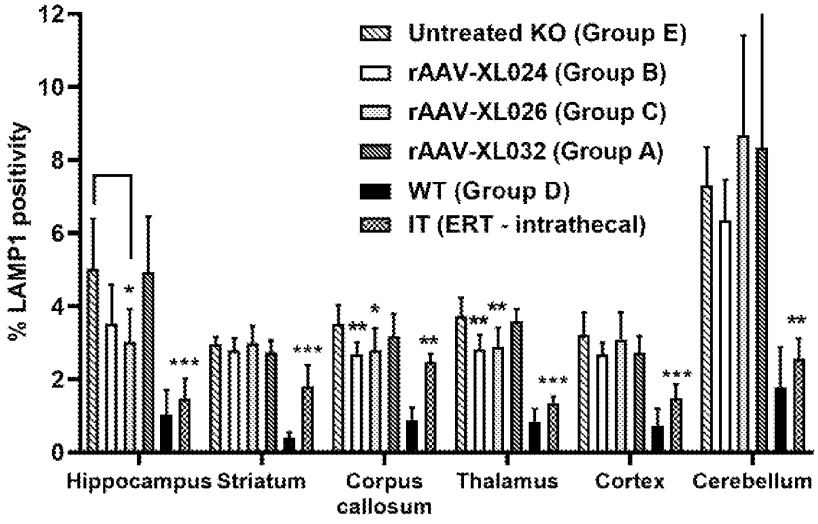


Figure 7B

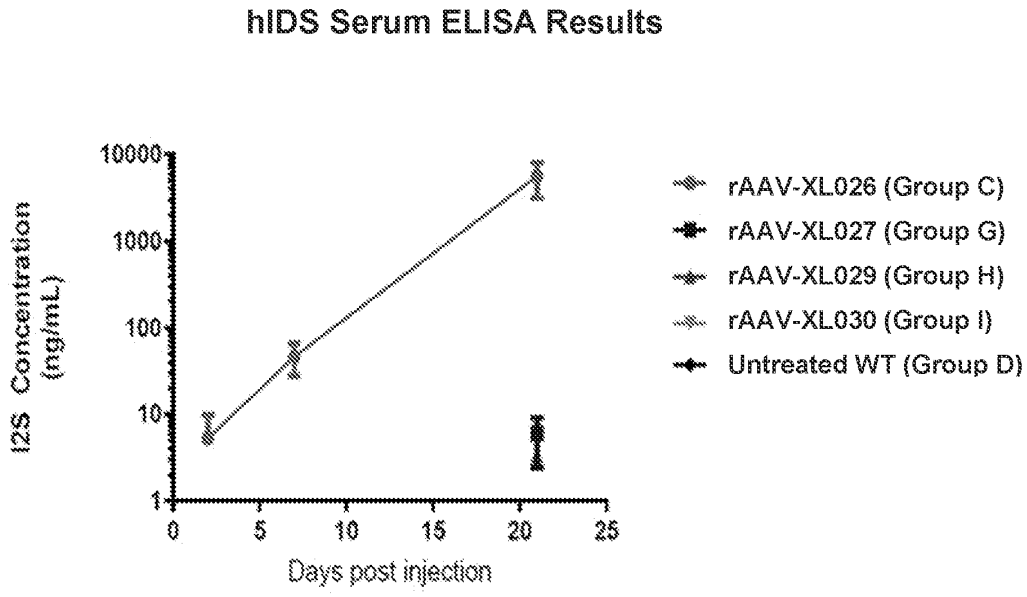

hIDS Serum ELISA Results
I2S Concentration (ng/mL)
10000
1000
100
10
1
0
5
10
15
20
25
Days post injection
rAAV-XL026 (Group C)
rAAV-XL027 (Group G)
rAAV-XL029 (Group H)
rAAV-XL030 (Group I)
Untreated WT (Group D)

Figure 8

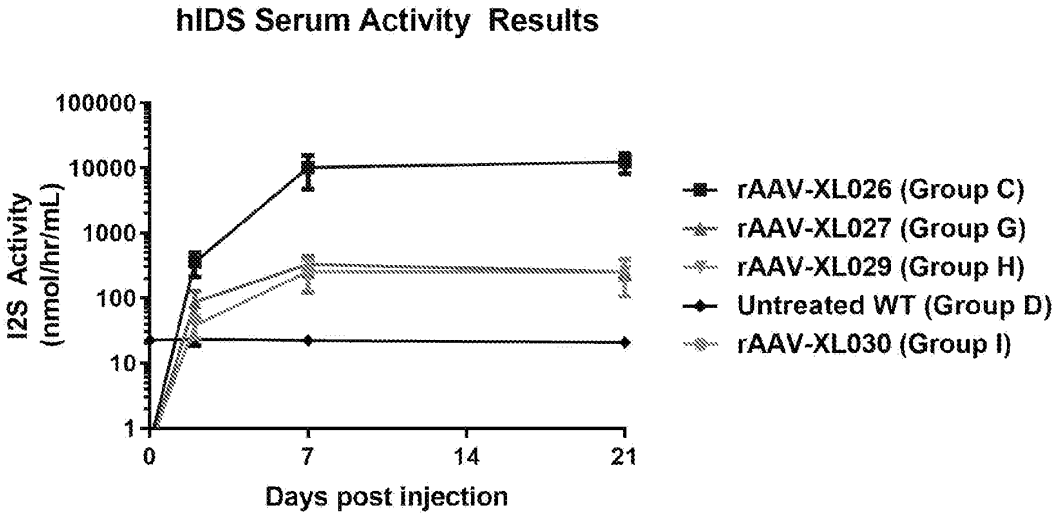

hIDS Serum Activity Results
I2S Activity (nmol/hr/mL)
100000
10000
1000
100
10
1
0
7
14
21
Days post injection
rAAV-XL026 (Group C)
rAAV-XL027 (Group G)
rAAV-XL029 (Group H)
Untreated WT (Group D)
rAAV-XL030 (Group I)

Figure 9

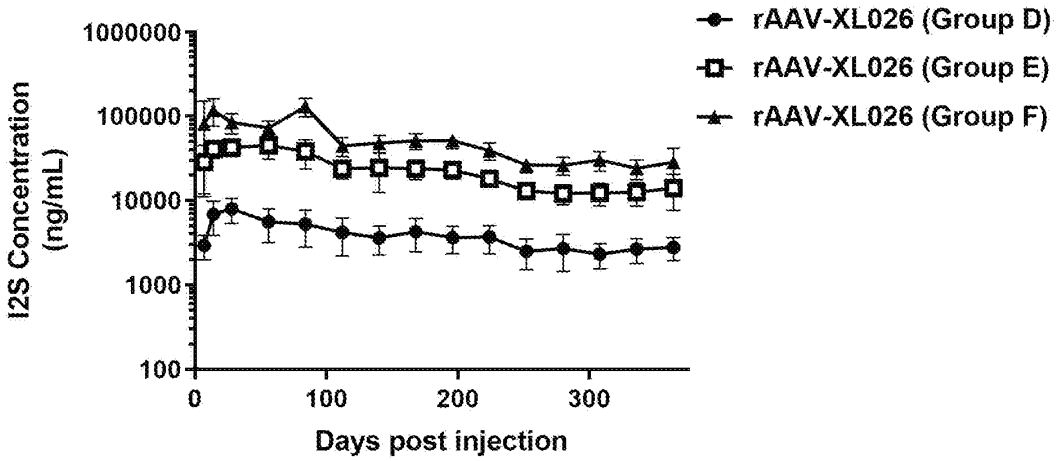


Figure 10

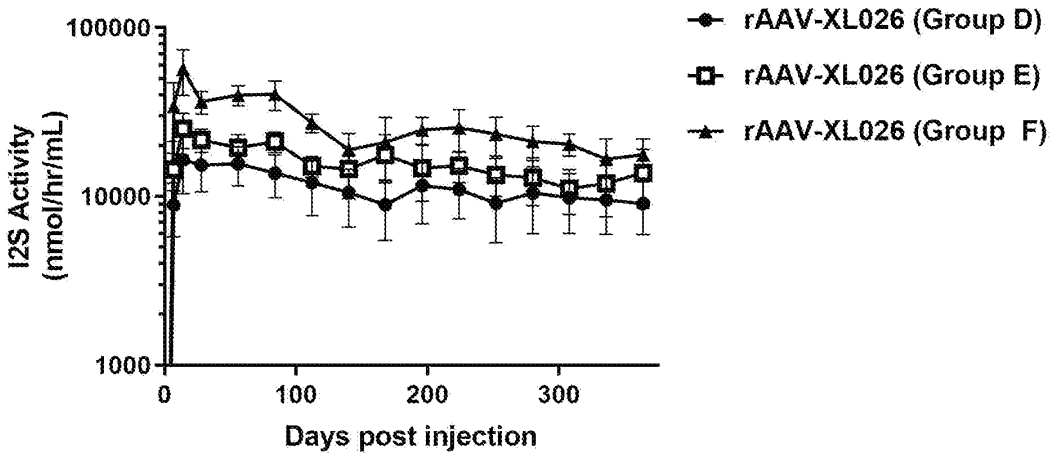


Figure 11

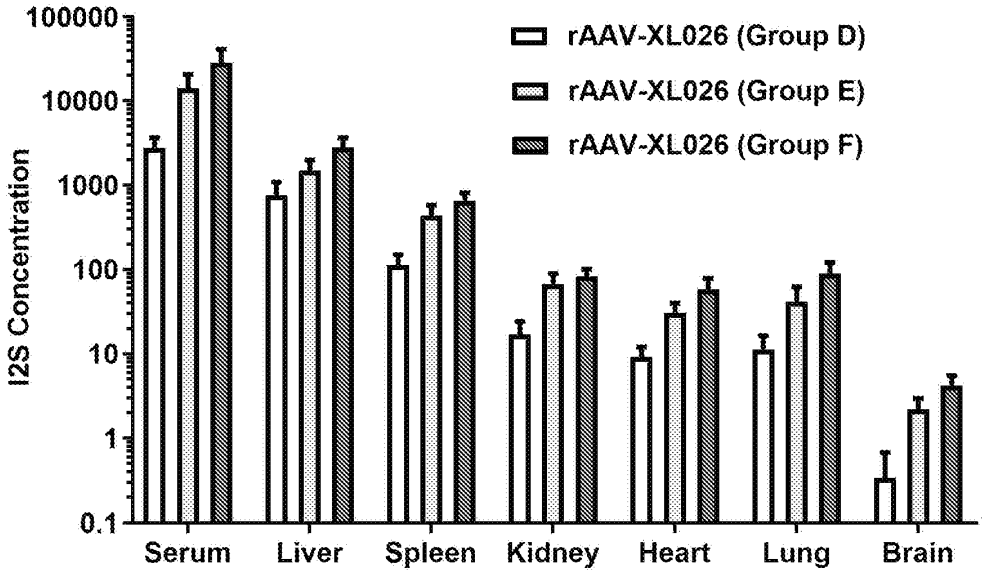


Figure 12A

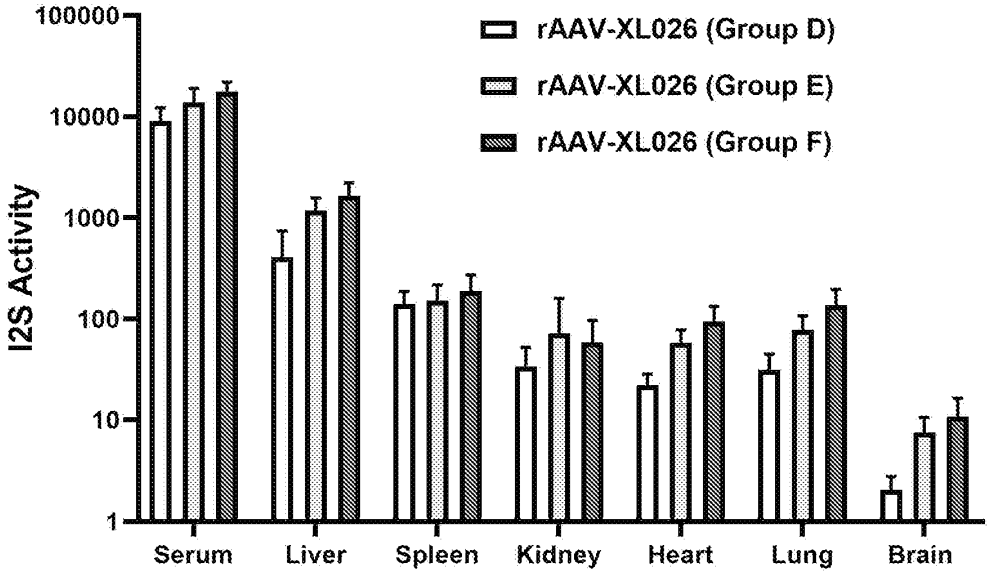


Figure 12B

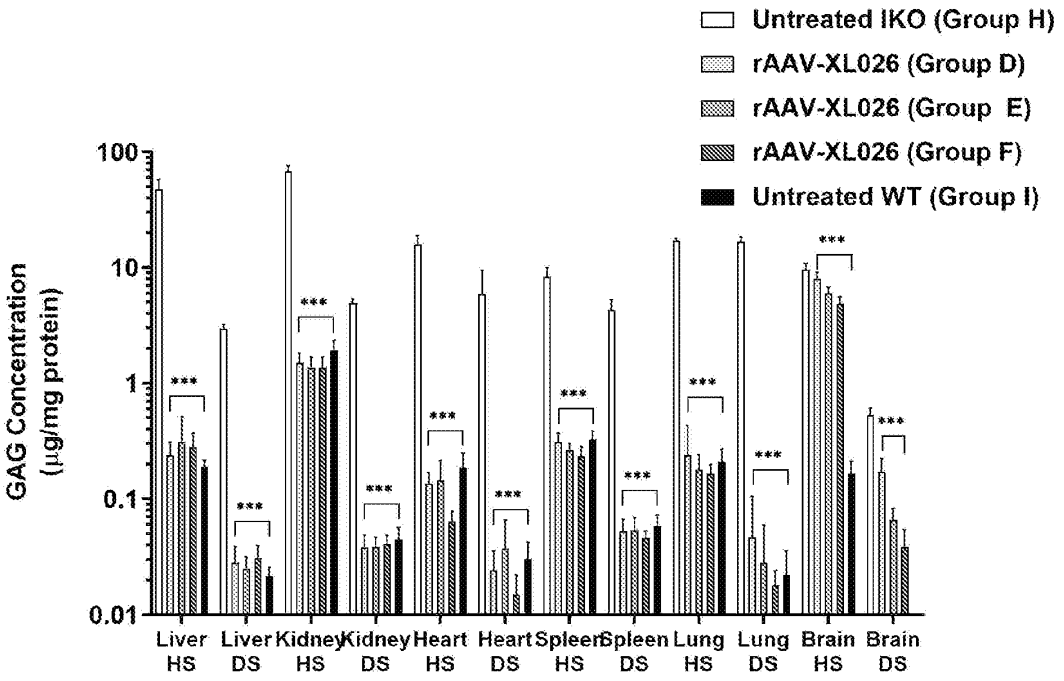


Figure 12C

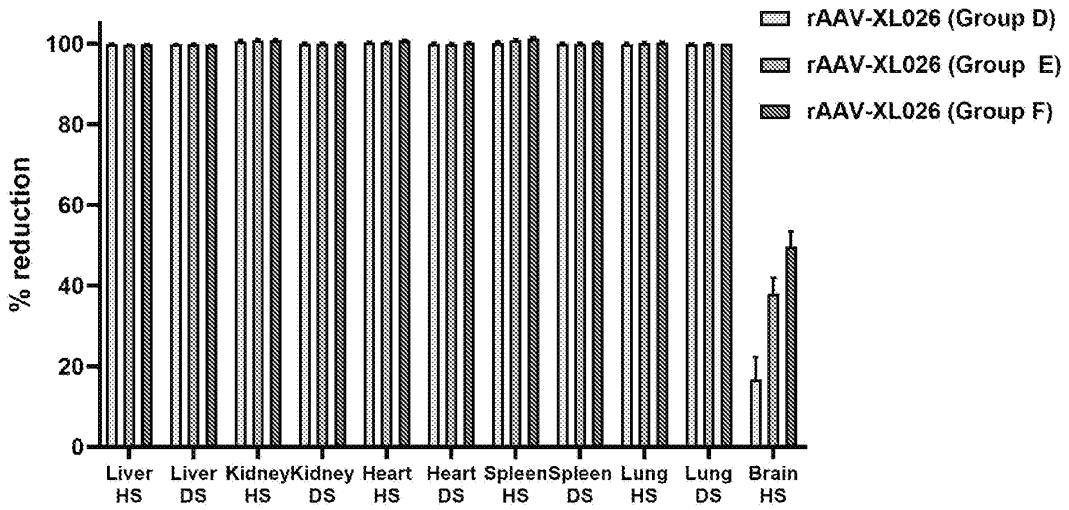


Figure 12D

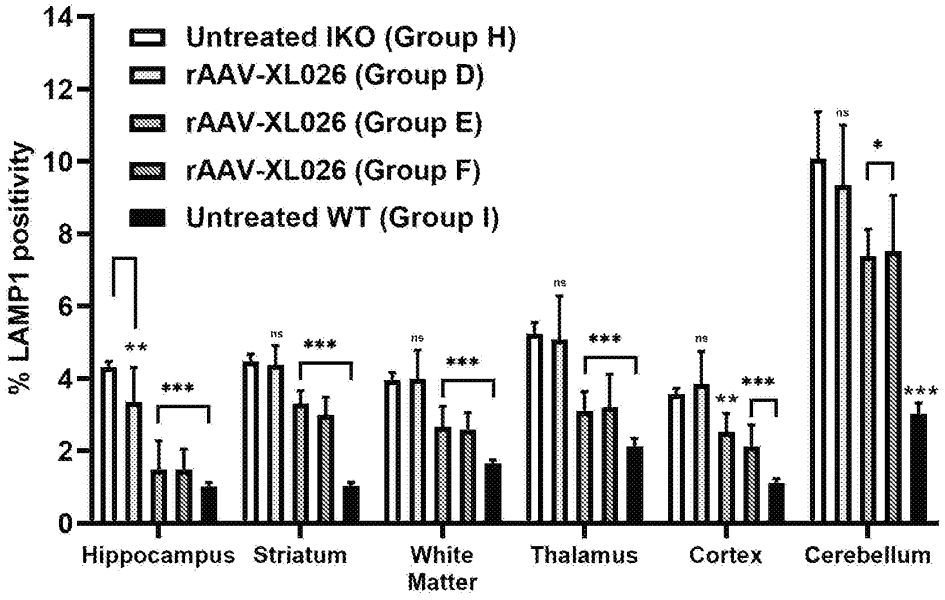

Untreated IKO (Group H)
rAAV-XL026 (Group D)
rAAV-XL026 (Group E)
rAAV-XL026 (Group F)
Untreated WT (Group I)
% LAMP1 positivity
0
2
4
6
8
10
12
14
**
***
ns
***
ns
***
ns
***
ns
**
***
ns
*
***
Hippocampus
Striatum
White Matter
Thalamus
Cortex
Cerebellum

Figure 12E

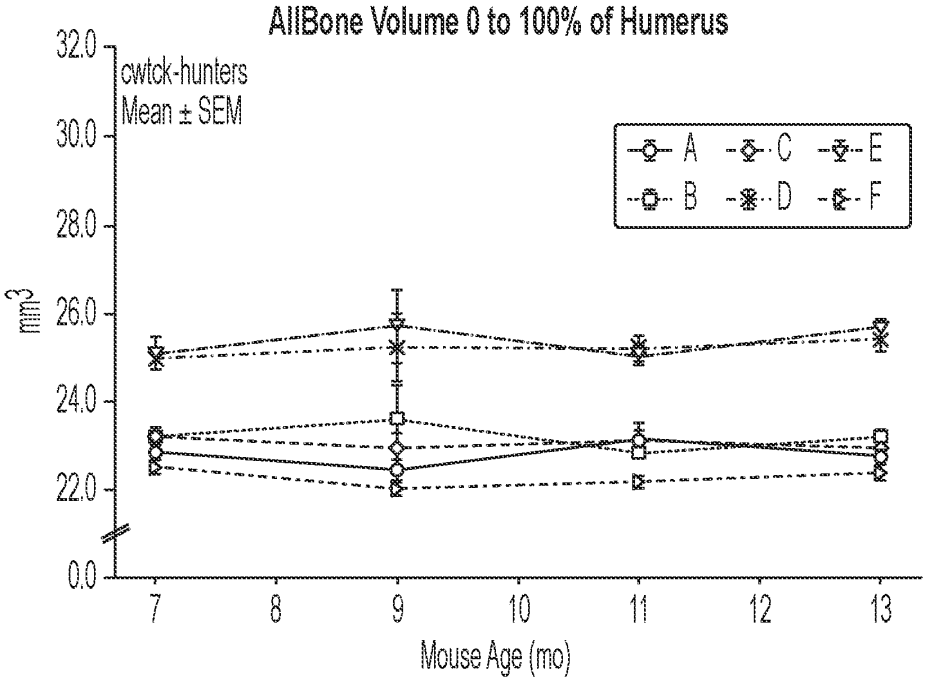


Figure 13A

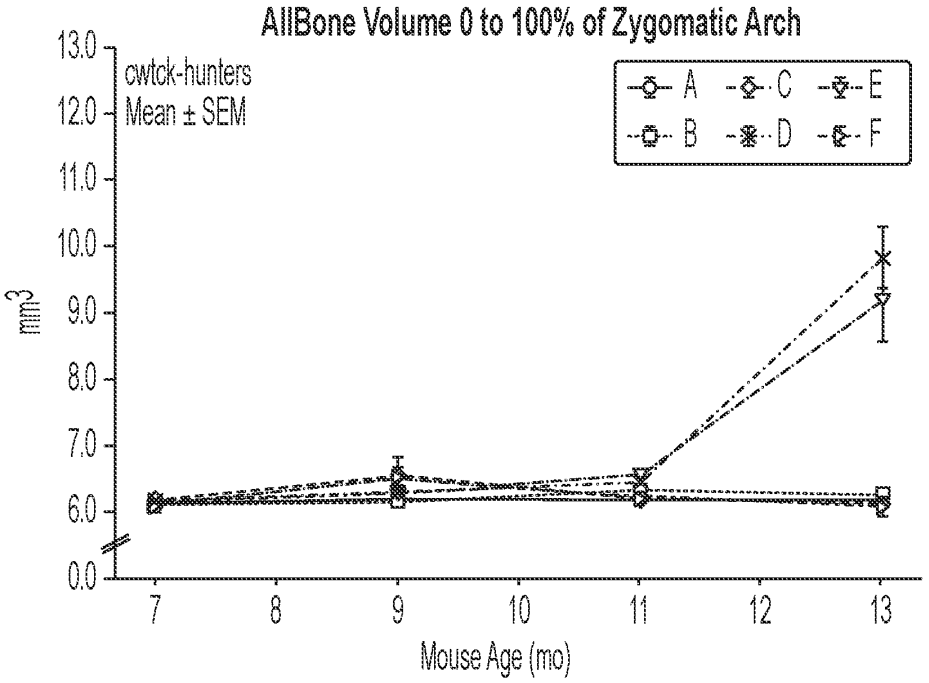


Figure 13B

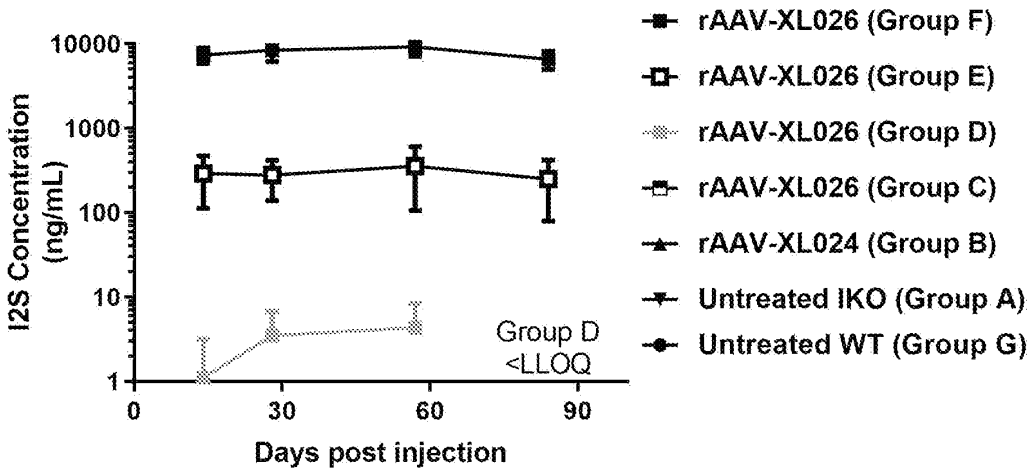


Figure 14A

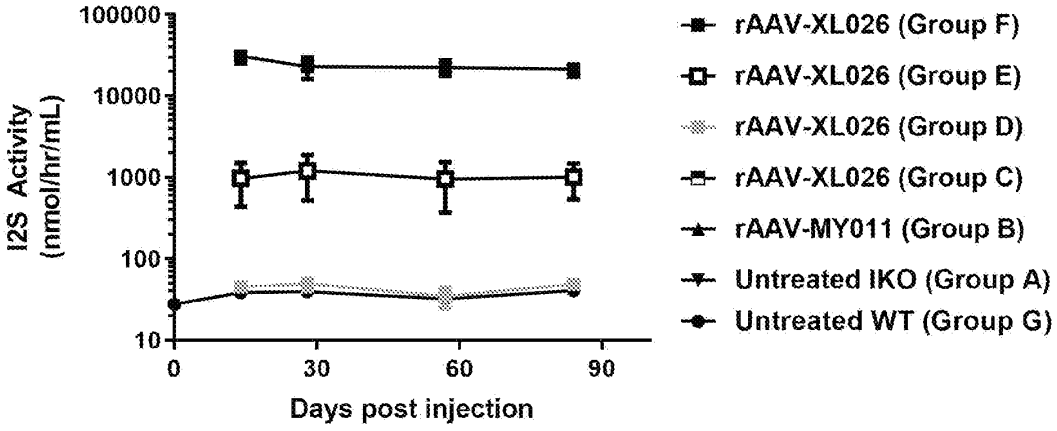


Figure 14B

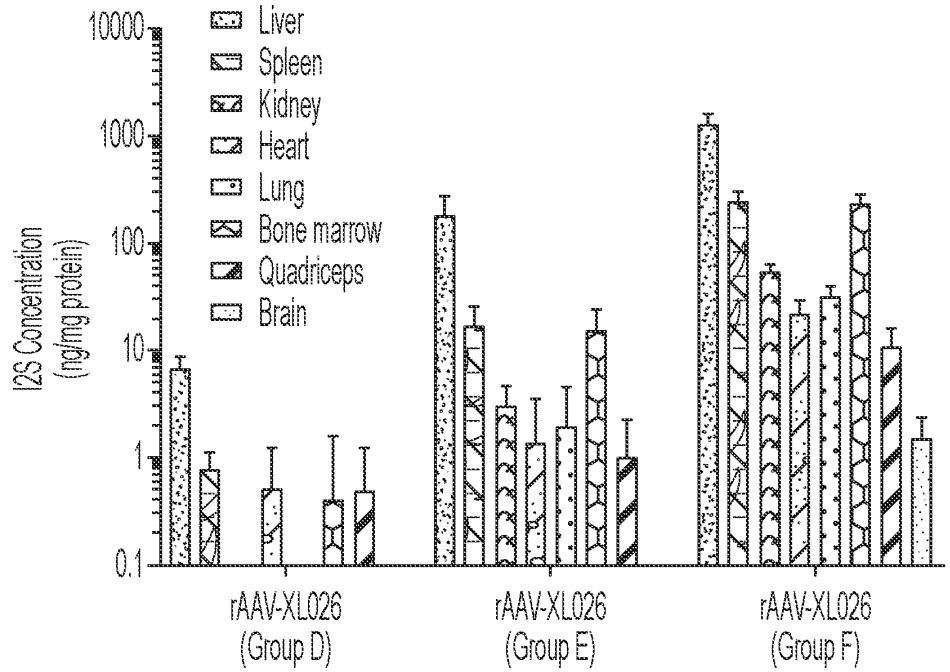


Figure 14C

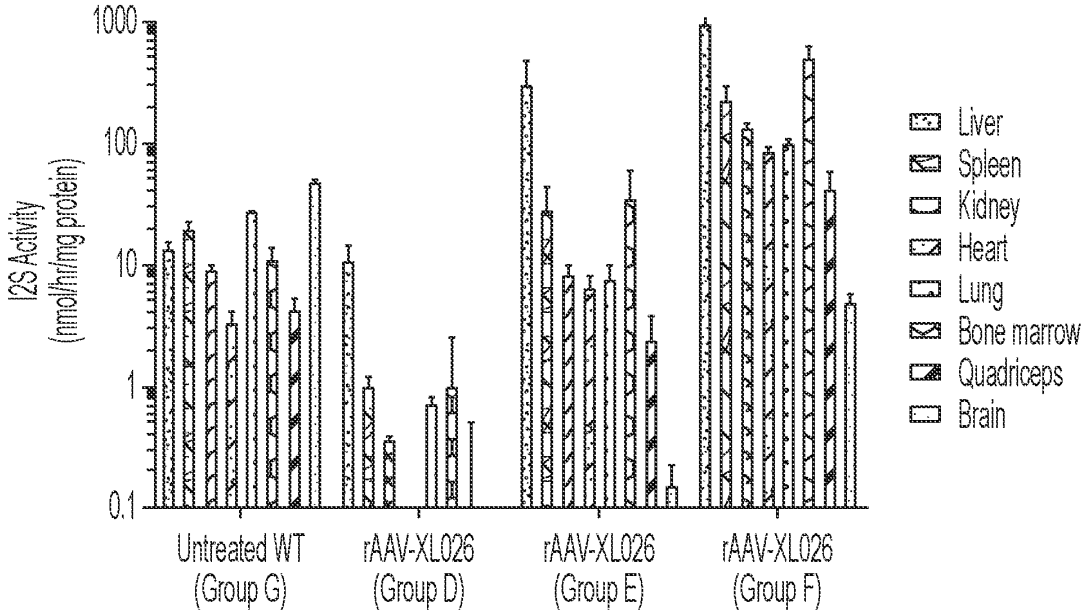


Figure 14D

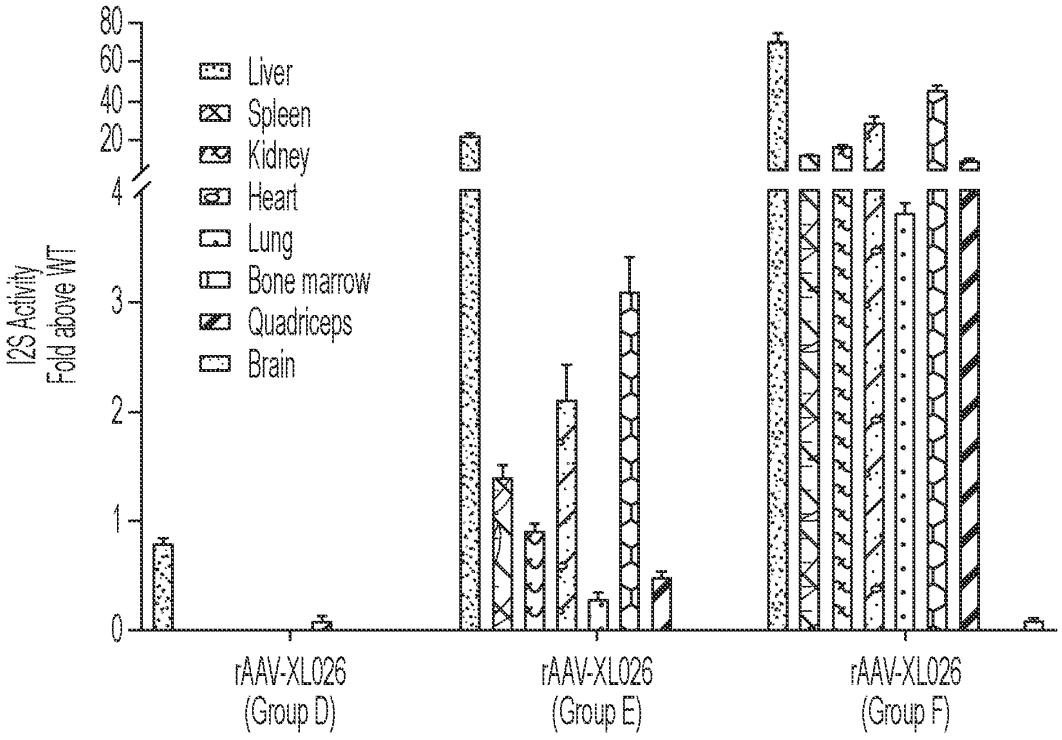

I2S Activity
Fold above WT
80
60
40
20
4
3
2
1
0
Liver
Spleen
Kidney
Heart
Lung
Bone marrow
Quadriceps
Brain
rAAV-XL026
(Group D)
rAAV-XL026
(Group E)
rAAV-XL026
(Group F)

Figure 14E

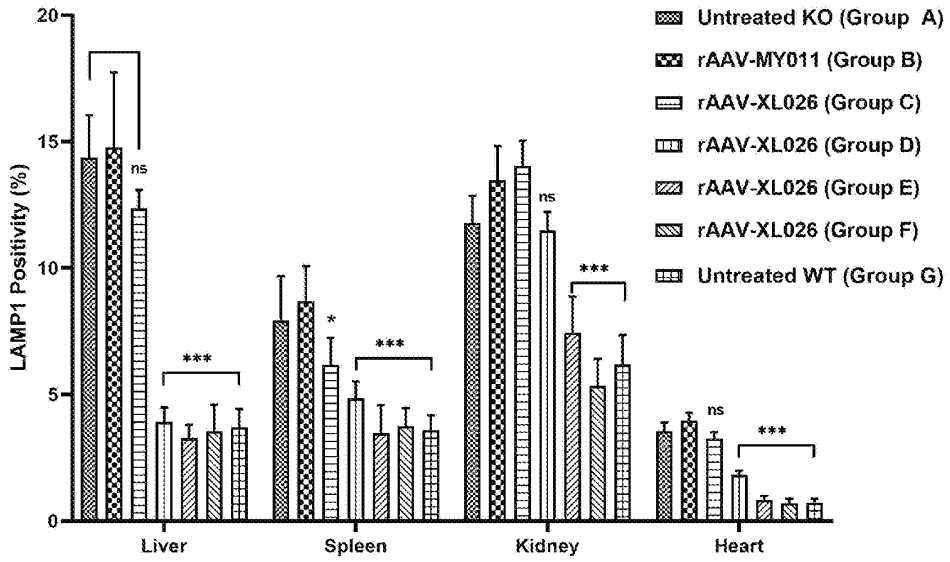


Figure 14F

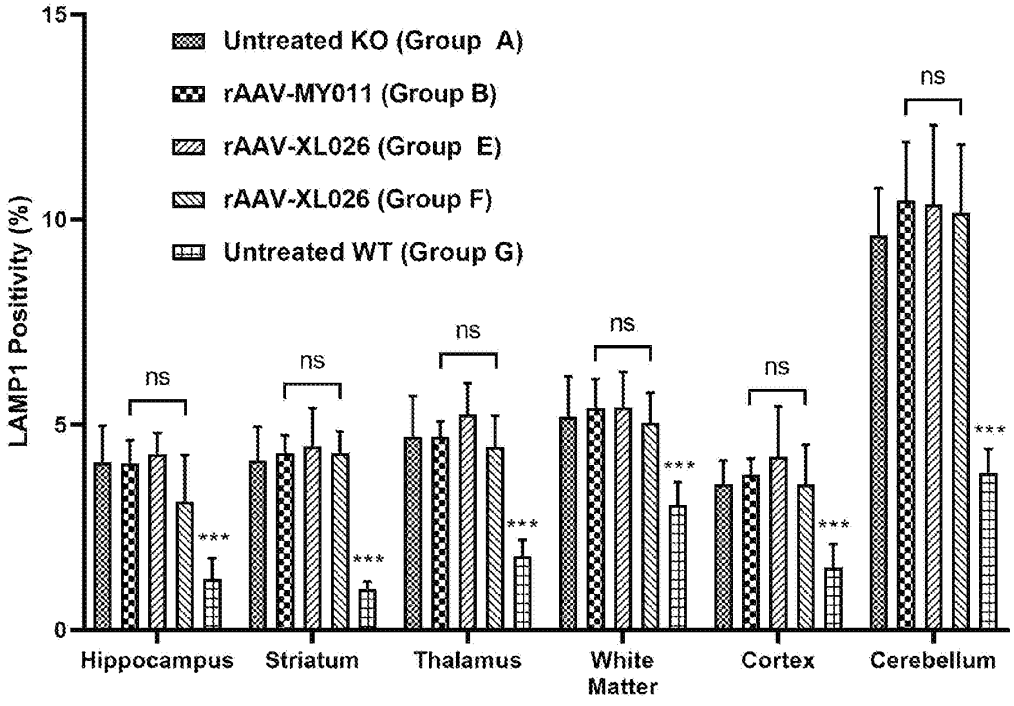


Figure 14G

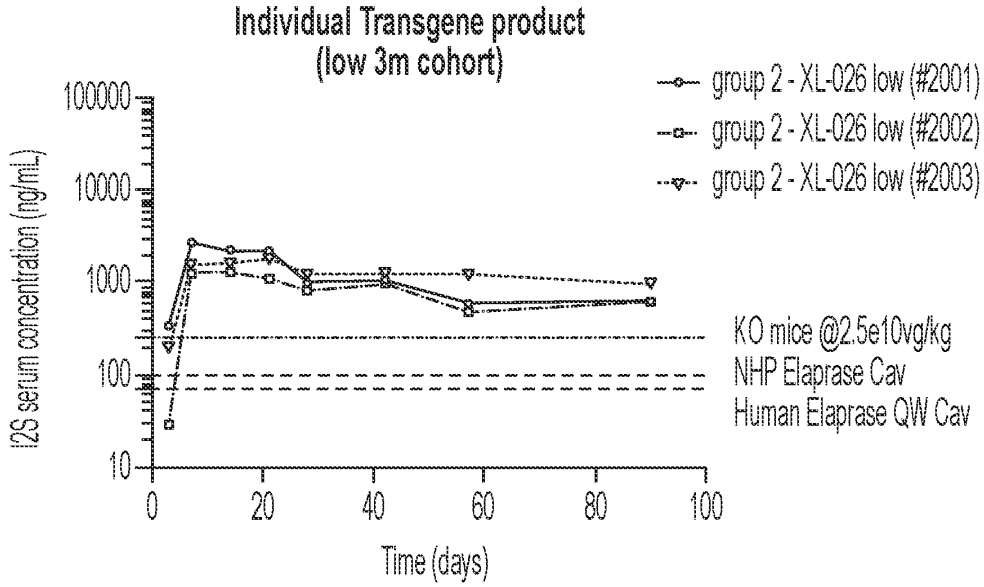


Figure 15A

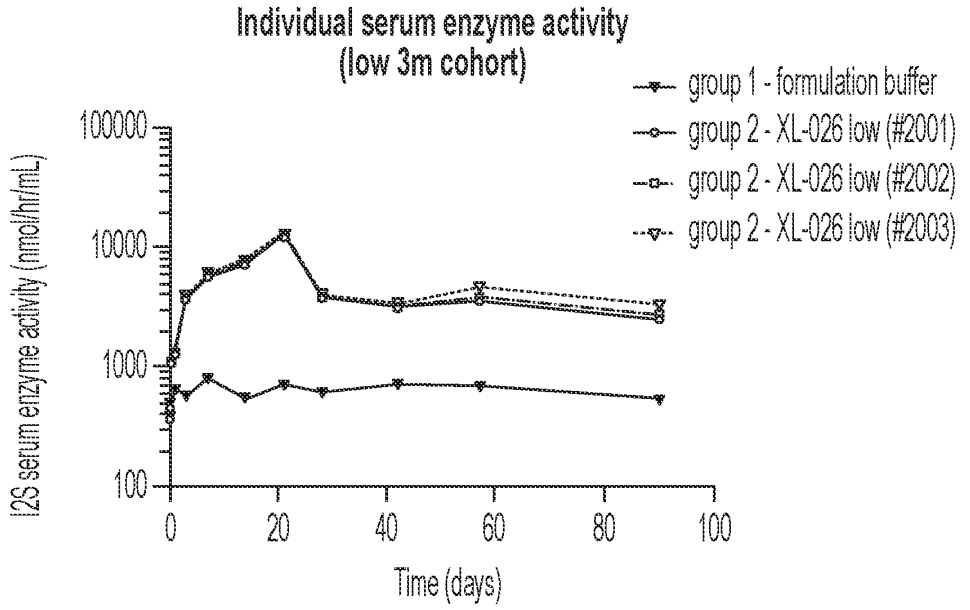


Figure 15B

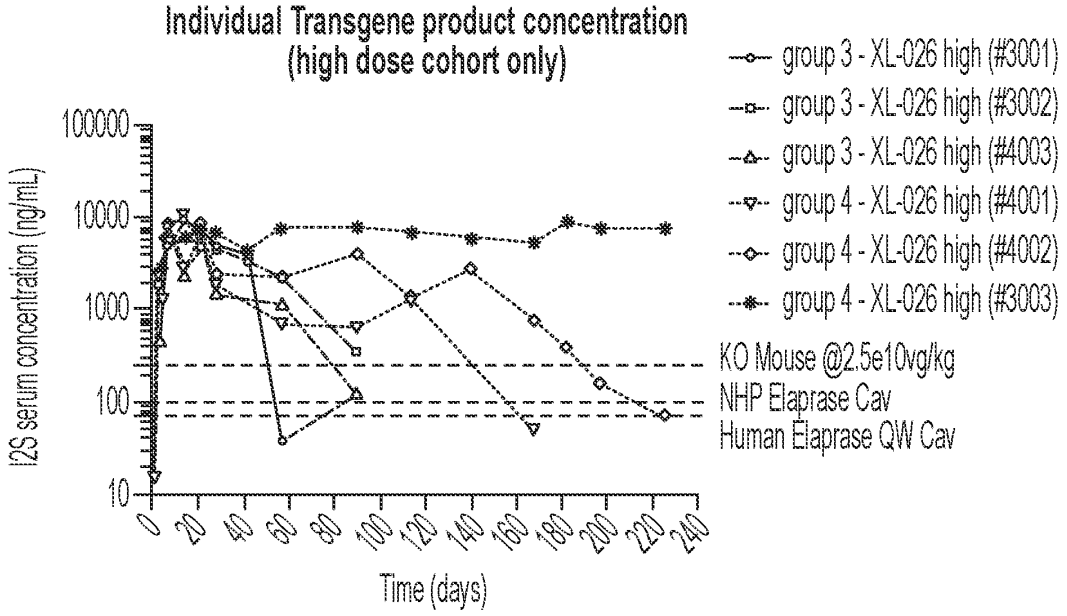


Figure 15C

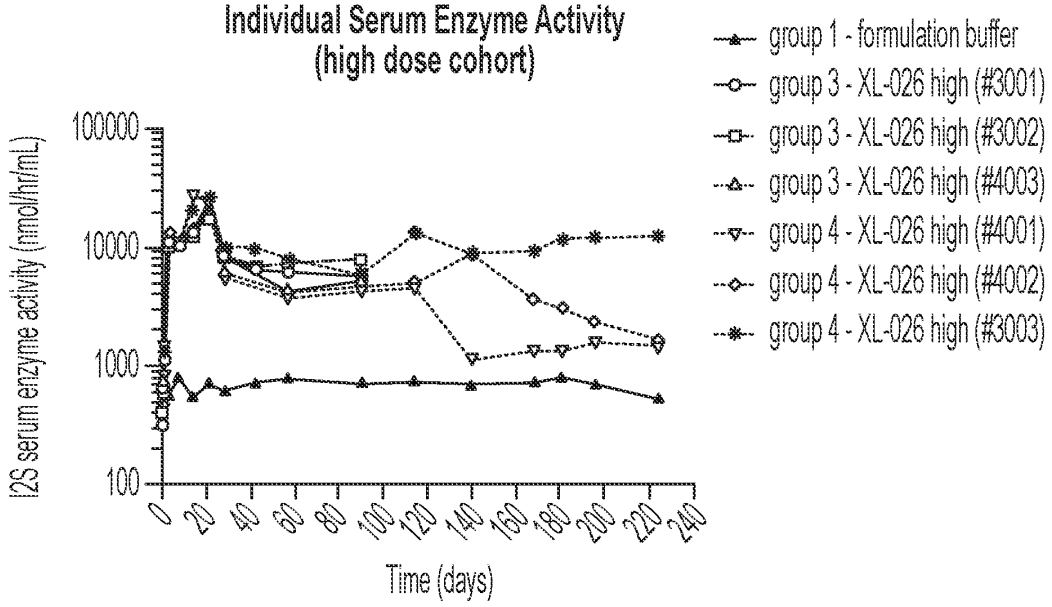


Figure 15D

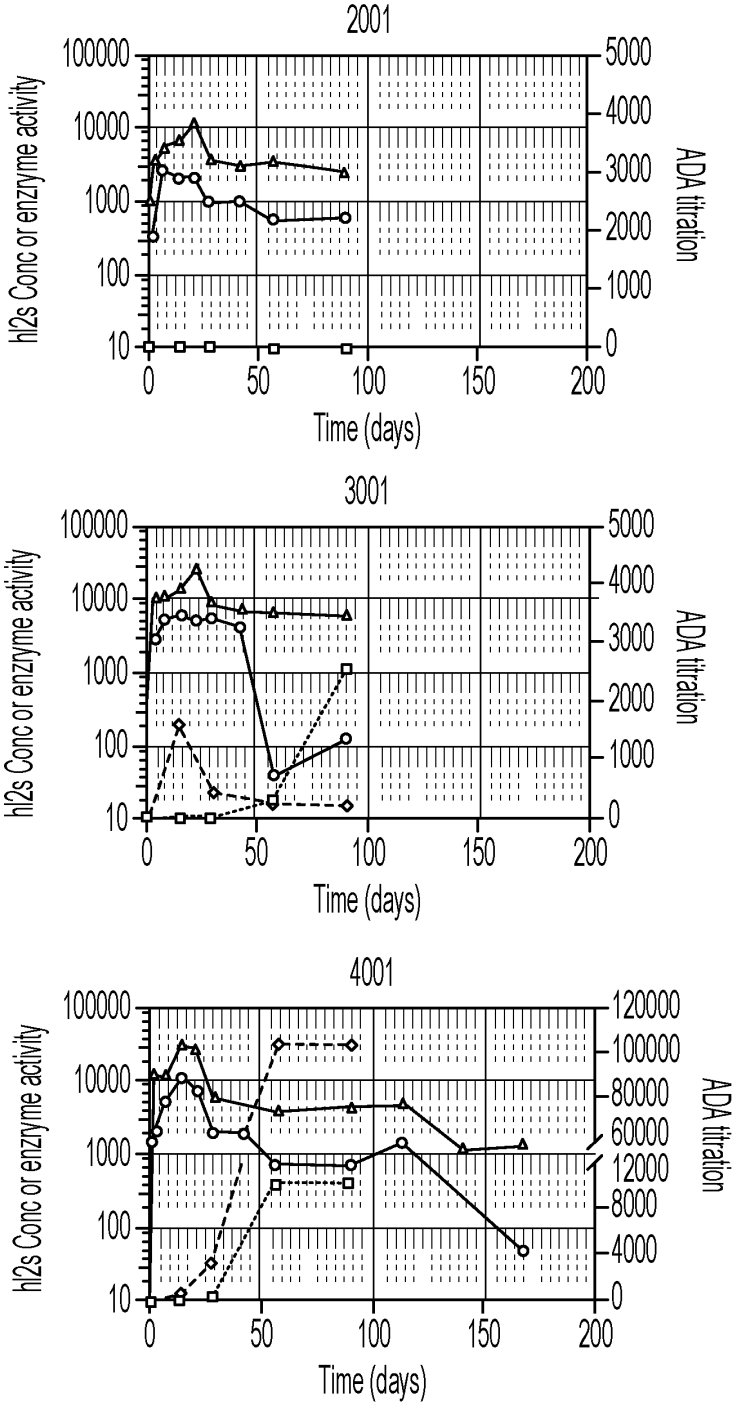

2001
hl2s Conc or enzyme activity
ADA titration
Time (days)
3001
hl2s Conc or enzyme activity
ADA titration
Time (days)
4001
hl2s Conc or enzyme activity
ADA titration
Time (days)

Figure 16

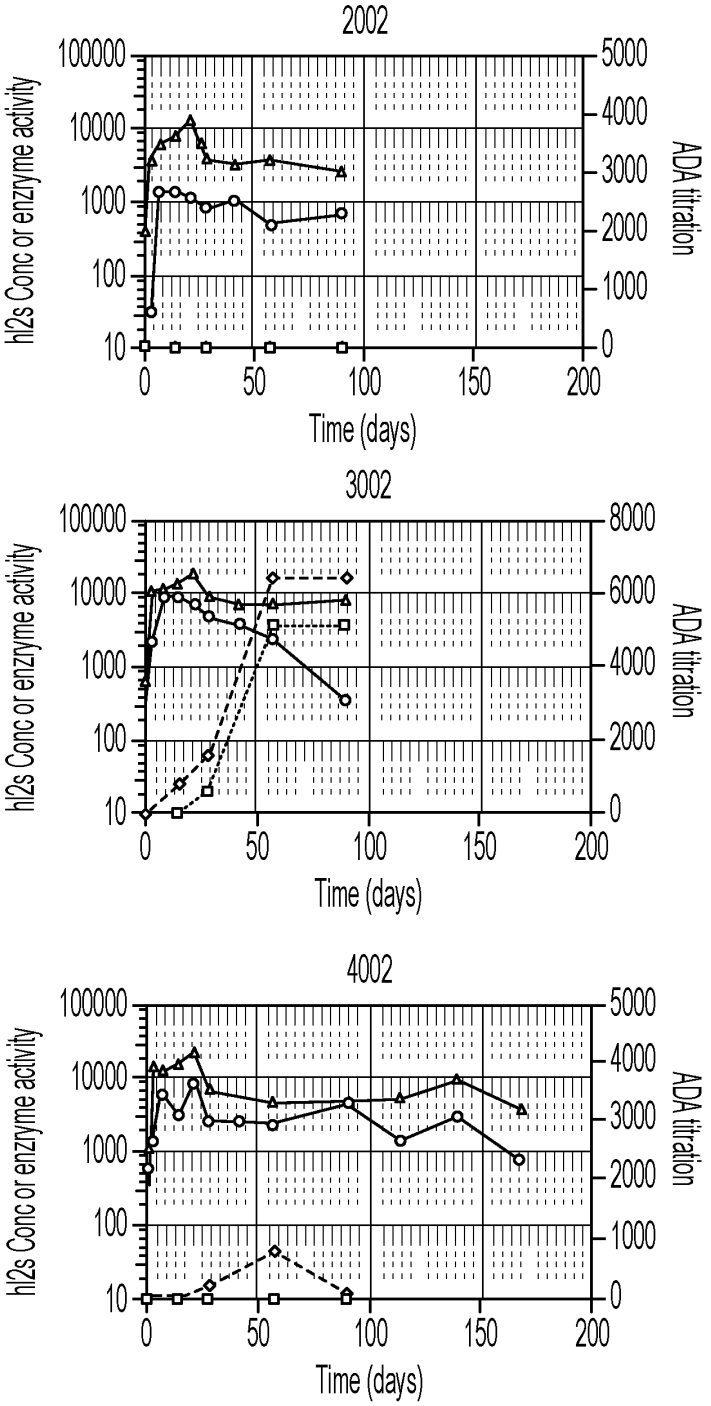


Figure 16 CONTINUED

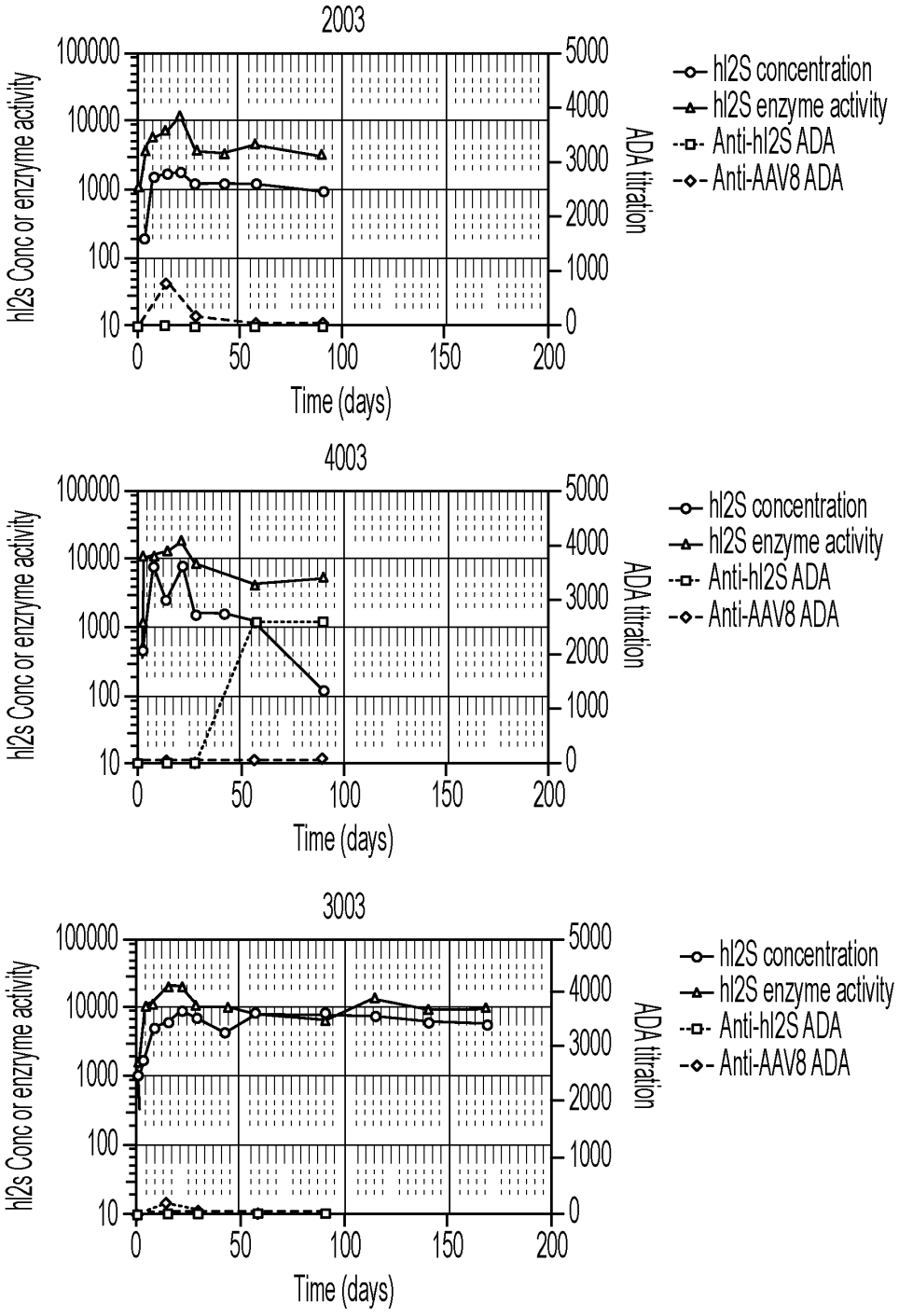


Figure 16 CONTINUED

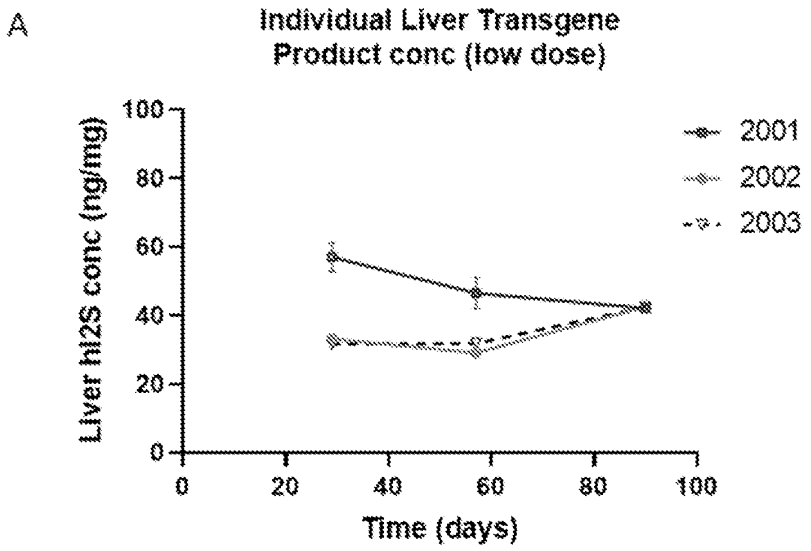


Figure 17A

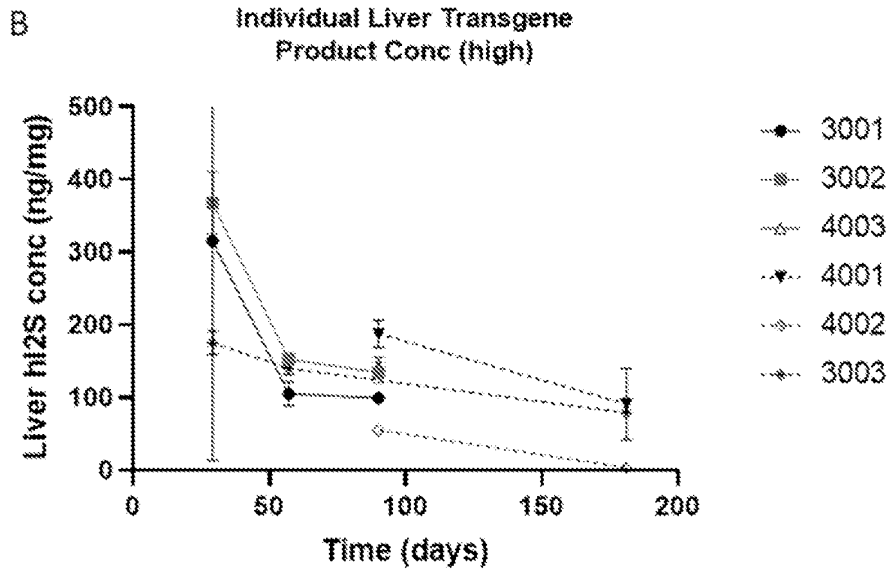


Figure 17B

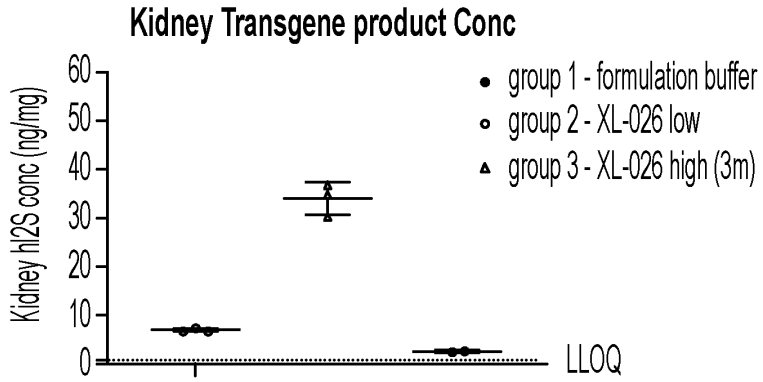


Figure 18A

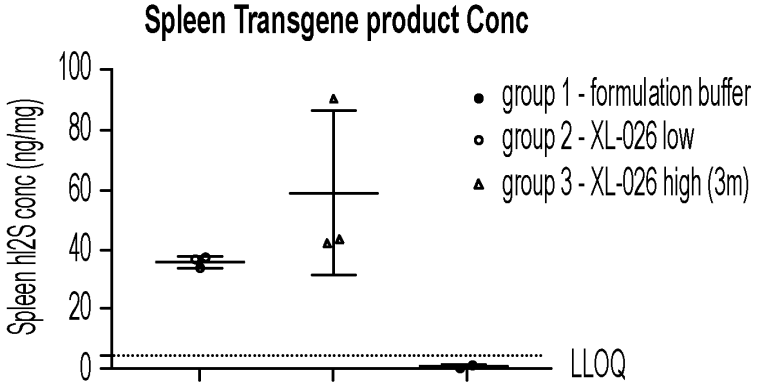


Figure 18B

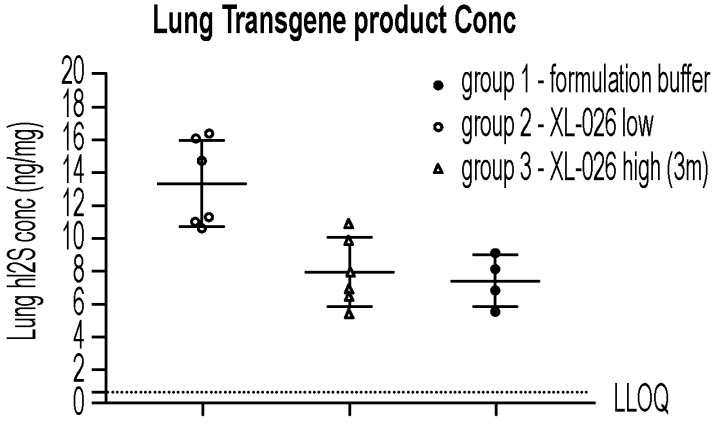


Figure 18C

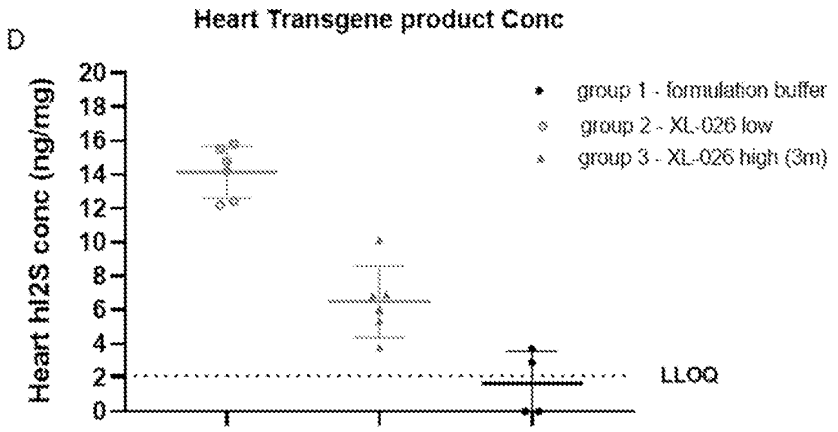


Figure 18D

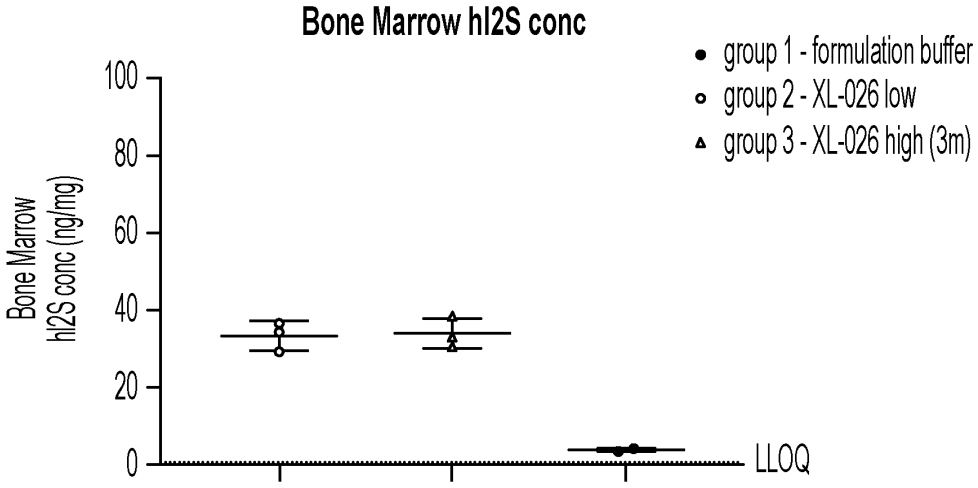


Figure 18E