Figure 1A

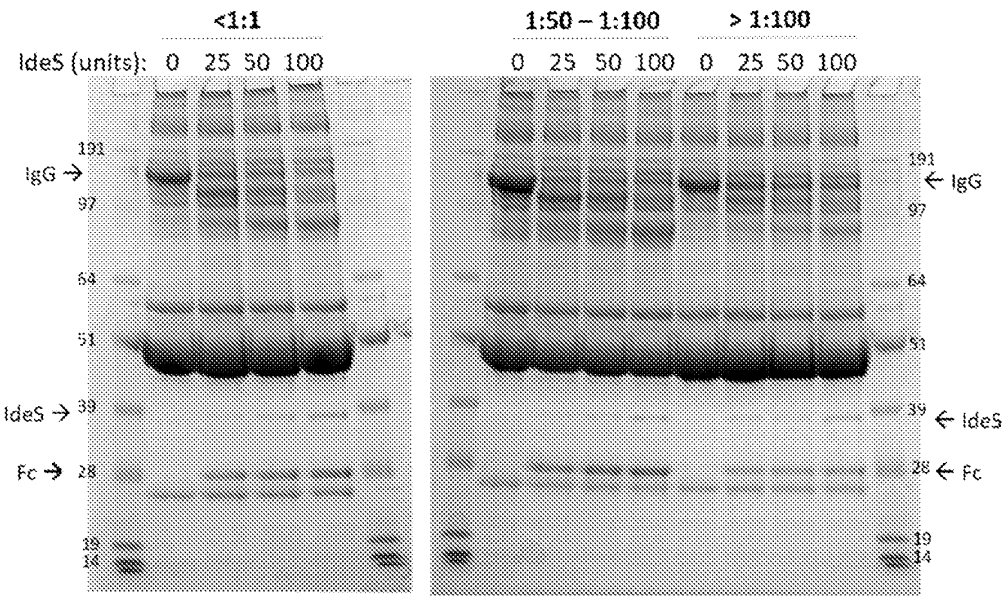

<1:1
1:50 – 1:100
> 1:100
IdeS (units): 0 25 50 100 0 25 50 100
191
IgG →
97
64
51
IdeS →
39
Fc →
28
19
14
← IgG
← IdeS
← Fc

Figure 1B

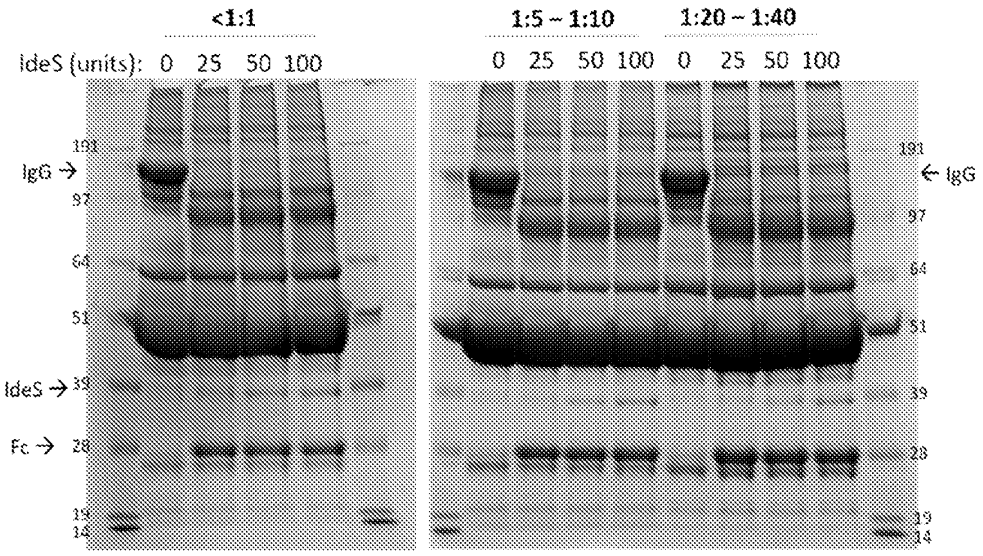

<1:1
1:5 ~ 1:10
1:20 ~ 1:40
IdeS (units): 0 25 50 100
0 25 50 100 0 25 50 100
191
IgG →
97
64
51
IdeS →
39
Fc →
28
19
14
191
← IgG
97
64
51
39
28
19
14

Figure 1C

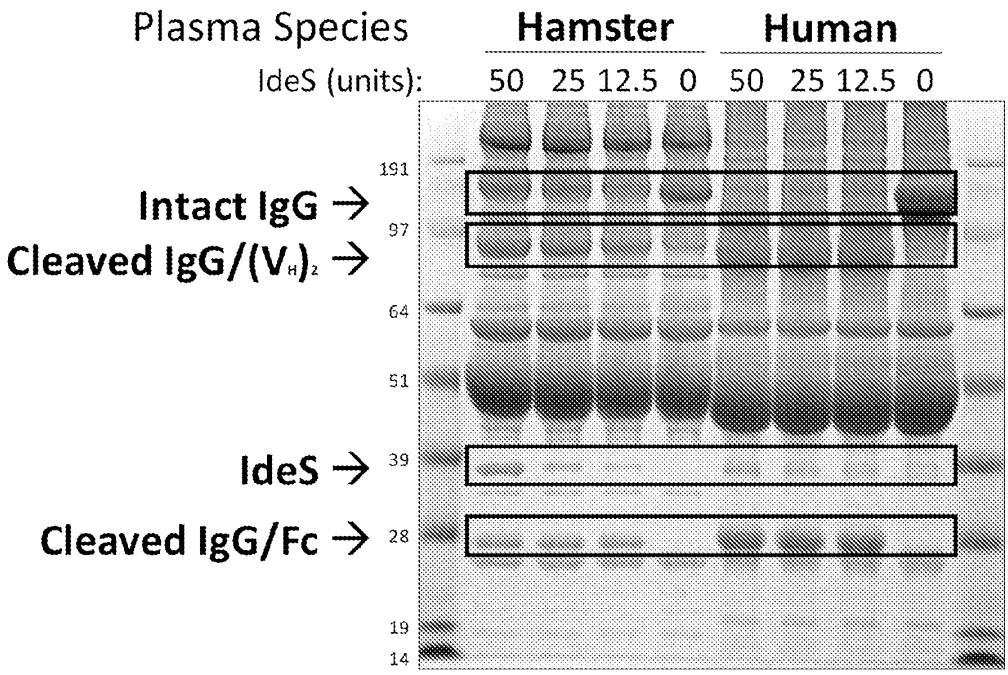

Plasma Species
Hamster
Human
IdeS (units):
50 25 12.5 0 50 25 12.5 0
191
97
64
51
39
28
19
14
Intact IgG →
Cleaved IgG/(V_H)_2 →
IdeS →
Cleaved IgG/Fc →

Figure 2

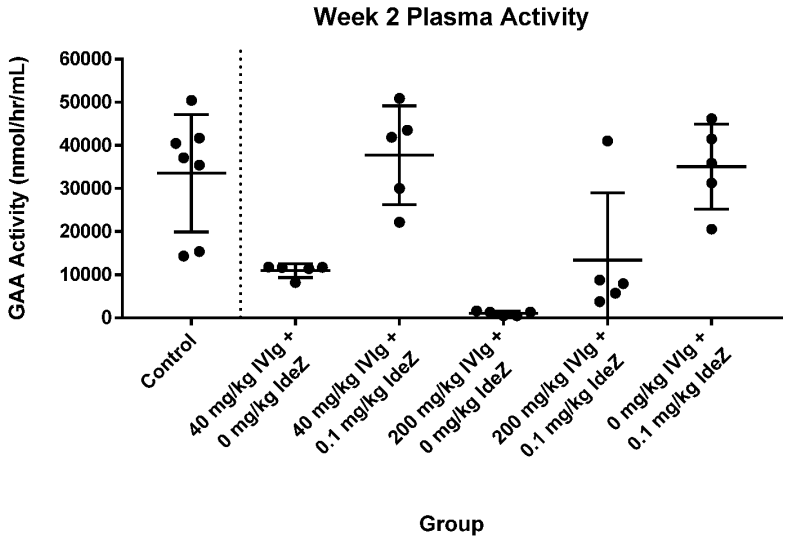

Week 2 Plasma Activity
GAA Activity (nmol/hr/mL)
60000
50000
40000
30000
20000
10000
0
Control
40 mg/kg IVIg + 0 mg/kg IdeZ
40 mg/kg IVIg + 0.1 mg/kg IdeZ
200 mg/kg IVIg + 0 mg/kg IdeZ
200 mg/kg IVIg + 0.1 mg/kg IdeZ
0 mg/kg IVIg + 0.1 mg/kg IdeZ
Group

Figure 3

	Pre-IdeS	Post-IdeS
1- Neg Control 0 mg/kg IVIg + 0 mg/kg IdeS	**<1:1**	**<1:1**
	<1:1	**<1:1**
	<1:1	Animal died
	<1:1	**<1:1**
	<1:1	**<1:1**
2- No IdeS 300 mg/kg IVIg + 0 mg/kg IdeS	*1:10-1:20*	*1:20-1:40*
	1:2.5-1:5	*1:5-1:10*
	1:10-1:20	*1:20-1:40*
	1:20-1:40	*1:10-1:20*
	1:20-1:40	*1:10-1:20*
3- IdeS Low 300 mg/kg IVIg + 0.4 mg/kg IdeS	*1:10-1:20*	***1:2.5-1:5***
	1:10-1:20	***1:1-1:2.5***
	1:10-1:20	***1:2.5-1:5***
	1:20-1:40	***1:2.5-1:5***
	1:10-1:20	**1:1-1:2.5**
4- Ides High 300 mg/kg IVIg + 4 mg/kg IdeS	*1:20-1:40*	**<1:1**
	1:20-1:40	**<1:1**
	1:40	**<1:1**
	1:20-1:40	**1:1-1:2.5**
	1:40	**<1:1**

Figure 4

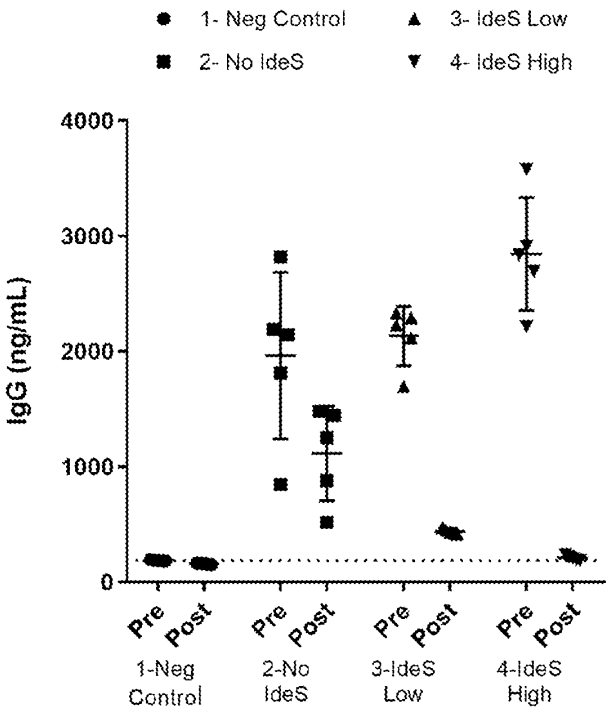
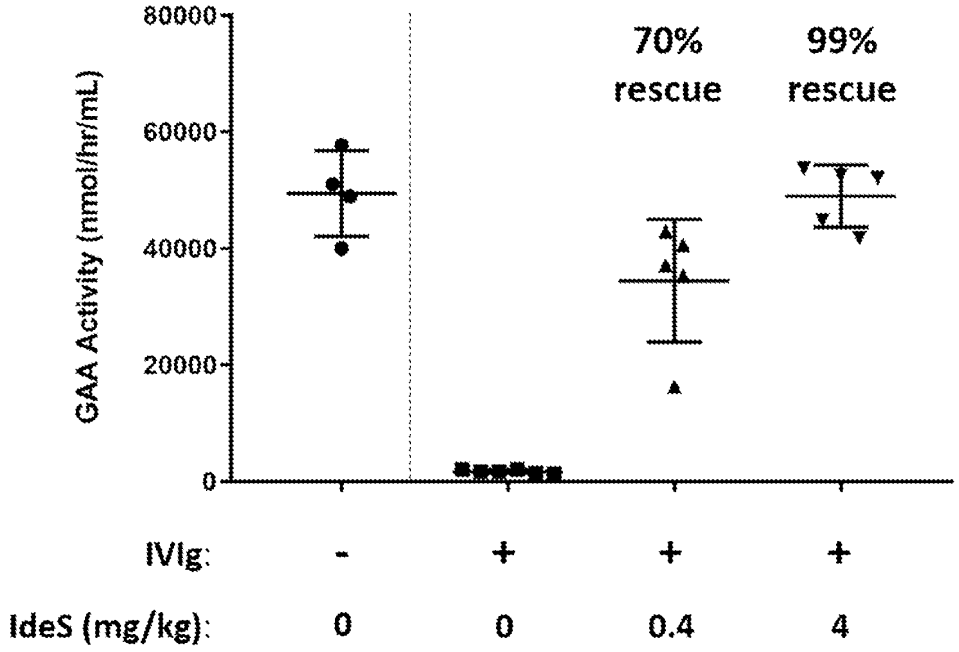
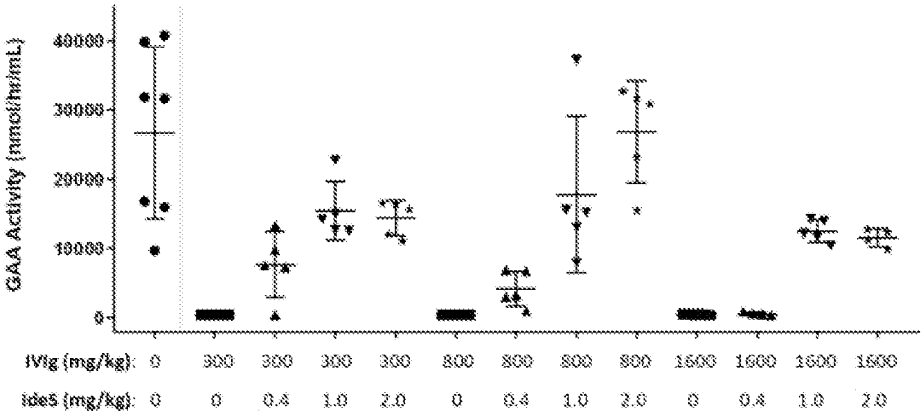

1- Neg Control
2- No IdeS
3- IdeS Low
4- IdeS High
IgG (ng/mL)
4000
3000
2000
1000
0
Pre
Post
1-Neg Control
2-No IdeS
3-IdeS Low
4-IdeS High

Figure 5



All animals received $2x10^{12}$ vg/kg AAV-Spk1-GAA

Figure 6



All animals received $2x10^{12}$ vg/kg AAV-Spk1-GAA

Figure 7

	Pre-IdeS	Post-IdeS
Neg Control 0 mg/kg IVIg + 0 mg/kg IdeS	< 1:2.5	< 1:2.5
	< 1:1	< 1:1
	< 1:1	< 1:1
	< 1:1	< 1:1
	< 1:1	< 1:1
No IdeS 300 mg/kg IVIg + 0 mg/kg IdeS	1:40-1:80	1:20-1:40
	1:40-1:80	1:20-1:40
	1:20-1:40	1:20-1:40
	1:20-1:40	1:20-1:40
	1:40-1:80	1:40-1:80
IdeS (Lot #1) 300mg/kg IVIg + 1 mg/kg IdeS	1:80-1:160	1:1-1:2.5
	1:40-1:80	< 1:1
	1:80-1:160	< 1:1
	1:80-1:160	n.d.
	1:80-1:160	< 1:2.5
IdeS (Lot #2) 300mg/kg IVIg + 1 mg/kg IdeS	1:40-1:80	1:1-1:2.5
	1:20-1:40	< 1:1
	> 1:160	< 1:1
	1:40-1:80	1:20-1:40
	1:40-1:80	1:1-1:2.5

n.d. - no data

Figure 8

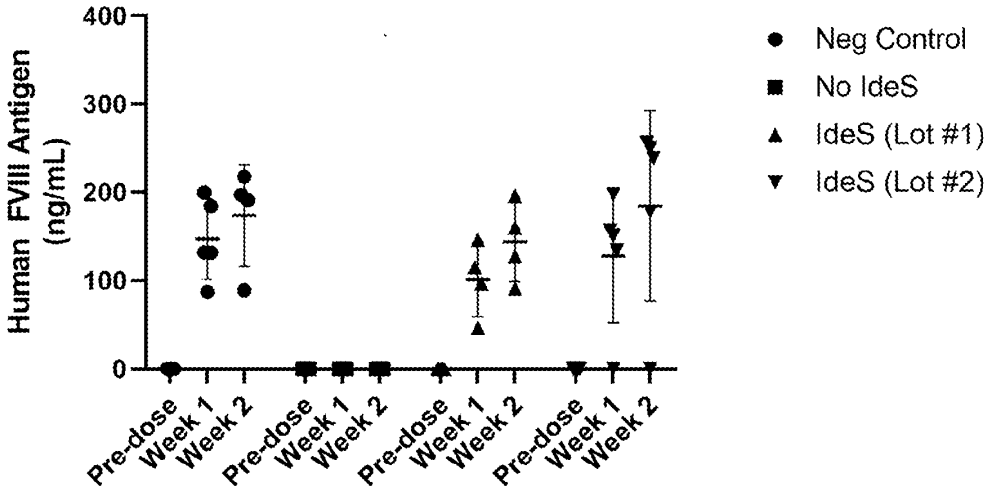

Human FVIII Antigen (ng/mL)
400
300
200
100
0
Pre-dose
Week 1
Week 2
Pre-dose
Week 1
Week 2
Pre-dose
Week 1
Week 2
Pre-dose
Week 1
Week 2
Neg Control
No IdeS
IdeS (Lot #1)
IdeS (Lot #2)

Figure 9

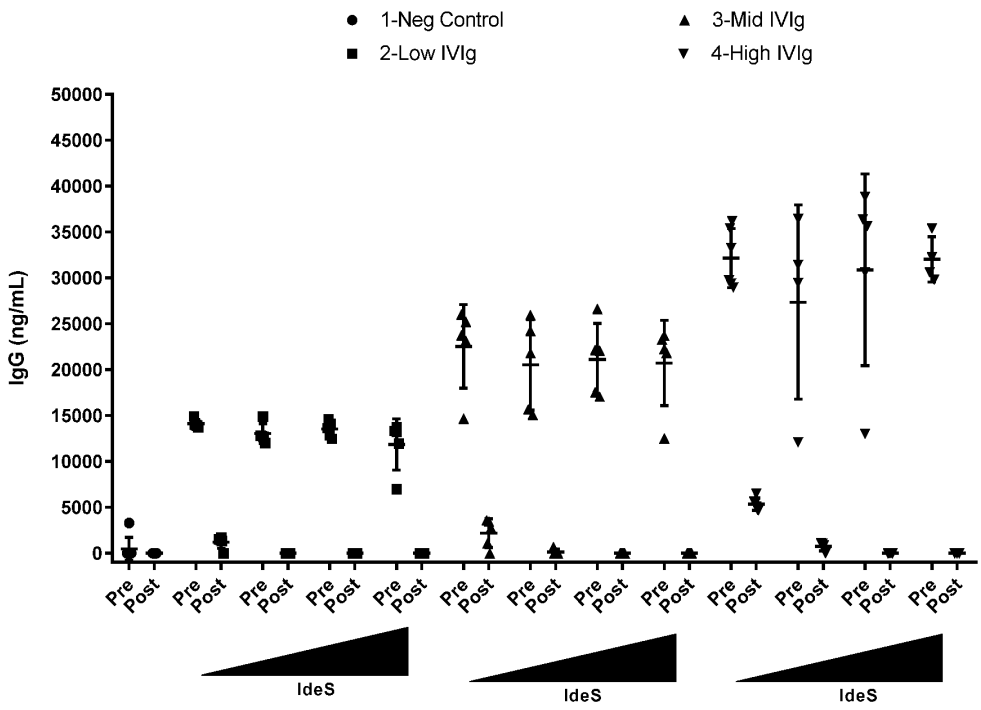

1-Neg Control
2-Low IVIg
3-Mid IVIg
4-High IVIg
IgG (ng/mL)
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
Pre
Post
IdeS
IdeS
IdeS

Figure 10

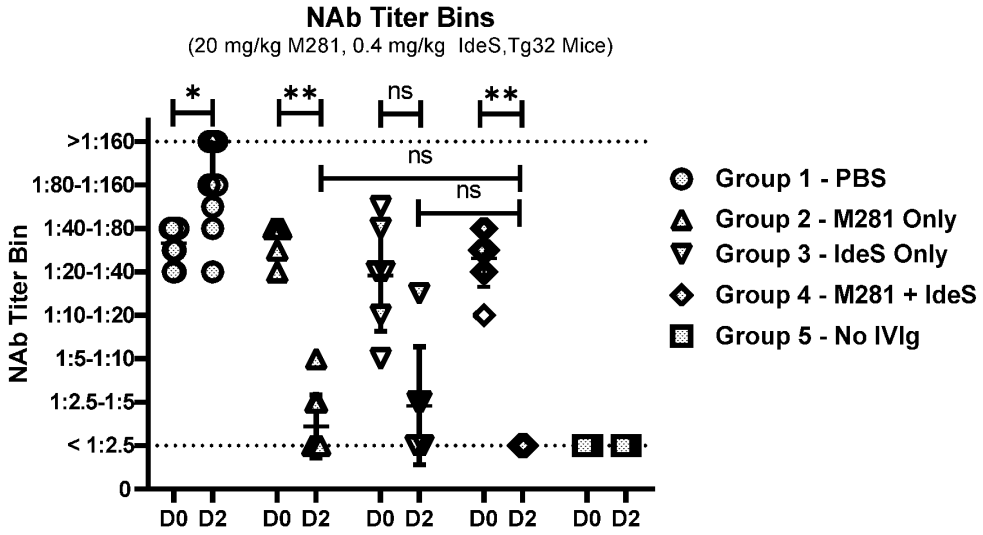

NAb Titer Bins
(20 mg/kg M281, 0.4 mg/kg IdeS,Tg32 Mice)
NAb Titer Bin
>1:160
1:80-1:160
1:40-1:80
1:20-1:40
1:10-1:20
1:5-1:10
1:2.5-1:5
< 1:2.5
0
*
**
ns
**
ns
ns
D0 D2 D0 D2 D0 D2 D0 D2 D0 D2
Group 1 - PBS
Group 2 - M281 Only
Group 3 - IdeS Only
Group 4 - M281 + IdeS
Group 5 - No IVIg

Figure 11

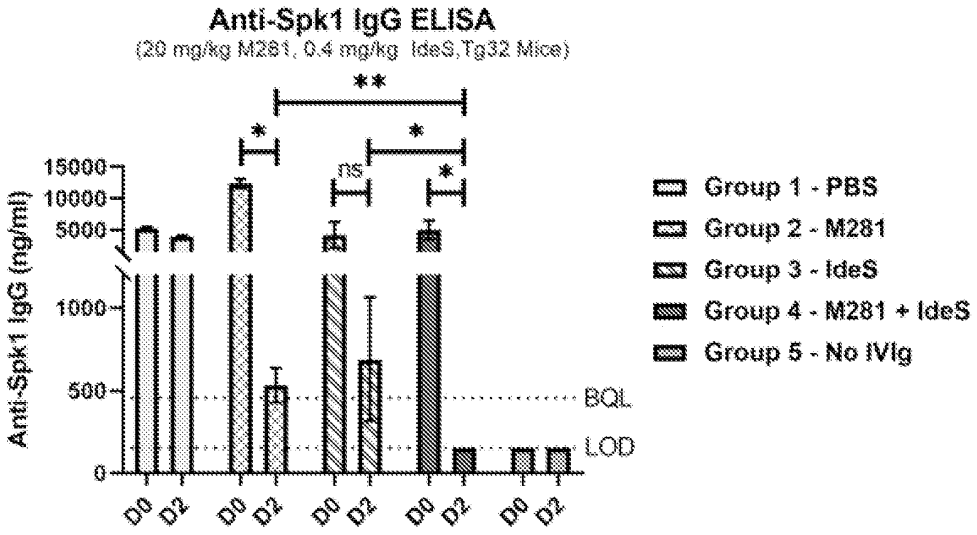

Anti-Spk1 IgG ELISA
(20 mg/kg M281, 0.4 mg/kg IdeS,Tg32 Mice)
**
*
*
ns
*
15000
10000
5000
1000
500
0
Anti-Spk1 IgG (ng/ml)
BQL
LOD
D0
D2
Group 1 - PBS
Group 2 - M281
Group 3 - IdeS
Group 4 - M281 + IdeS
Group 5 - No IVIg

Figure 12

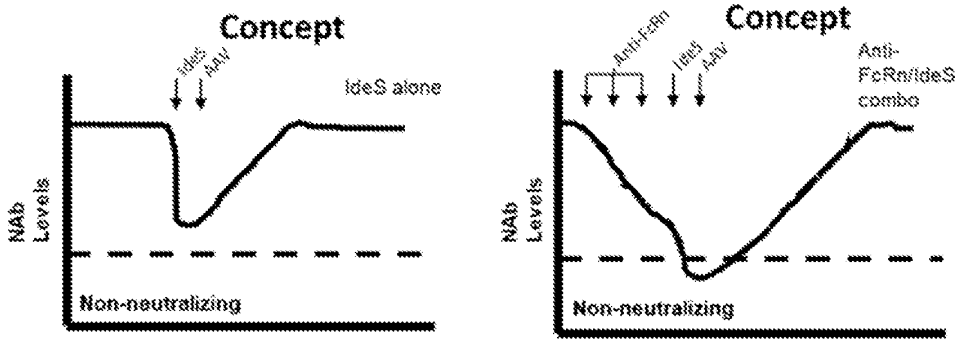

Concept
IdeS
AAV
IdeS alone
NAb Levels
Non-neutralizing
Concept
Anti-FcRn
IdeS
AAV
Anti-FcRn/IdeS combo
NAb Levels
Non-neutralizing

Figure 13

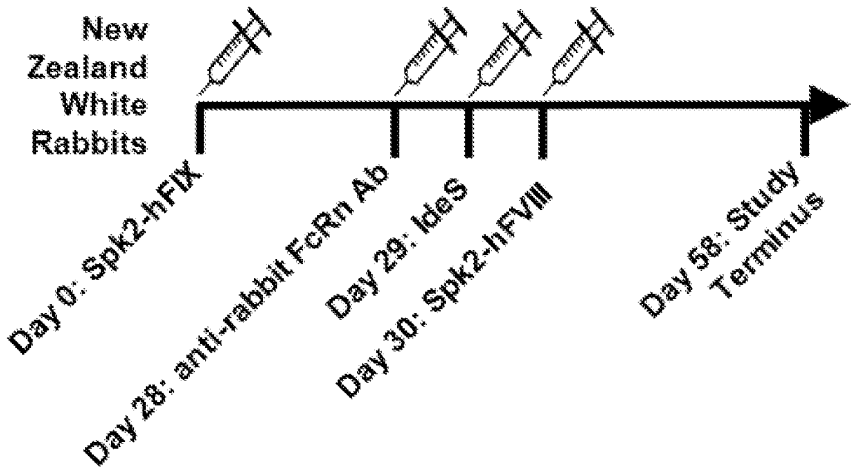

New Zealand White Rabbits
Day 0: Spk2-hFIX
Day 28: anti-rabbit FcRn Ab
Day 29: IdeS
Day 30: Spk2-hFVIII
Day 58: Study Terminus

Figure 14

