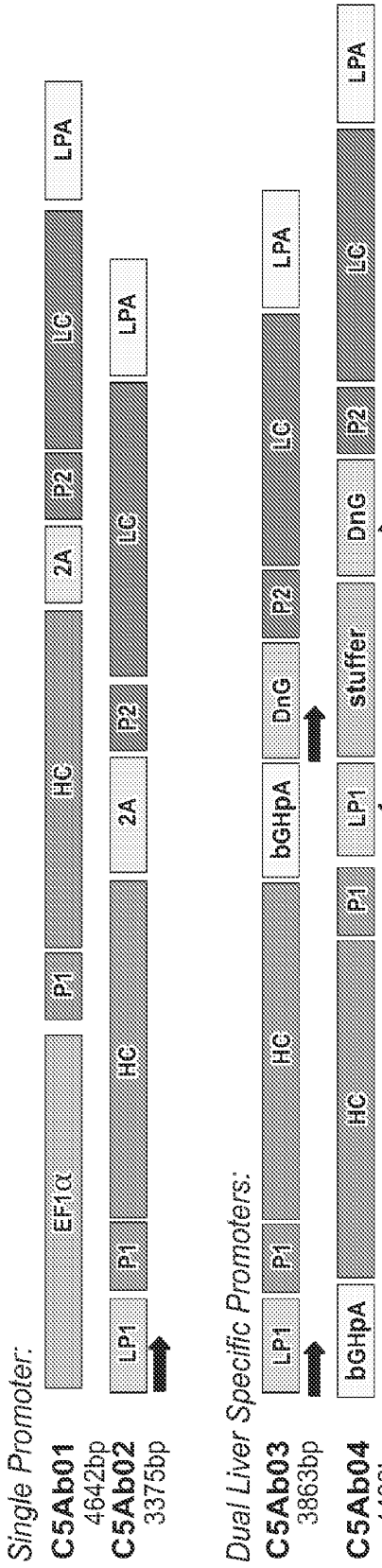
Single Promoter:
C5Ab01
4642bp
EF1α
P1
HC
2A
P2
LC
LPA
C5Ab02
3375bp
LP1
P1
HC
2A
P2
LC
LPA
Dual Liver Specific Promoters:
C5Ab03
3863bp
LP1
P1
HC
bGHpA
DnG
P2
LC
LPA
C5Ab04
4483bp
bGHpA
HC
P1
LP1
stuffer
DnG
P2
LC
LPA

FIG. 1

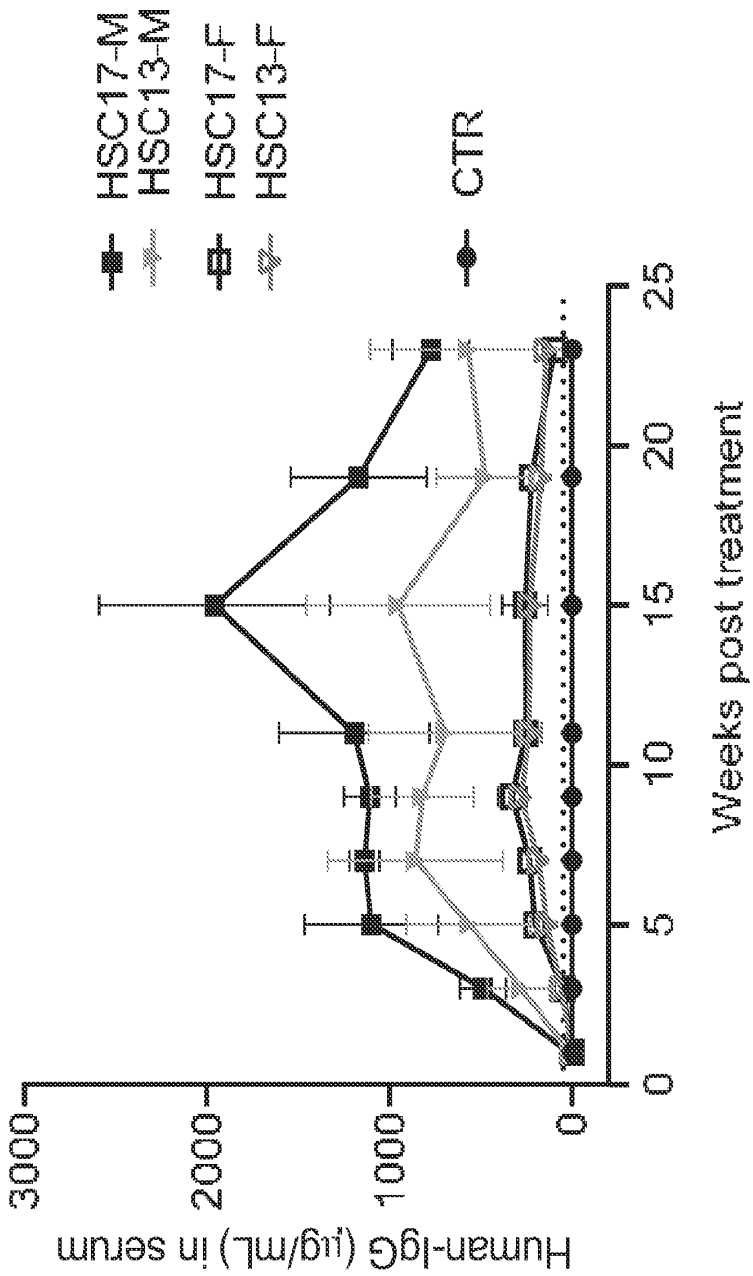
HSC17-M
HSC13-M
HSC17-F
HSC13-F
CTR
Human-IgG (µg/mL) in serum
3000
2000
1000
0
0
5
10
15
20
25
Weeks post treatment

FIG. 2A

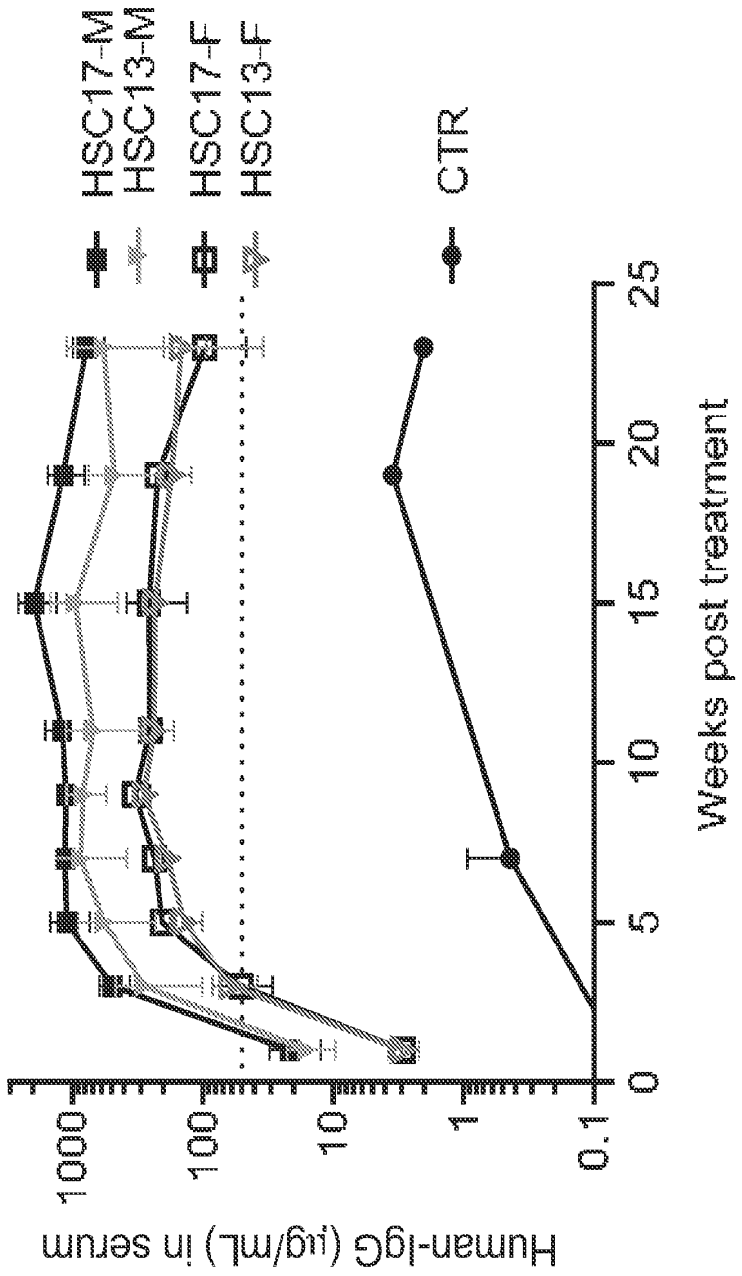
HSC17-M
HSC13-M
HSC17-F
HSC13-F
CTR
Human-IgG (µg/mL) in serum
1000
100
10
1
0.1
0
5
10
15
20
25
Weeks post treatment

FIG. 2B

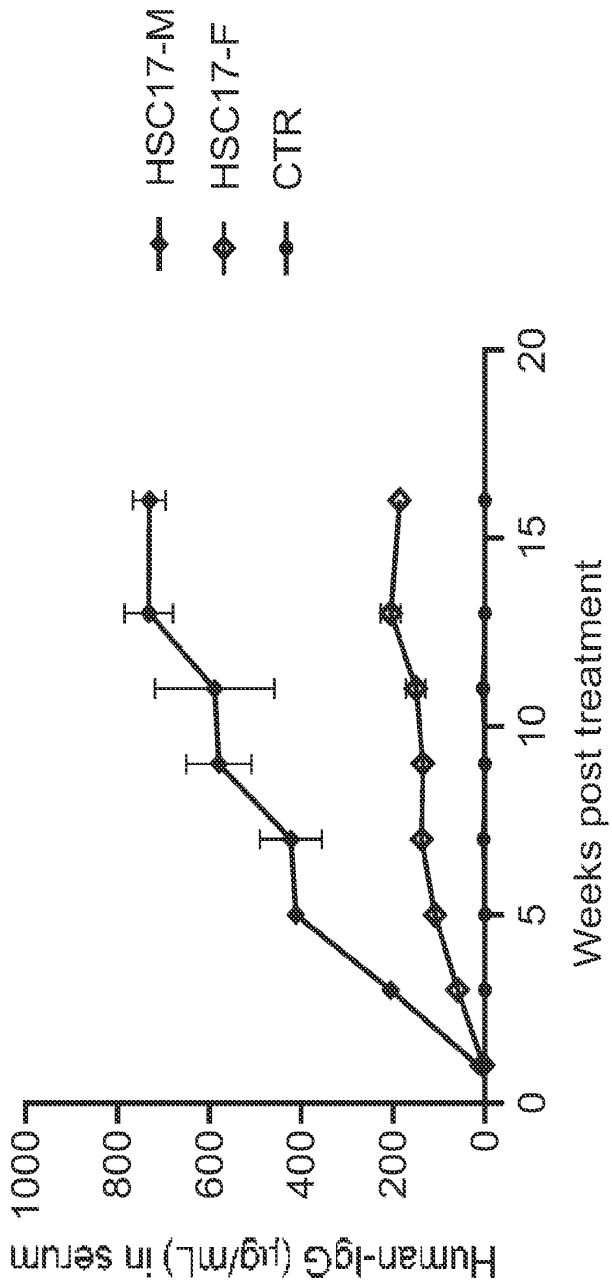
HSC17-M
HSC17-F
CTR
Human-IgG (µg/mL) in serum
1000
800
600
400
200
0
0
5
10
15
20
Weeks post treatment

FIG. 2C

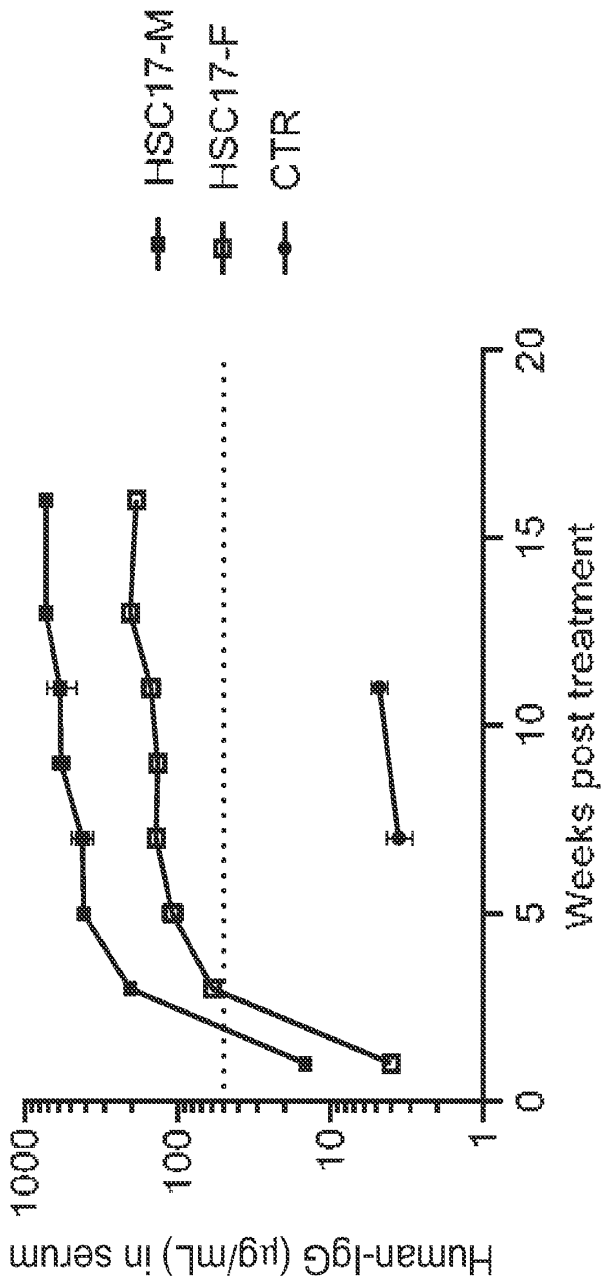
HSC17-M
HSC17-F
CTR
1000
100
10
1
0
5
10
15
20
Weeks post treatment
Human-IgG (µg/mL) in serum

FIG. 2D

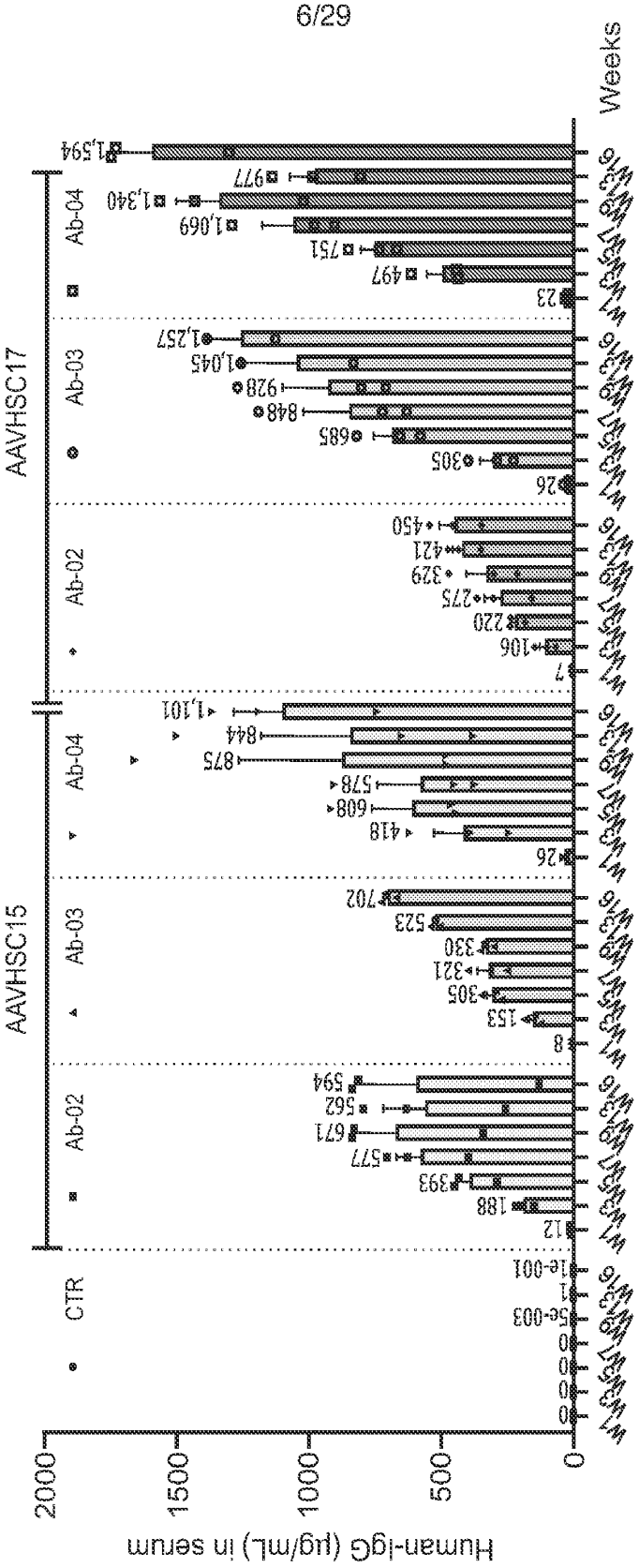
Weeks
AAVHSC17
AAVHSC15
CTR
Ab-02
Ab-03
Ab-04
Human-IgG (µg/mL) in serum
0
500
1000
1500
2000

FIG. 2E

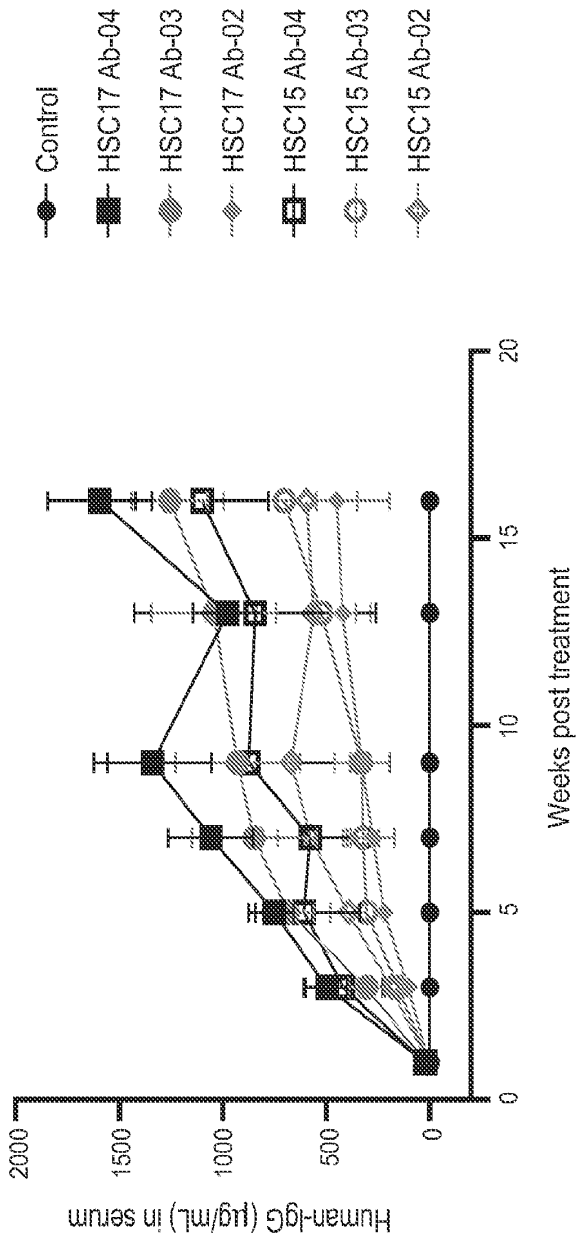
Control
HSC17 Ab-04
HSC17 Ab-03
HSC17 Ab-02
HSC15 Ab-04
HSC15 Ab-03
HSC15 Ab-02
Human-IgG (µg/mL) in serum
2000
1500
1000
500
0
0
5
10
15
20
Weeks post treatment

FIG. 2F

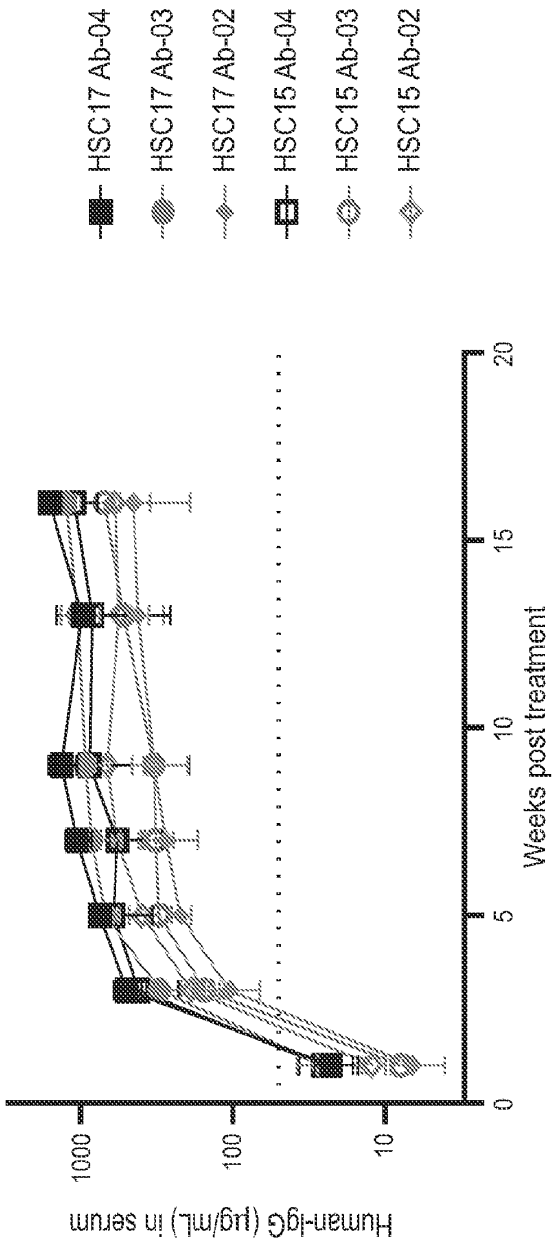
HSC17 Ab-04
HSC17 Ab-03
HSC17 Ab-02
HSC15 Ab-04
HSC15 Ab-03
HSC15 Ab-02
Human-IgG (µg/mL) in serum
1000
100
10
0
5
10
15
20
Weeks post treatment

FIG. 2G

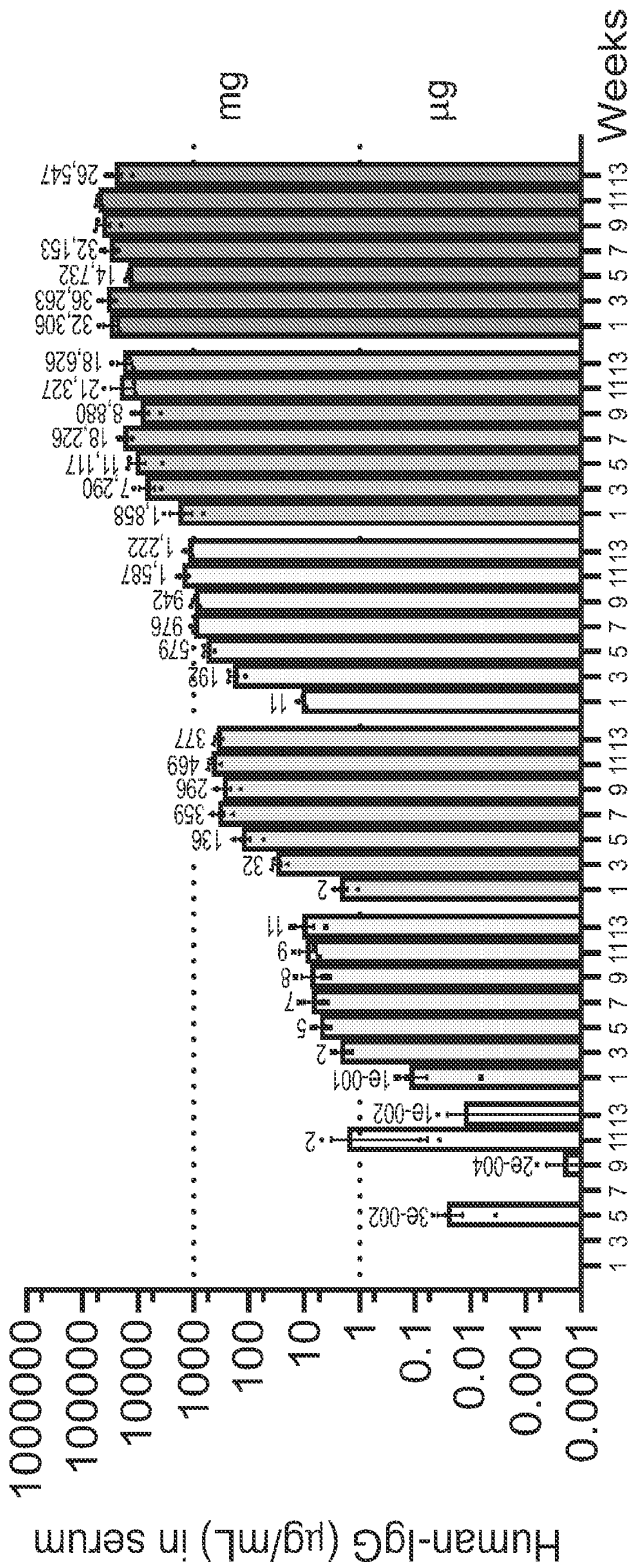
Ab.Liv.01.20
Human-IgG (µg/mL) in serum
1000000
100000
10000
1000
100
10
1
0.1
0.01
0.001
0.0001
CTR
5e11
5e12
1.4e13
4.4e13
1.8e14
mg
µg
Weeks
1 3 5 7 9 11 13
36e-002
2e-004
2
1e-002
1e-001
2
5
7
8
9
11
2
32
136
359
296
469
377
11
192
579
976
942
1,587
1,222
1,858
7,290
11,117
18,226
8,880
21,327
18,626
32,306
36,263
14,732
32,153
26,547

FIG. 2H

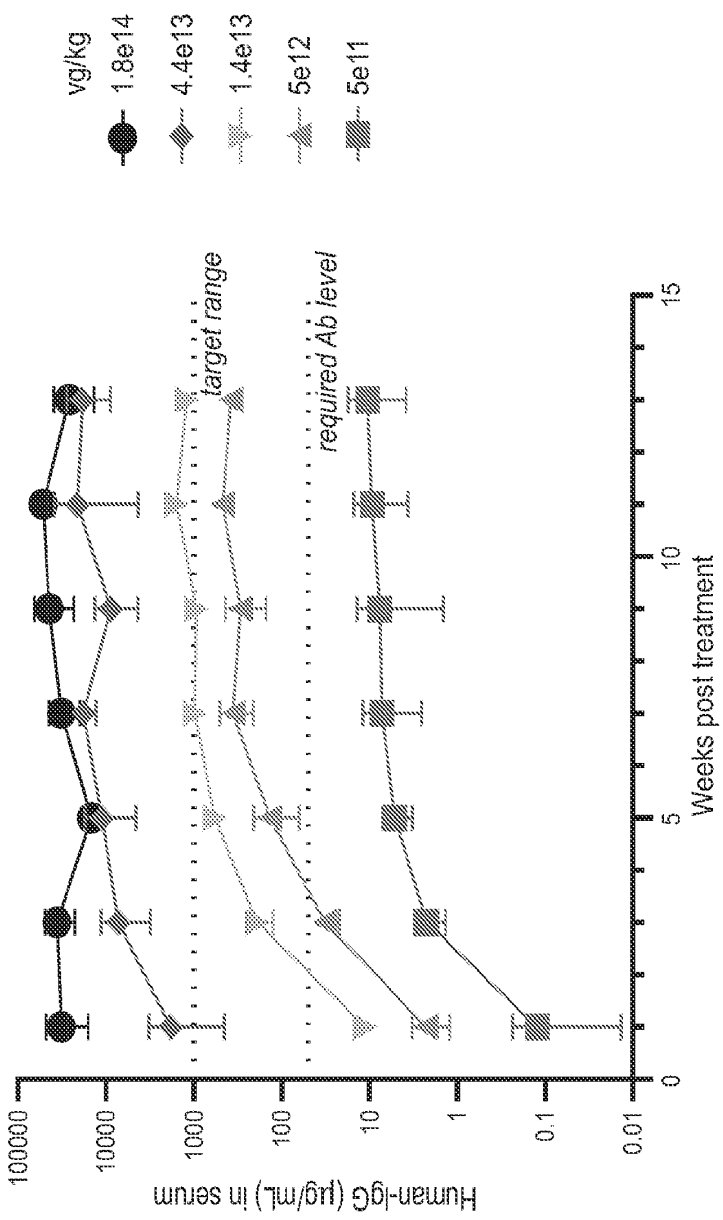
vg/kg
1.8e14
4.4e13
1.4e13
5e12
5e11
target range
required Ab level
Human-IgG (µg/mL) in serum
100000
10000
1000
100
10
1
0.1
0.01
0
5
10
15
Weeks post treatment

FIG. 2I

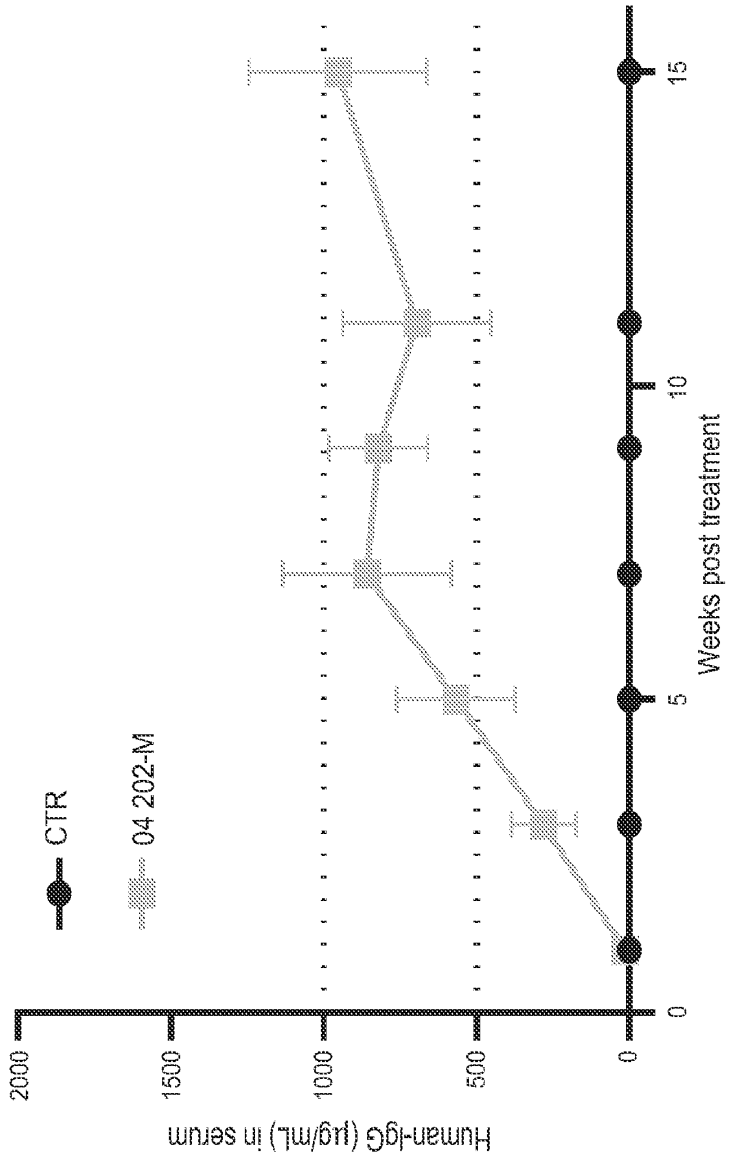
AAVHSC13
CTR
04 202-M
Human-IgG (µg/mL) in serum
2000
1500
1000
500
0
0
5
10
15
Weeks post treatment

FIG. 3A

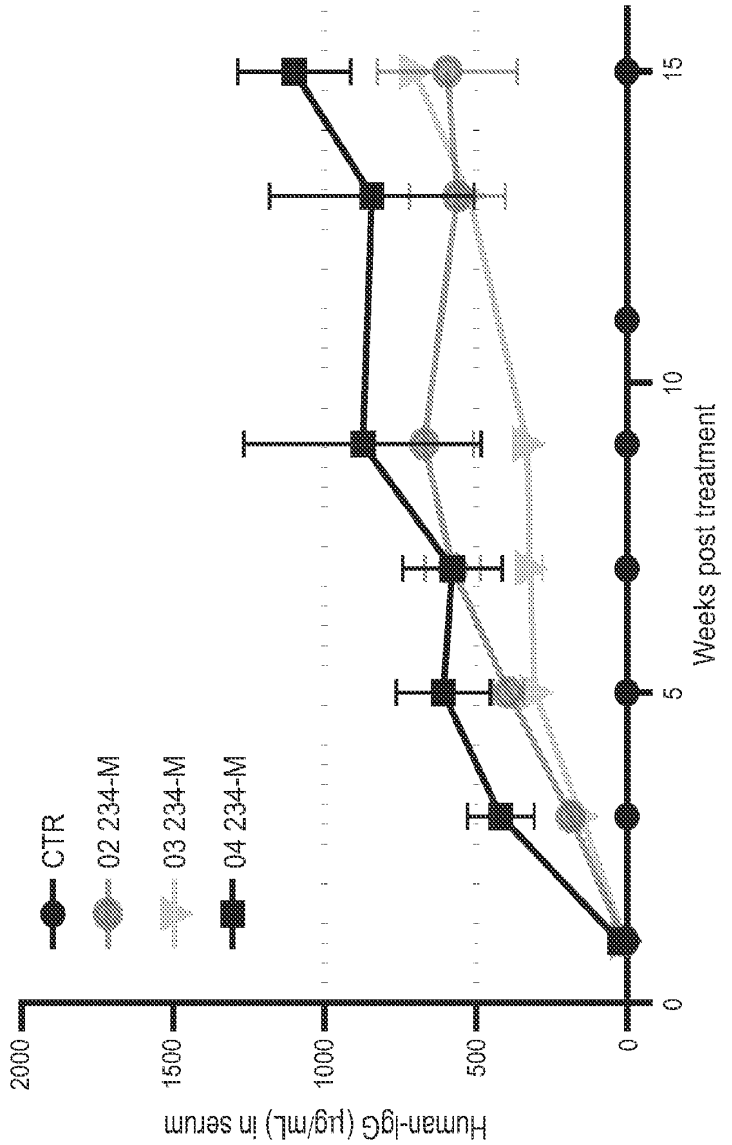
AAVHSC15
CTR
02 234-M
03 234-M
04 234-M
Human-IgG (µg/mL) in serum
2000
1500
1000
500
0
0
5
10
15
Weeks post treatment

FIG. 3B

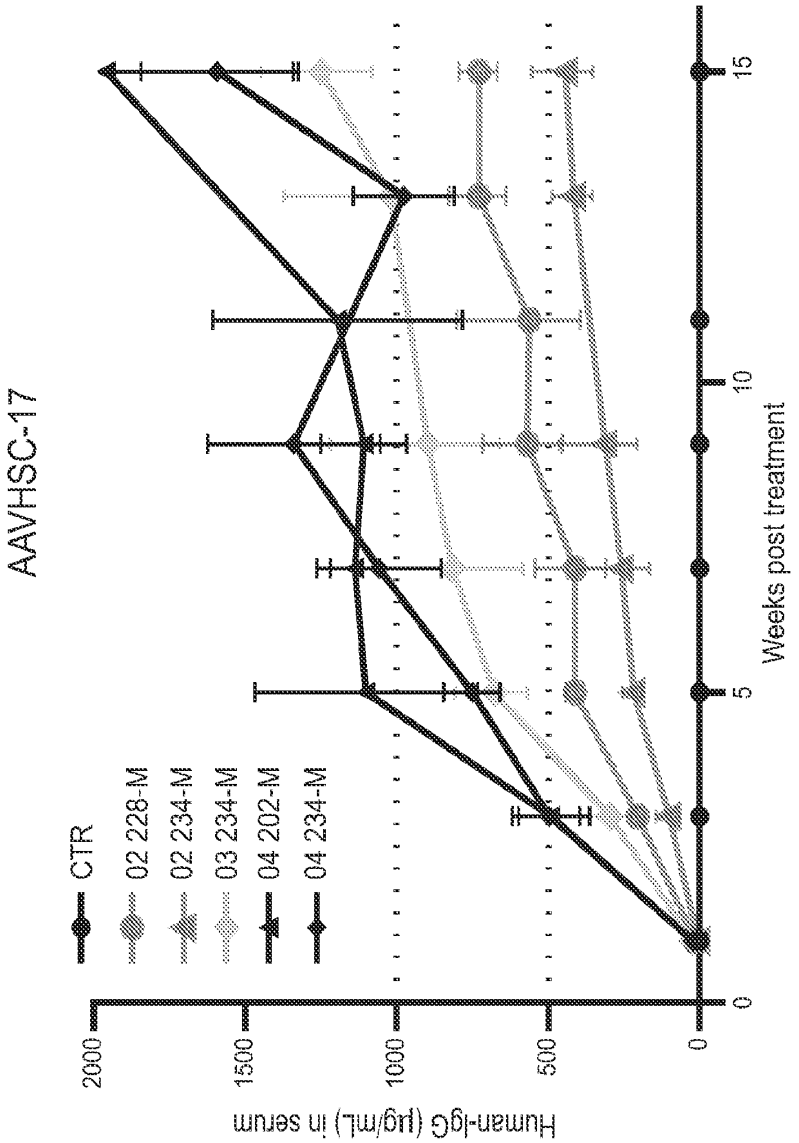
AAVHSC-17
CTR
02 228-M
02 234-M
03 234-M
04 202-M
04 234-M
Human-IgG (µg/mL) in serum
2000
1500
1000
500
0
0
5
10
15
Weeks post treatment

FIG. 3C

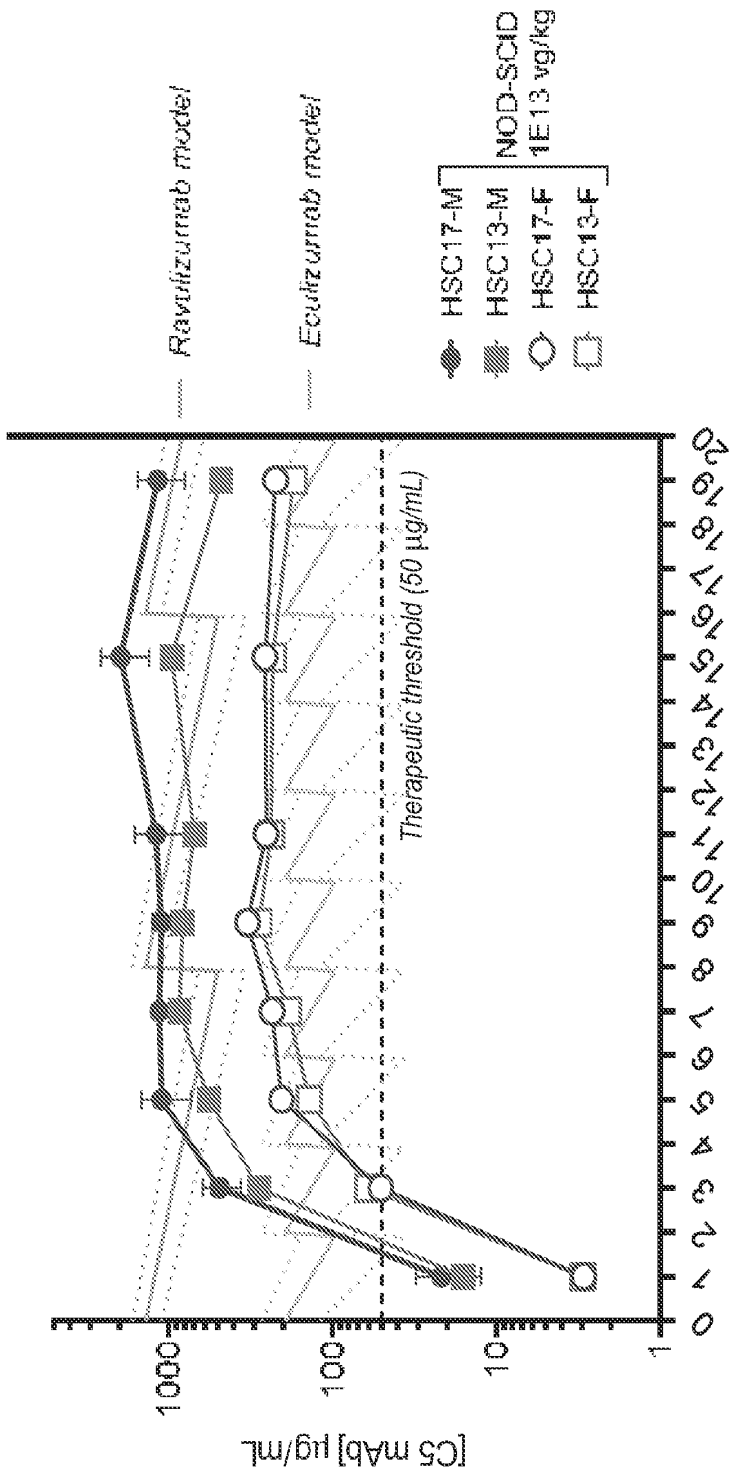
Ravulizumab model
Eculizumab model
HSC17-M
HSC13-M
HSC17-F
HSC13-F
NOD-SCID
1E13 vg/kg
Therapeutic threshold (50 µg/mL)
[C5 mAb] µg/mL
1000
100
10
1
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Weeks Post Treatment

FIG. 4A

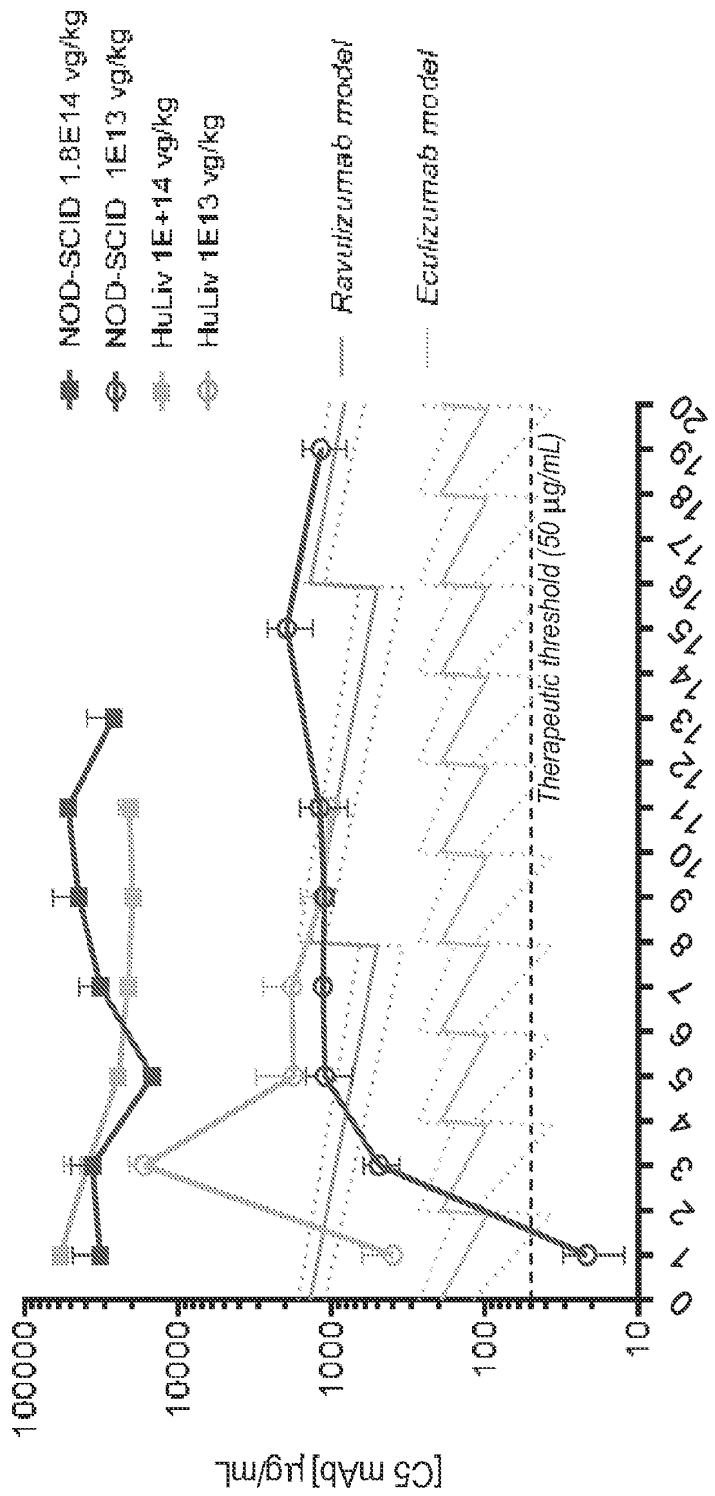
NOD-SCID 1.8E14 vg/kg
NOD-SCID 1E13 vg/kg
HuLiv 1E+14 vg/kg
HuLiv 1E13 vg/kg
Ravulizumab model
Eculizumab model
Therapeutic threshold (50 µg/mL)
[C5 mAb] µg/mL
100000
10000
1000
100
10
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Weeks Post Treatment

FIG. 4B

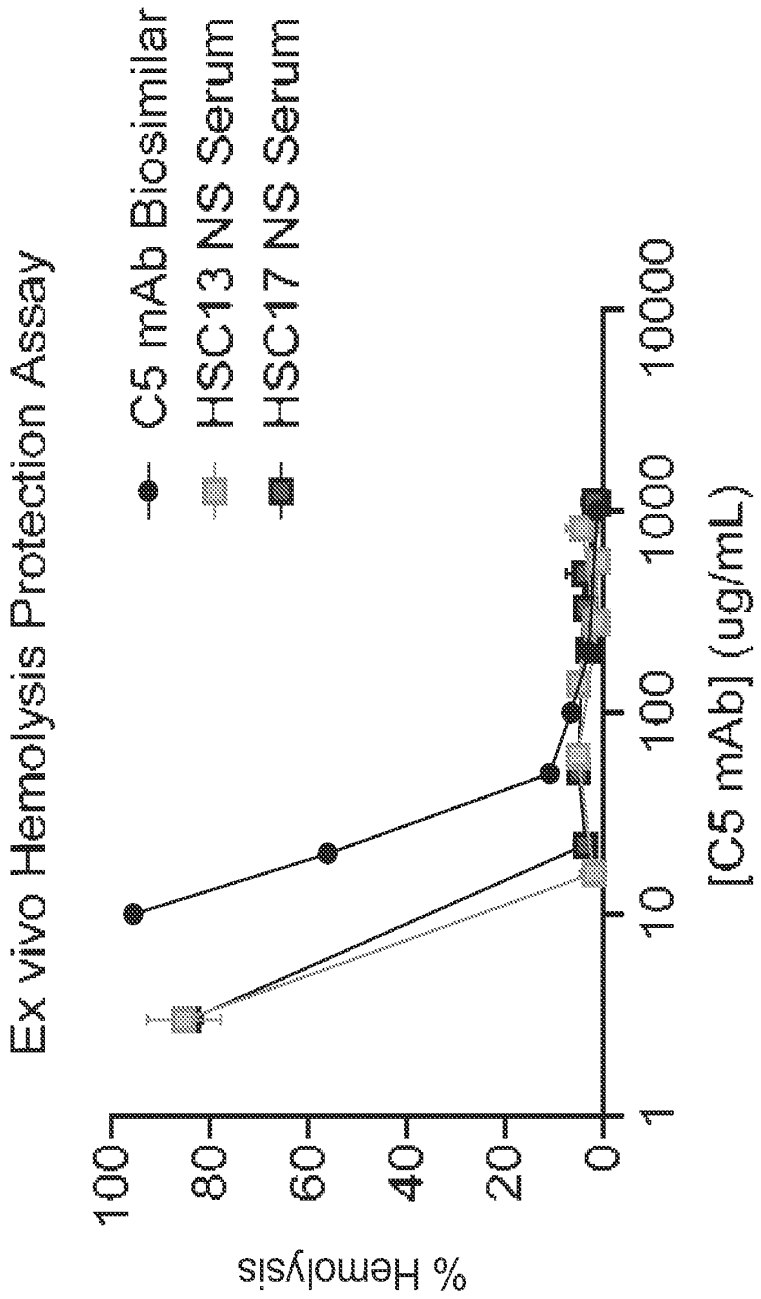
Ex vivo Hemolysis Protection Assay
C5 mAb Biosimilar
HSC13 NS Serum
HSC17 NS Serum
% Hemolysis
100
80
60
40
20
0
1
10
100
1000
10000
[C5 mAb] (ug/mL)

FIG. 5

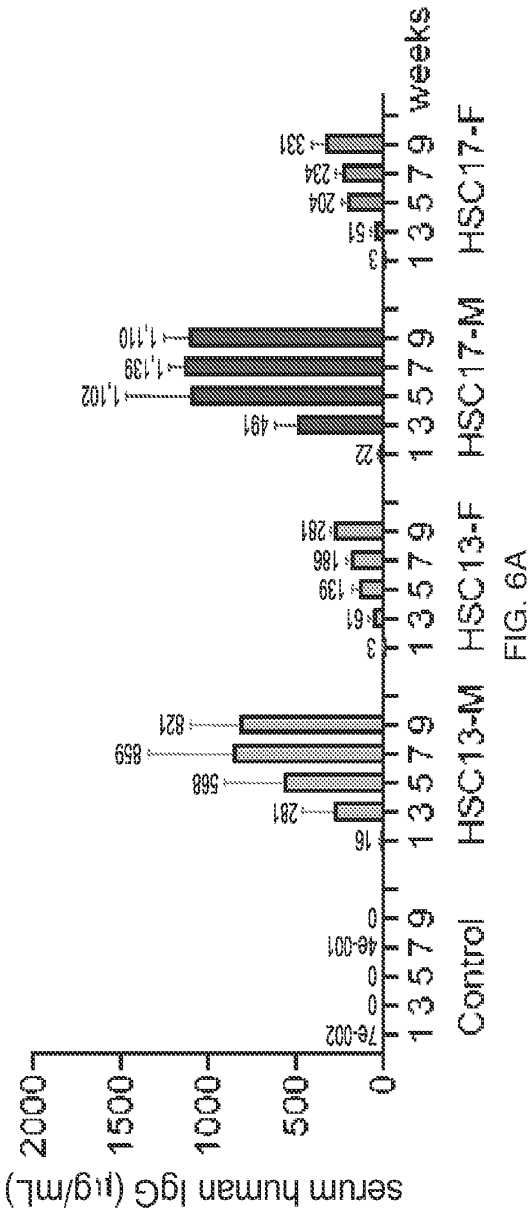
serum human IgG (µg/mL)
2000
1500
1000
500
0
7e-002
0
0
4e-001
0
16
281
568
859
821
3
61
139
186
281
22
491
1,102
1,139
1,110
3
51
204
234
331
1 3 5 7 9 1 3 5 7 9 1 3 5 7 9 1 3 5 7 9
Control HSC13-M HSC13-F HSC17-M HSC17-F
weeks

FIG. 6A

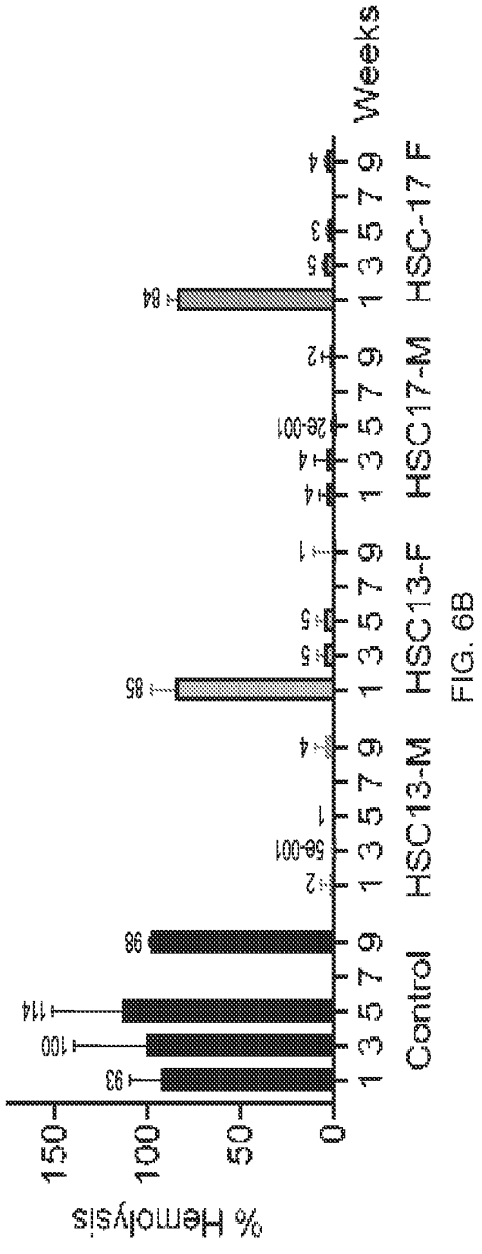
% Hemolysis
150
100
50
0
93
100
114
98
2
56-001
1
4
85
5
5
1
4
4
26-001
2
84
5
3
4
1 3 5 7 9 1 3 5 7 9 1 3 5 7 9 1 3 5 7 9
Control HSC13-M HSC13-F HSC17-M HSC-17 F
Weeks

FIG. 6B

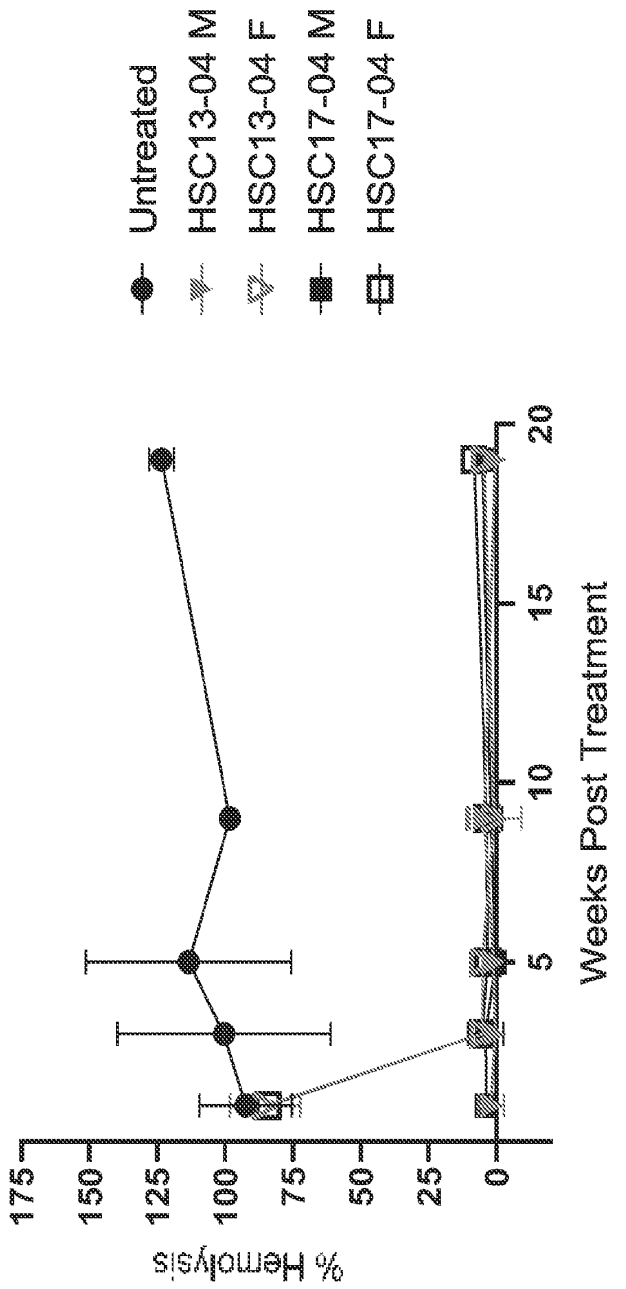
Untreated
HSC13-04 M
HSC13-04 F
HSC17-04 M
HSC17-04 F
% Hemolysis
175
150
125
100
75
50
25
0
5
10
15
20
Weeks Post Treatment

FIG. 6C

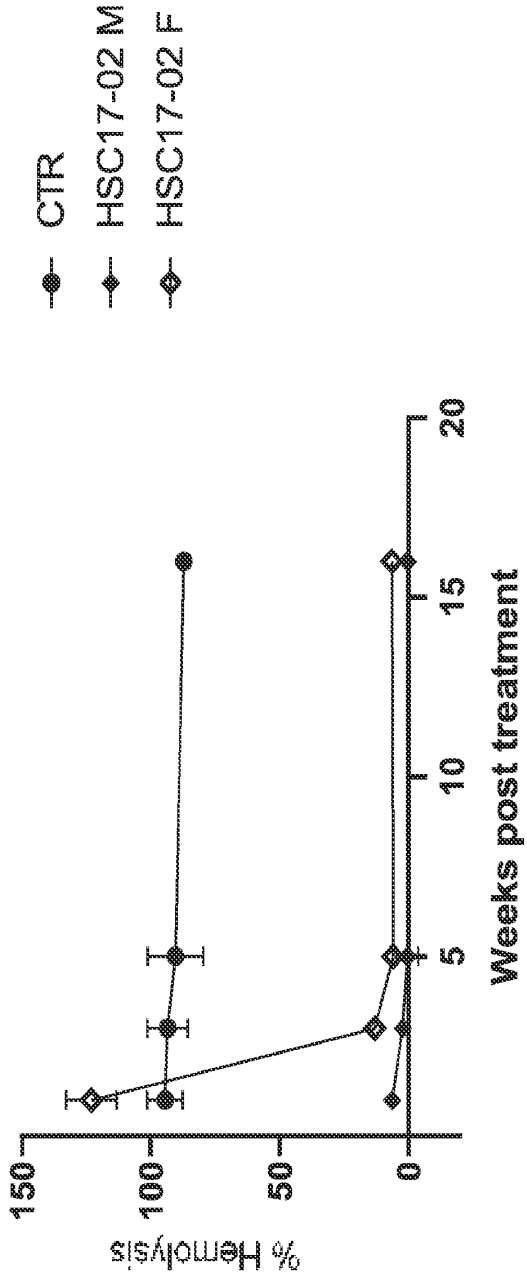
CTR
HSC17-02 M
HSC17-02 F
% Hemolysis
150
100
50
0
5
10
15
20
Weeks post treatment

FIG. 6D

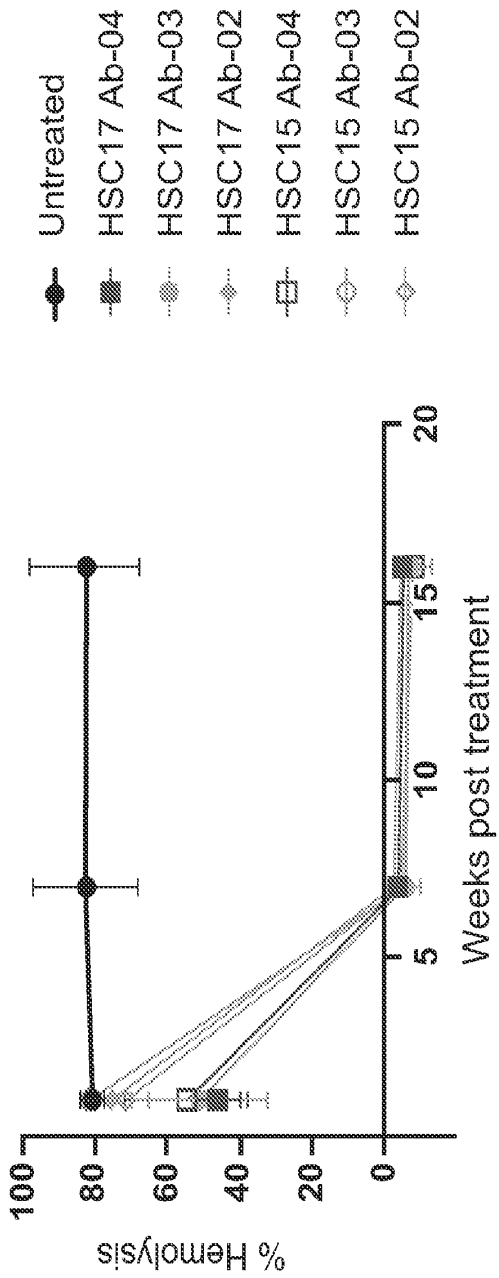
Untreated
HSC17 Ab-04
HSC17 Ab-03
HSC17 Ab-02
HSC15 Ab-04
HSC15 Ab-03
HSC15 Ab-02
% Hemolysis
100
80
60
40
20
0
5
10
15
20
Weeks post treatment

FIG. 6E

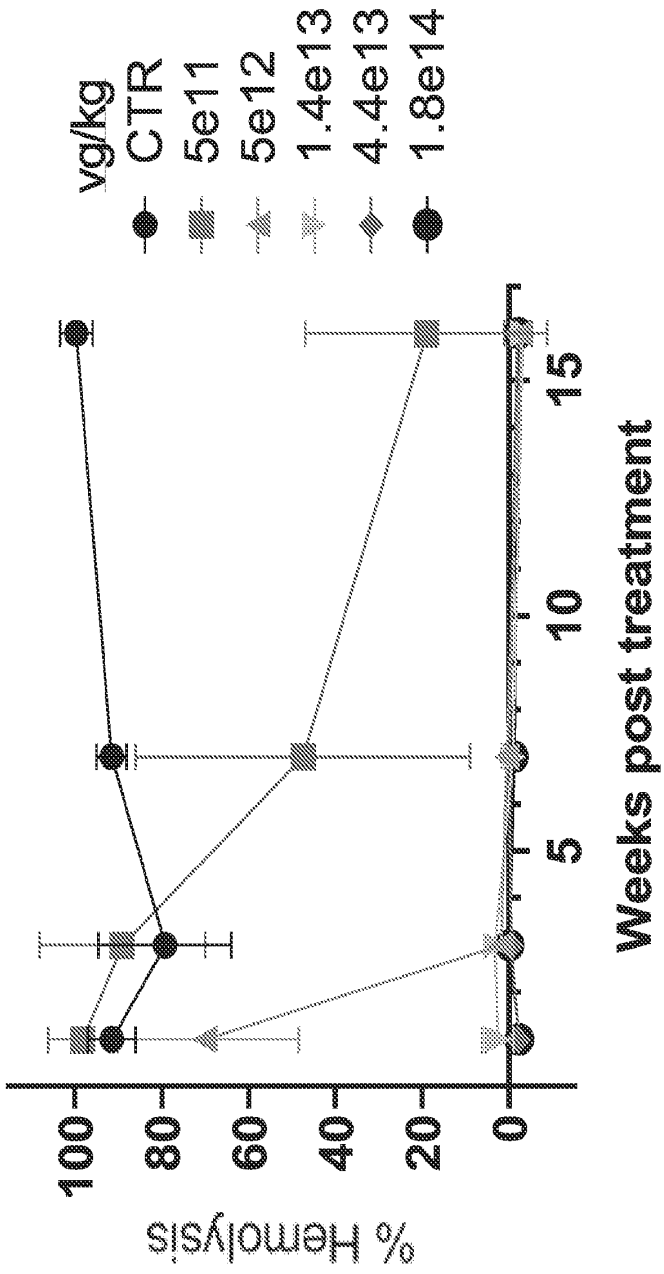
vg/kg
CTR
5e11
5e12
1.4e13
4.4e13
1.8e14
% Hemolysis
100
80
60
40
20
0
5
10
15
Weeks post treatment

FIG. 6F

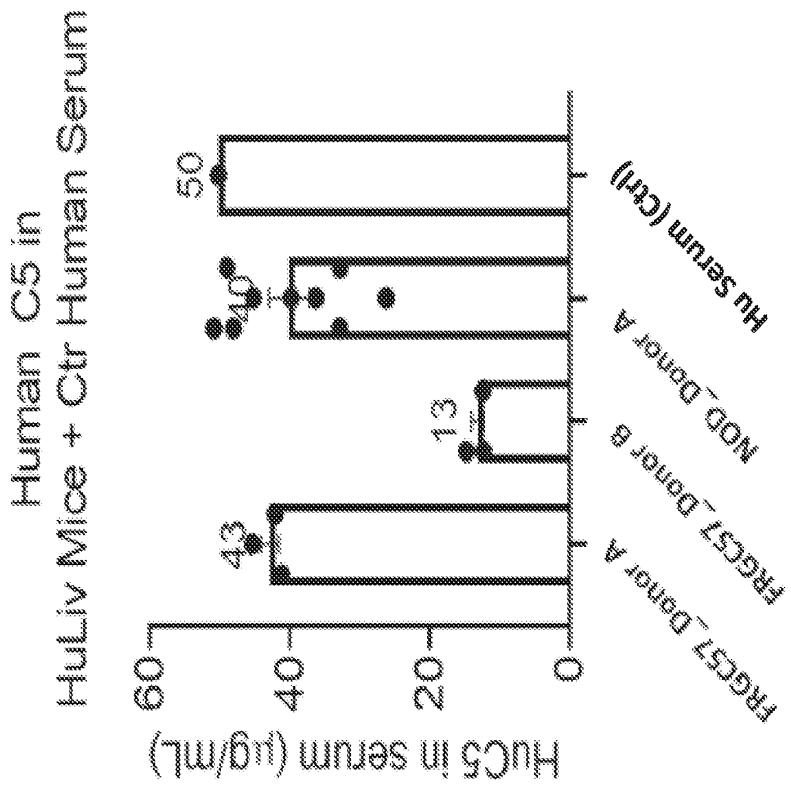
Human C5 in
HuLiv Mice + Ctr Human Serum
HuC5 in serum (µg/mL)
0
20
40
60
43
13
50
RGCS7_Donor A
RGCS7_Donor B
NOD_Donor A
Hu Serum (Ctrl)

FIG. 7A

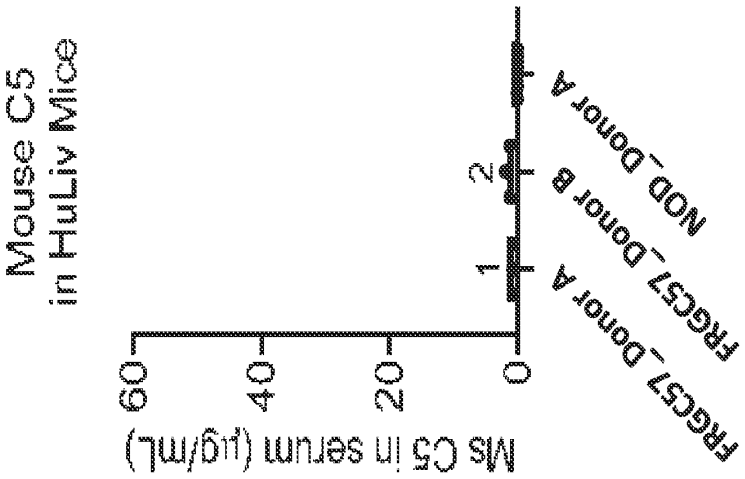
Mouse C5
in HuLiv Mice
Ms C5 in serum (µg/mL)
0
20
40
60
1
2
FRGCS7_Donor A
FRGCS7_Donor B
NOD_Donor A

FIG. 7B

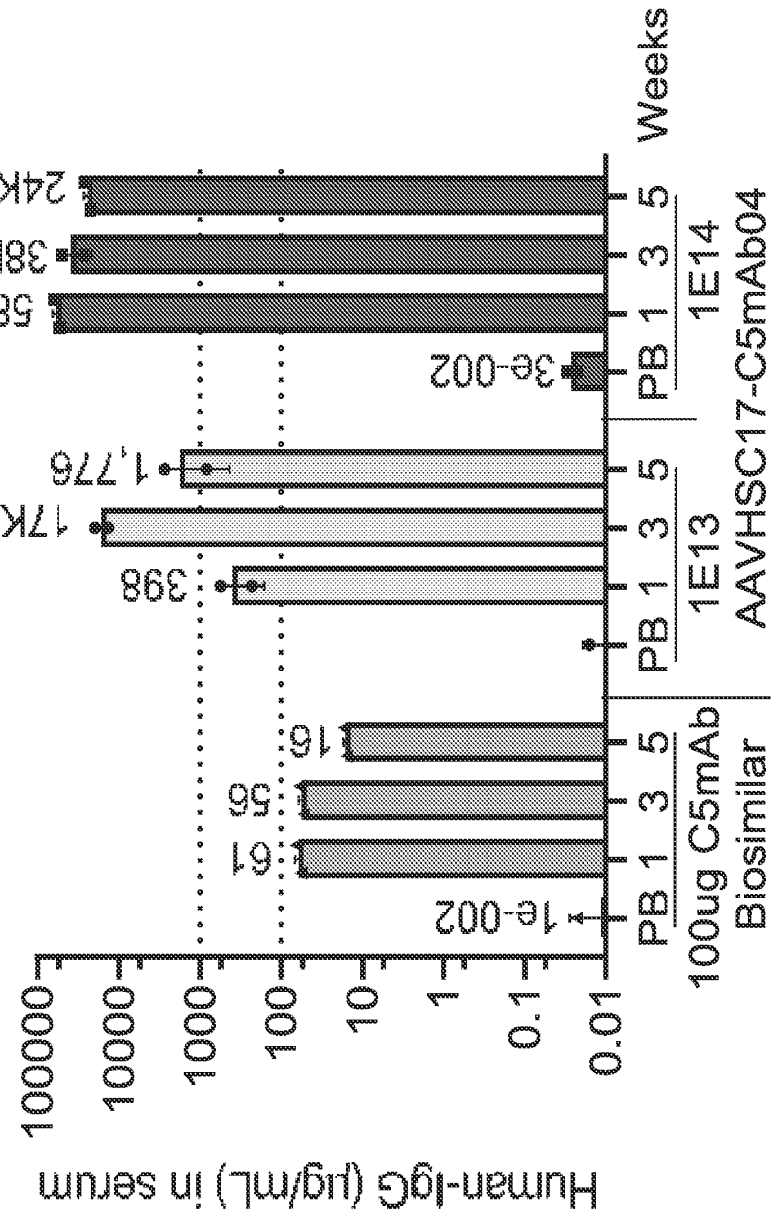
Human-IgG (µg/mL) in serum
100000
10000
1000
100
10
1
0.1
0.01
1e-002
61
56
16
398
17K
1,776
3e-002
58K
38K
24K
PB 1 3 5
100ug C5mAb Biosimilar
1E13
1E14
AAVHSC17-C5mAb04
Weeks

FIG. 8A

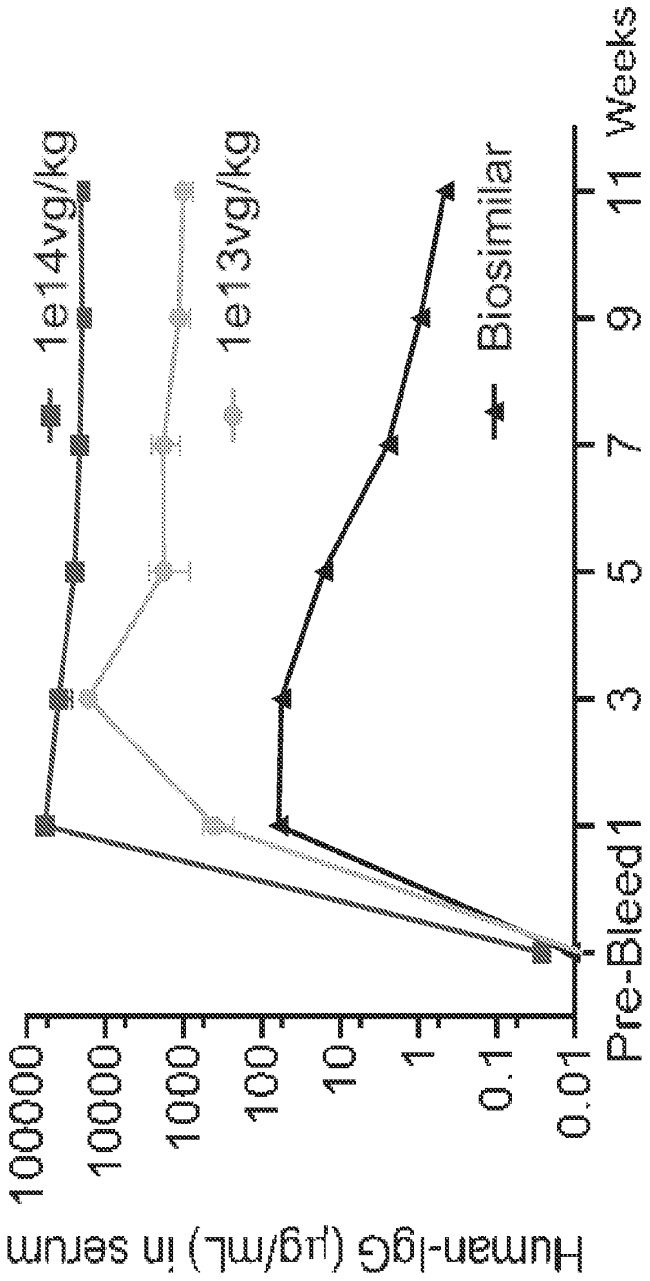
Human-IgG (µg/mL) in serum
100000
10000
1000
100
10
1
0.1
0.01
Pre-Bleed
1
3
5
7
9
11
Weeks
1e14vg/kg
1e13vg/kg
Biosimilar

FIG. 8B

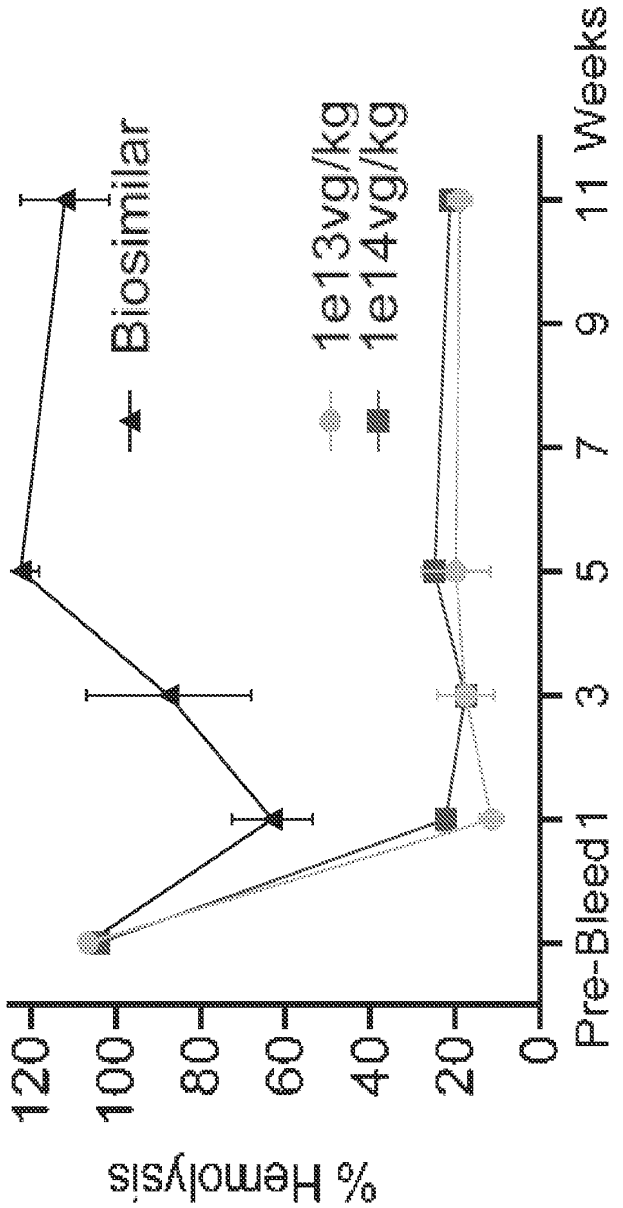
% Hemolysis
120
100
80
60
40
20
0
Pre-Bleed
1
3
5
7
9
11 Weeks
Biosimilar
1e13vg/kg
1e14vg/kg

FIG. 8C

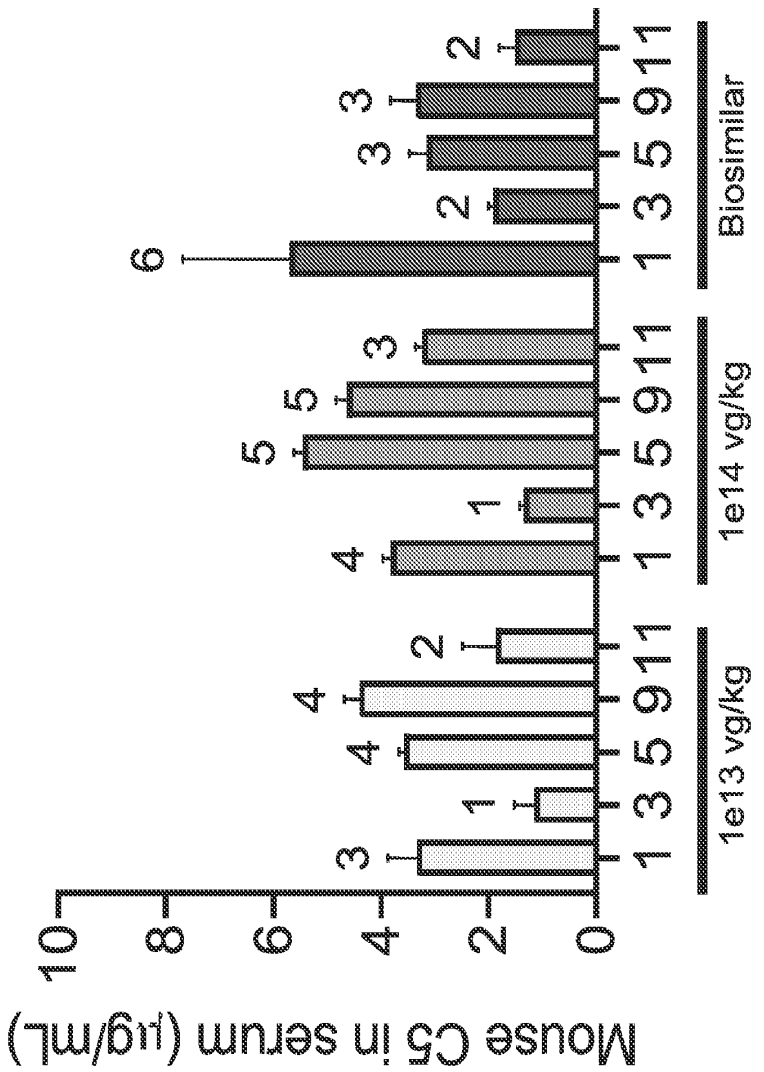
Mouse C5 in serum (μg/mL)
0
2
4
6
8
10
1 3 5 9 11
1e13 vg/kg
1 3 5 9 11
1e14 vg/kg
1 3 5 9 11
Biosimilar

FIG. 8D

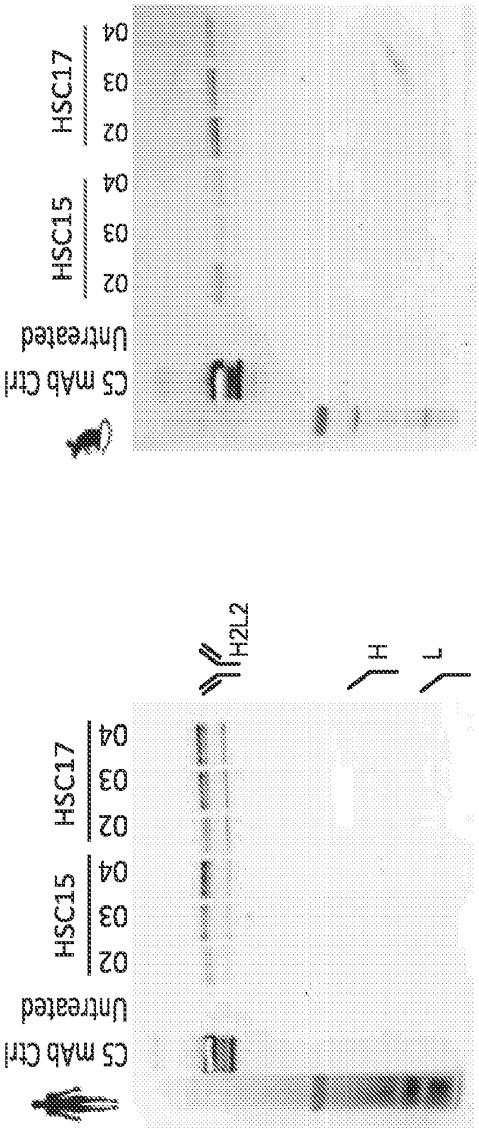
C5 mAb Ctrl
Untreated
HSC15
02
03
04
HSC17
02
03
04
H2L2
H
L
Western Blot

FIG. 9A

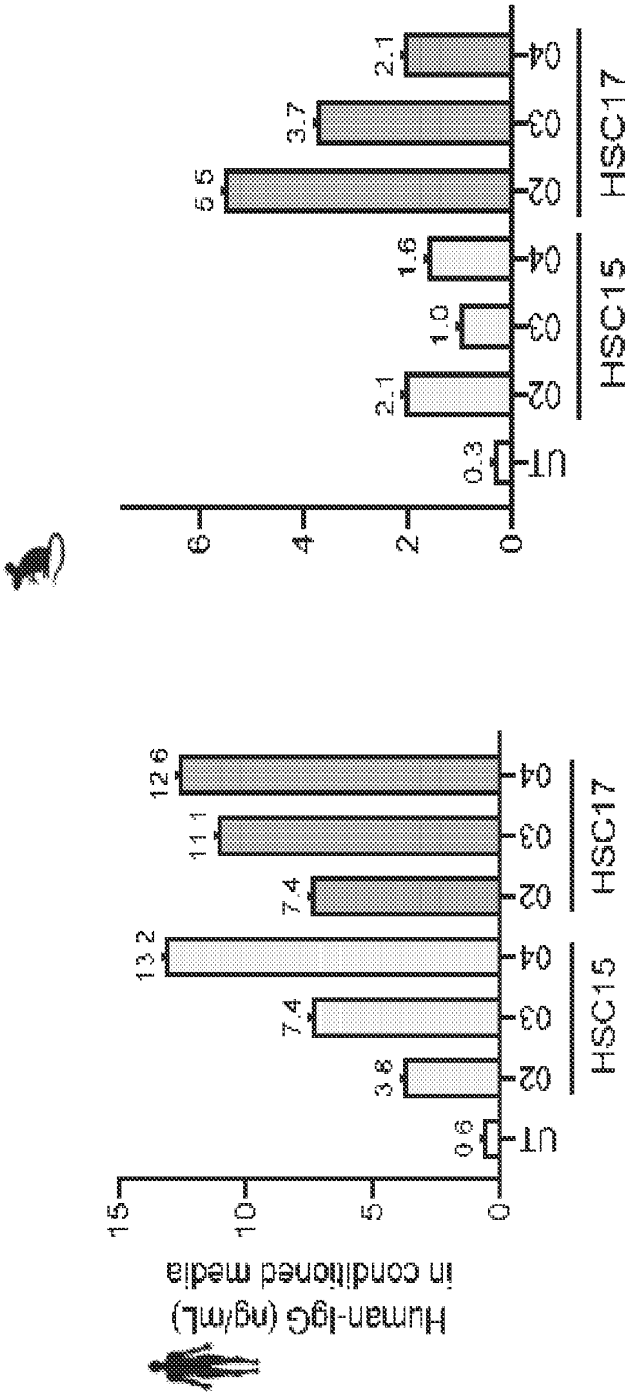
Human-IgG (ng/mL)
in conditioned media
Human IgG ELISA
UT
02
03
04
HSC15
HSC17
0.6
3.8
7.4
13.2
7.4
11.1
12.6
0.3
2.1
1.0
1.6
5.5
3.7
2.1

FIG. 9B