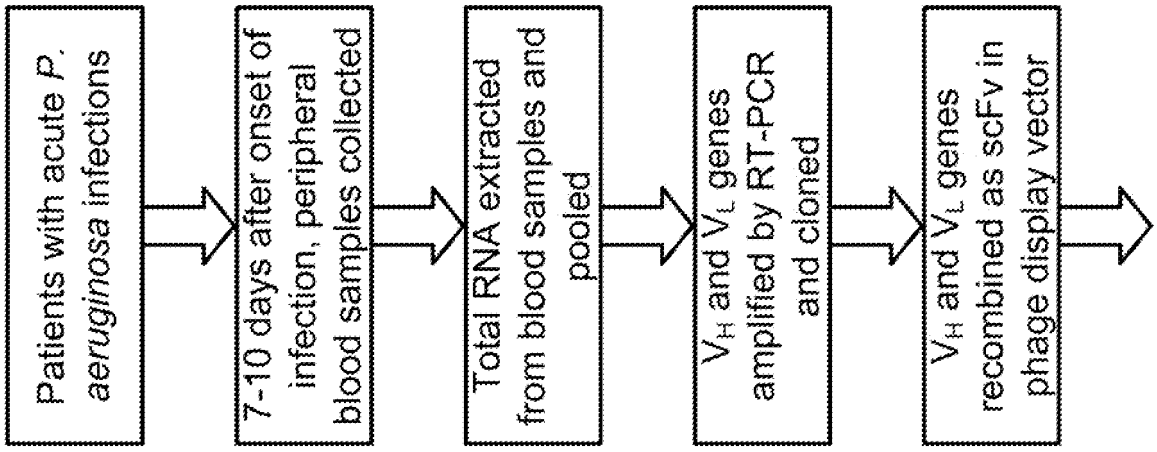
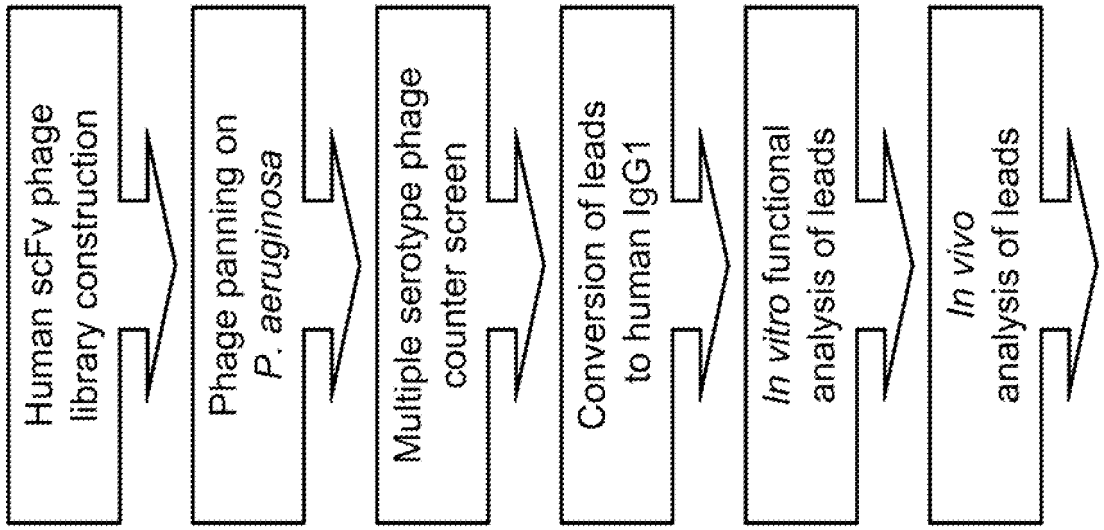

Patients with acute P. aeruginosa infections
7-10 days after onset of infection, peripheral blood samples collected
Total RNA extracted from blood samples and pooled
V_H and V_L genes amplified by RT-PCR and cloned
V_H and V_L genes recombined as scFv in phage display vector

1B.


Human scFv phage library construction
Phage panning on P. aeruginosa
Multiple serotype phage counter screen
Conversion of leads to human IgG1
In vitro functional analysis of leads
In vivo analysis of leads

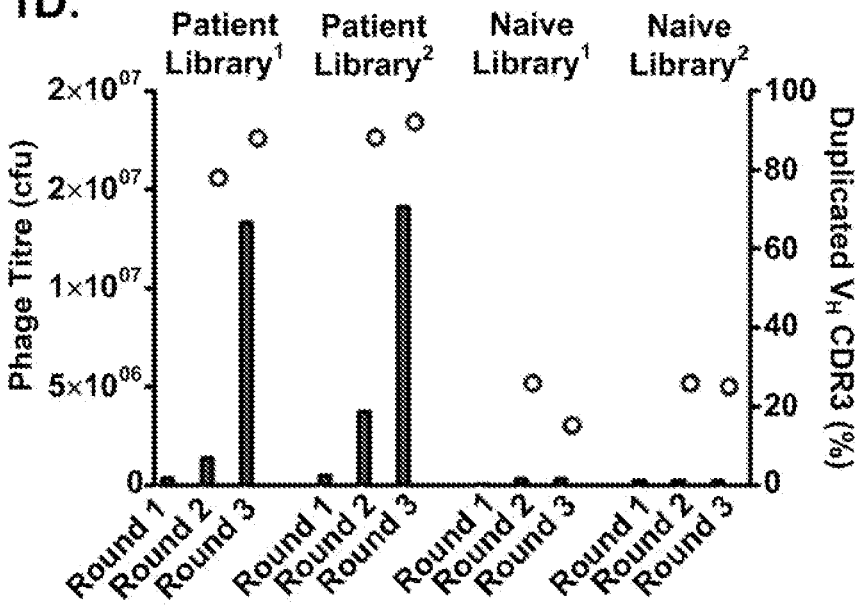
1A.

FIG. 1

1C.

Patient Library Data	
V_H library size:	5.2×10^8
V_K library size:	1.6×10^7
V_λ library size:	3.5×10^7
scFv library size:	5.4×10^8
Full length, in-frame scFv:	279/352 (79%)
Unique V_HCDR3 sequences:	234/279 (84%)

1D.



1E.

	P. aeruginosa 3039	*P. aeruginosa* 3064	*P. aeruginosa* PA01	*P. aeruginosa* 33356	*P. aeruginosa* 33359	*E. coli* TG1	BSA
CAM-003 scFv	1.28	1.46	1.22	1.06	1.31	0.09	0.07
CAM-004 scFv	0.91	1.15	0.84	0.82	1.03	0.06	0.08
CAM-005 scFv	0.33	0.55	0.27	0.23	0.33	0.07	0.08
CAM-006 scFv	0.51	0.65	0.47	0.45	0.62	0.05	0.06
CAM-007 scFv	0.99	1.12	0.77	0.76	1.06	0.05	0.06
CAM-008 scFv	0.17	0.25	0.13	0.16	0.17	0.07	0.06
CAM-009 scFv	0.99	1.15	0.88	0.87	1.02	0.08	0.07
CAM-010 scFv	0.74	1.03	0.66	0.63	0.91	0.07	0.07
Irrelevant scFv	0.06	0.06	0.07	0.06	0.06	0.07	0.05

FIG. 1

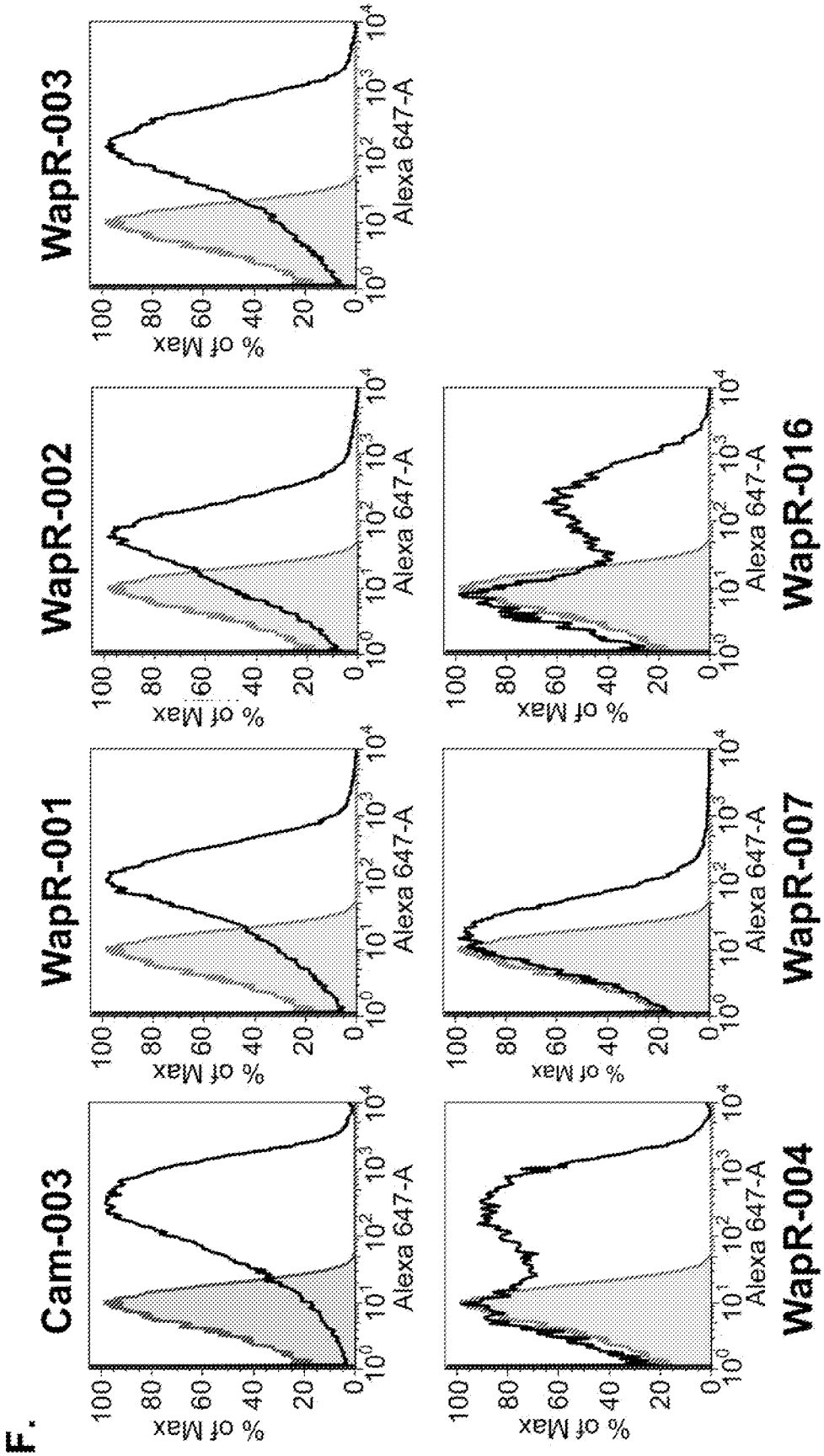

1F.
Cam-003
WapR-001
WapR-002
WapR-003
WapR-004
WapR-007
WapR-016
% of Max
Alexa 647-A
Human IgG Ctrl (30-µg/mL)
mAb (30-µg/mL)

FIG. 1

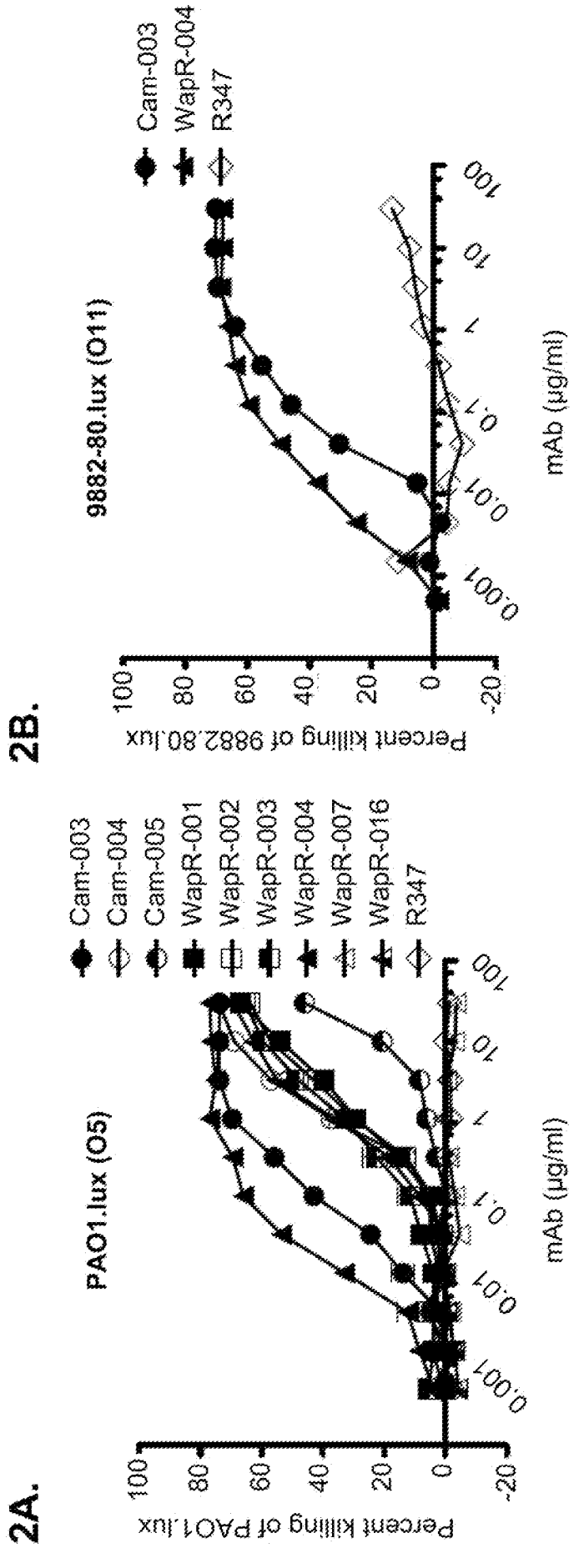

2A.
PAO1.lux (O5)
Cam-003
Cam-004
Cam-005
WapR-001
WapR-002
WapR-003
WapR-004
WapR-007
WapR-016
R347
Percent killing of PAO1.lux
100
80
60
40
20
0
-20
100
10
1
0.1
0.01
0.001
mAb (µg/ml)
2B.
9882-80.lux (O11)
Cam-003
WapR-004
R347
Percent killing of 9882.80.lux
100
80
60
40
20
0
-20
100
10
1
0.1
0.01
0.001
mAb (µg/ml)

FIG. 2

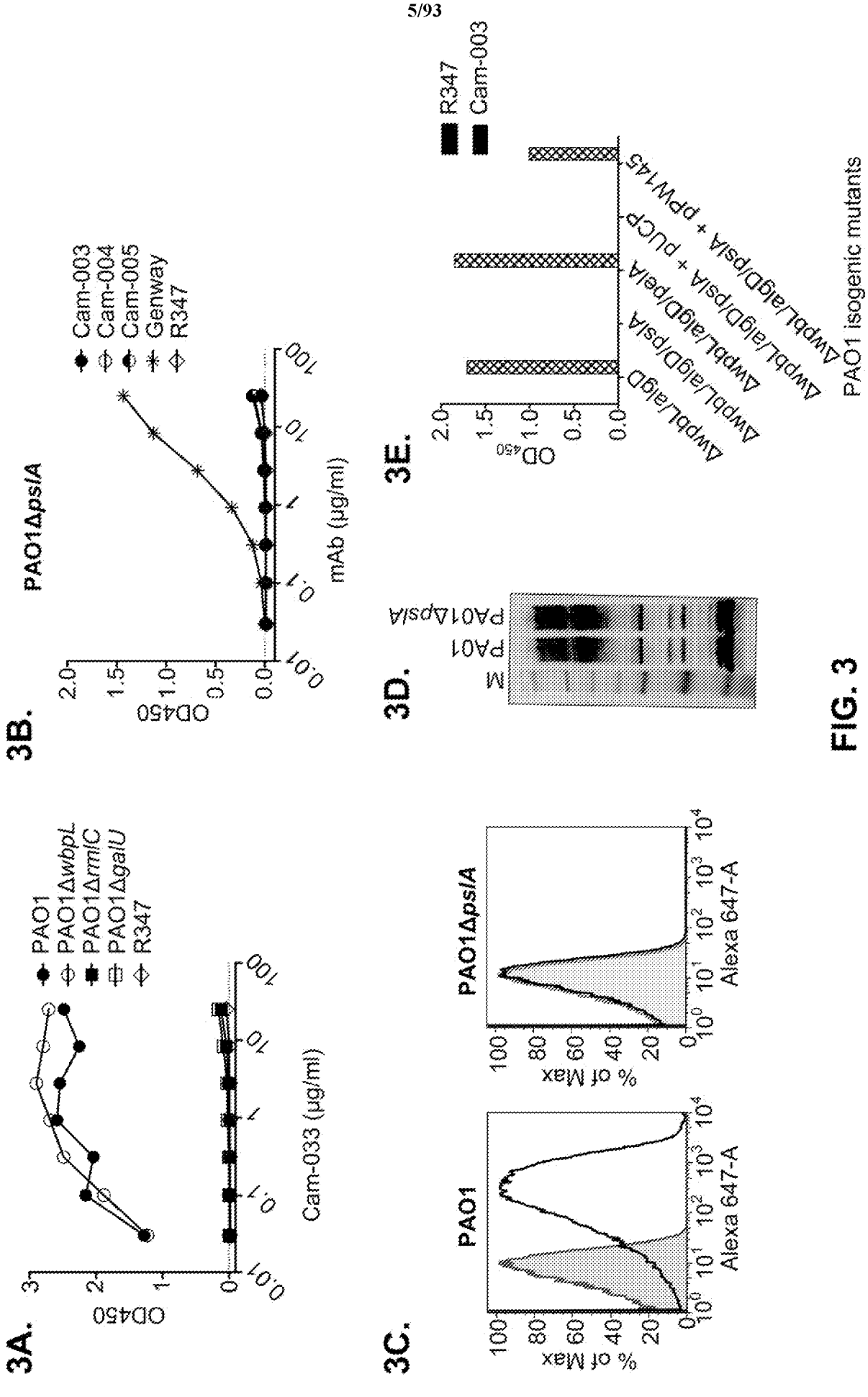

3A.
PAO1
PAO1ΔwbpL
PAO1ΔrmlC
PAO1ΔgalU
R347
OD450
Cam-033 (μg/ml)
3B.
PAO1ΔpslA
Cam-003
Cam-004
Cam-005
Genway
R347
OD450
mAb (μg/ml)
3C.
PAO1
PAO1ΔpslA
% of Max
Alexa 647-A
3D.
M
PA01
PA01ΔpslA
3E.
R347
Cam-003
OD450
ΔwbpL/algD
ΔwbpL/algD/pslA
ΔwbpL/algD/pelA
ΔwbpL/algD/pslA + pUCP
ΔwbpL/algD/pslA + pPW145
PAO1 isogenic mutants

FIG. 3

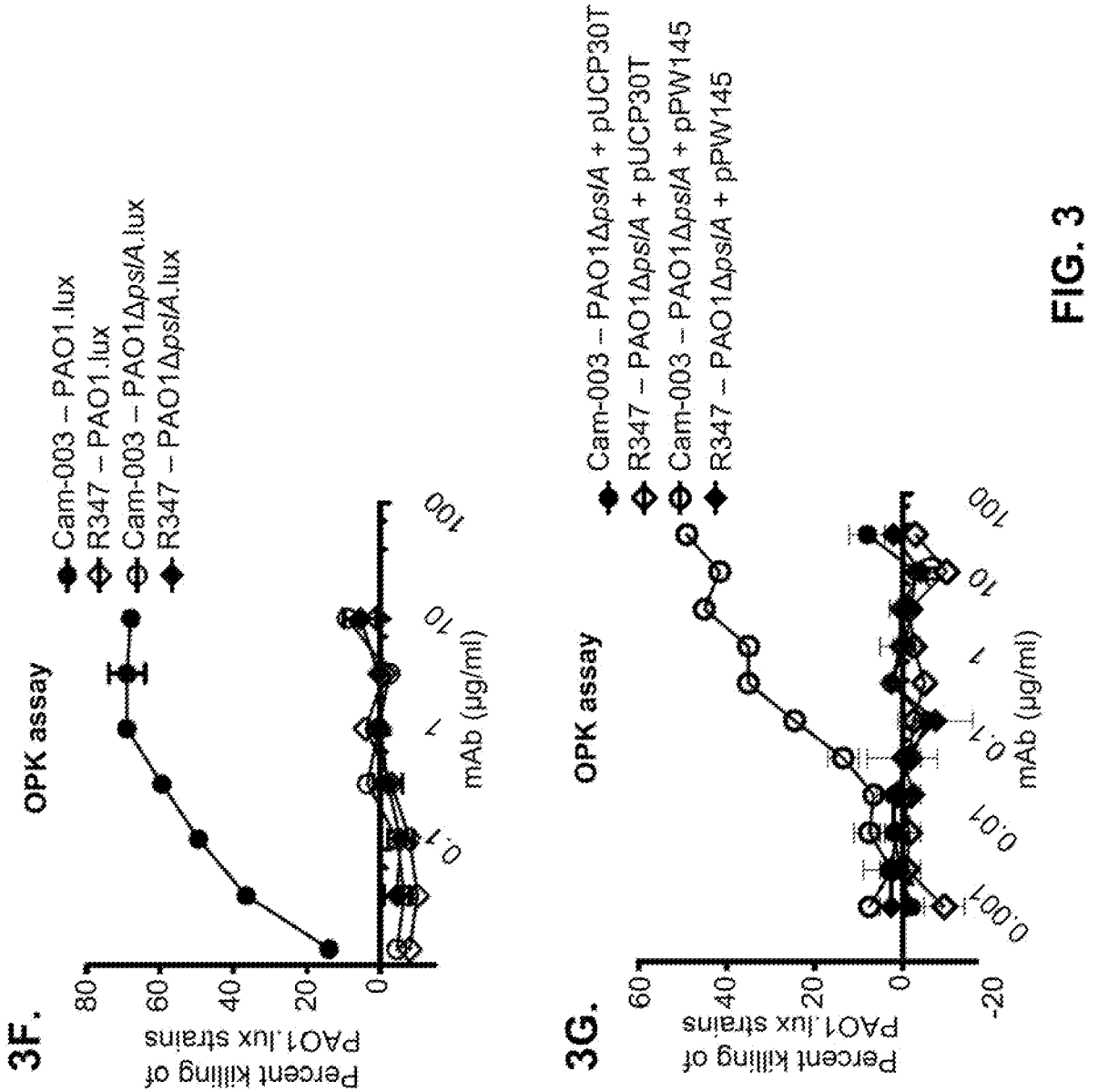

3F.
OPK assay
Cam-003 – PAO1.lux
R347 – PAO1.lux
Cam-003 – PAO1ΔpslA.lux
R347 – PAO1ΔpslA.lux
Percent killing of PAO1.lux strains
mAb (µg/ml)
0
20
40
60
80
0.1
1
10
100
3G.
OPK assay
Cam-003 – PAO1ΔpslA + pUCP30T
R347 – PAO1ΔpslA + pUCP30T
Cam-003 – PAO1ΔpslA + pPW145
R347 – PAO1ΔpslA + pPW145
Percent killing of PAO1.lux strains
mAb (µg/ml)
-20
0
20
40
60
0.001
0.01
0.1
1
10
100

FIG. 3

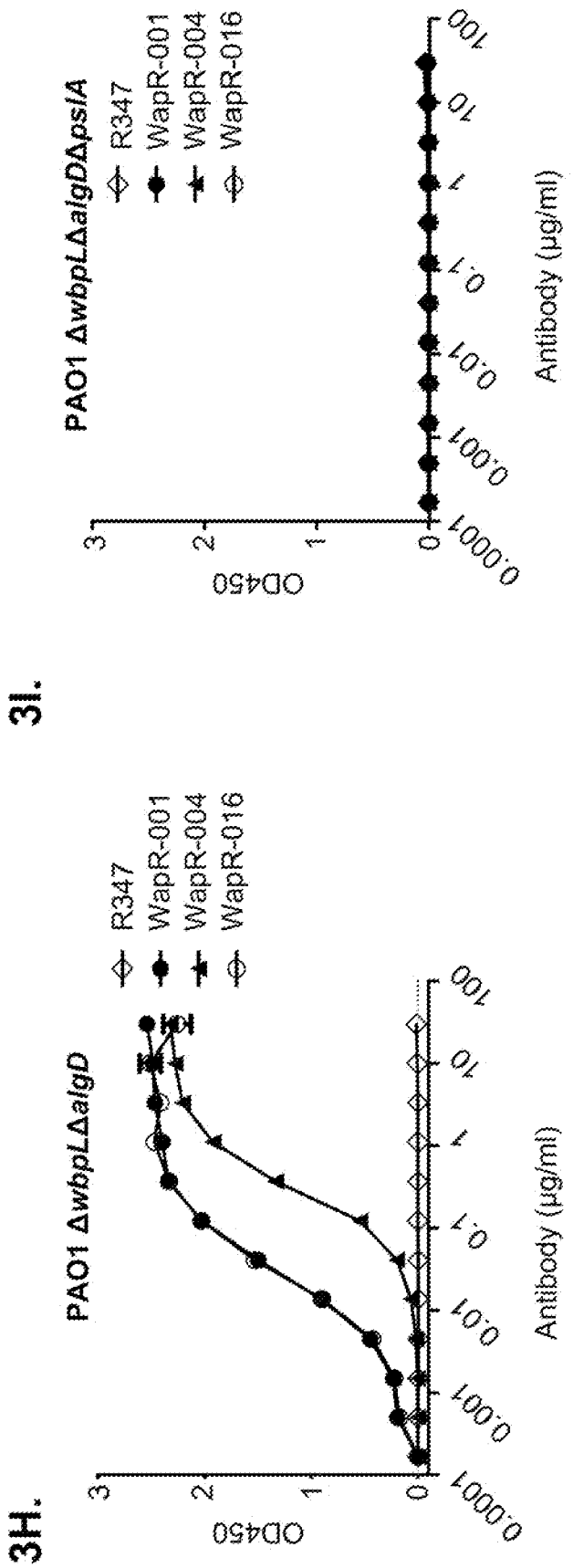

3I.
PAO1 ΔwbpLΔalgDΔpslA
R347
WapR-001
WapR-004
WapR-016
OD450
Antibody (µg/ml)
3H.
PAO1 ΔwbpLΔalgD
R347
WapR-001
WapR-004
WapR-016
OD450
Antibody (µg/ml)

FIG. 3

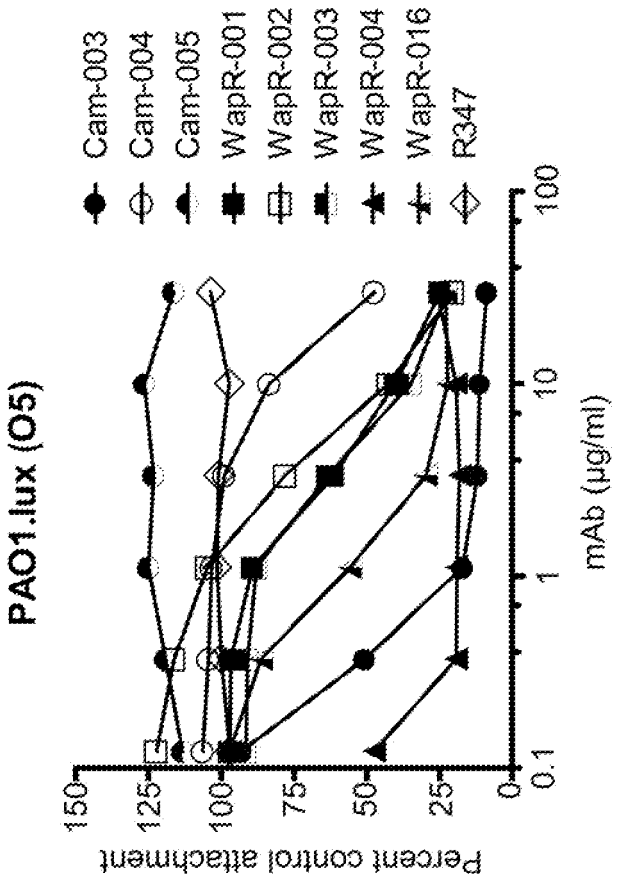

PAO1.lux (O5)
Cam-003
Cam-004
Cam-005
WapR-001
WapR-002
WapR-003
WapR-004
WapR-016
R347
Percent control attachment
150
125
100
75
50
25
0
0.1
1
10
100
mAb (µg/ml)

FIG. 4

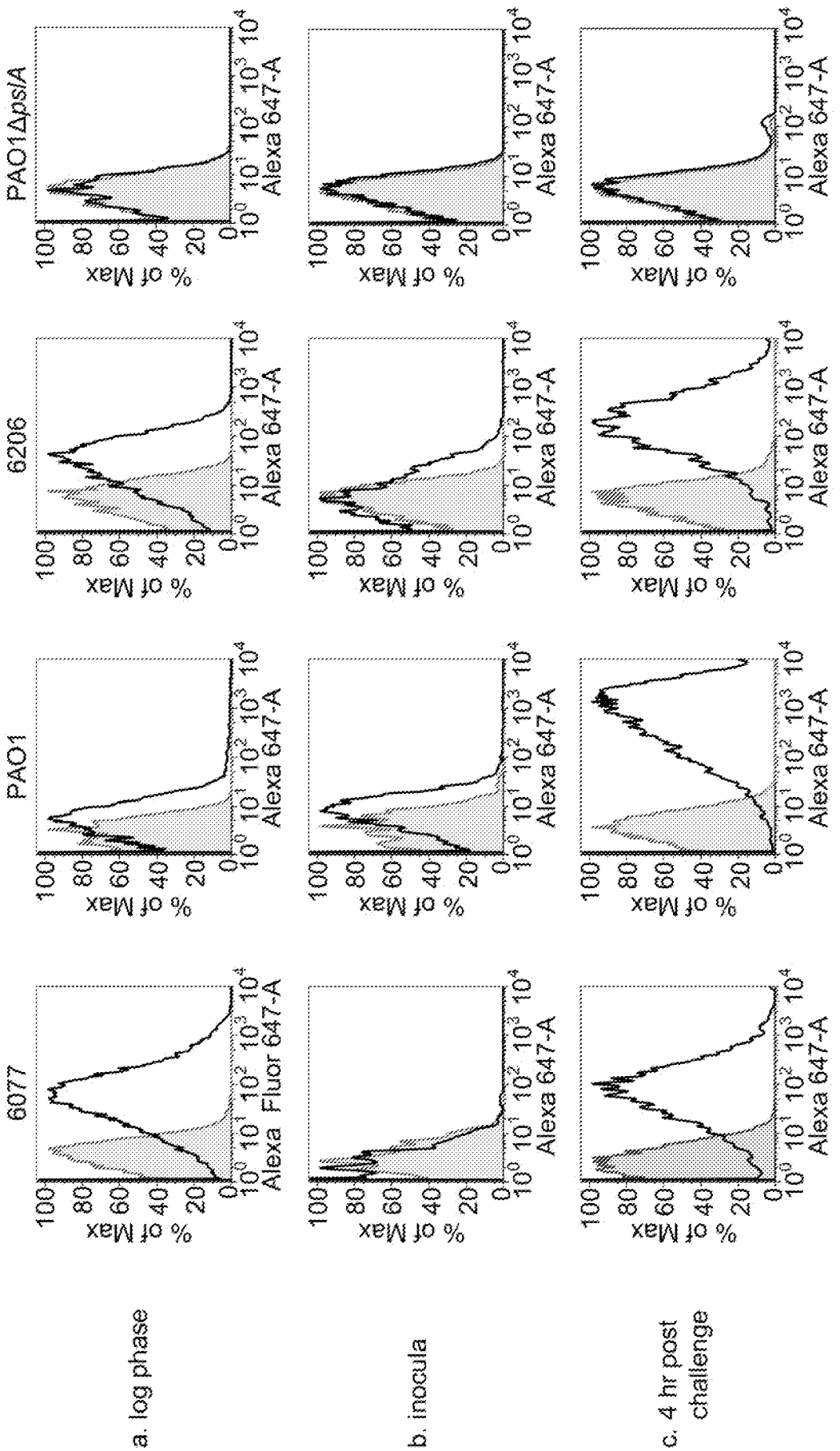

6077
PAO1
6206
PAO1Δpsl A
a. log phase
b. inocula
c. 4 hr post challenge
% of Max
Alexa Fluor 647-A
Alexa 647-A
Human IgG Control (30 µg/mL)
Cam-003 mAb (30 µg/mL)

FIG. 5

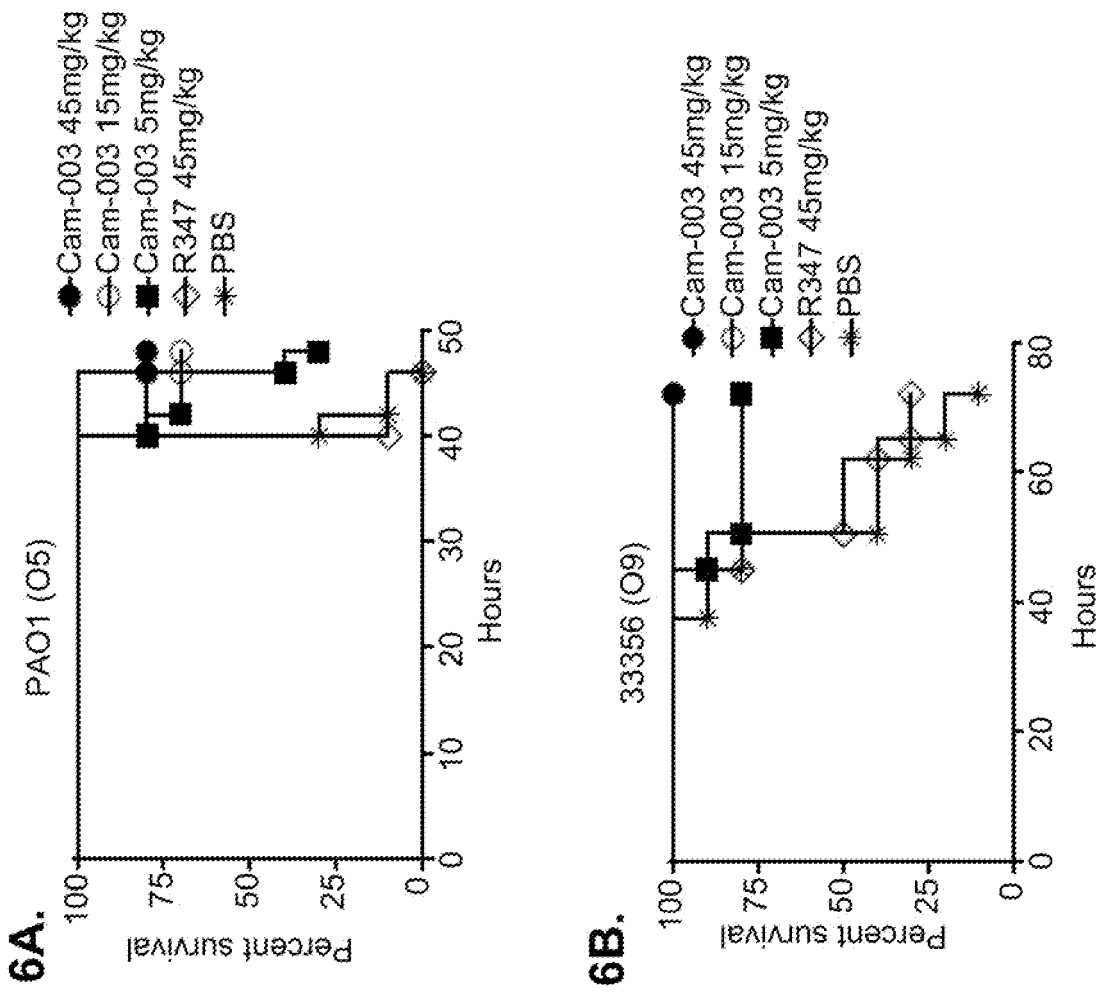

6A.
PAO1 (O5)
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
R347 45mg/kg
PBS
Percent survival
Hours
0
25
50
75
100
0
10
20
30
40
50
6B.
33356 (O9)
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
R347 45mg/kg
PBS
Percent survival
Hours
0
25
50
75
100
0
20
40
60
80

FIG. 6

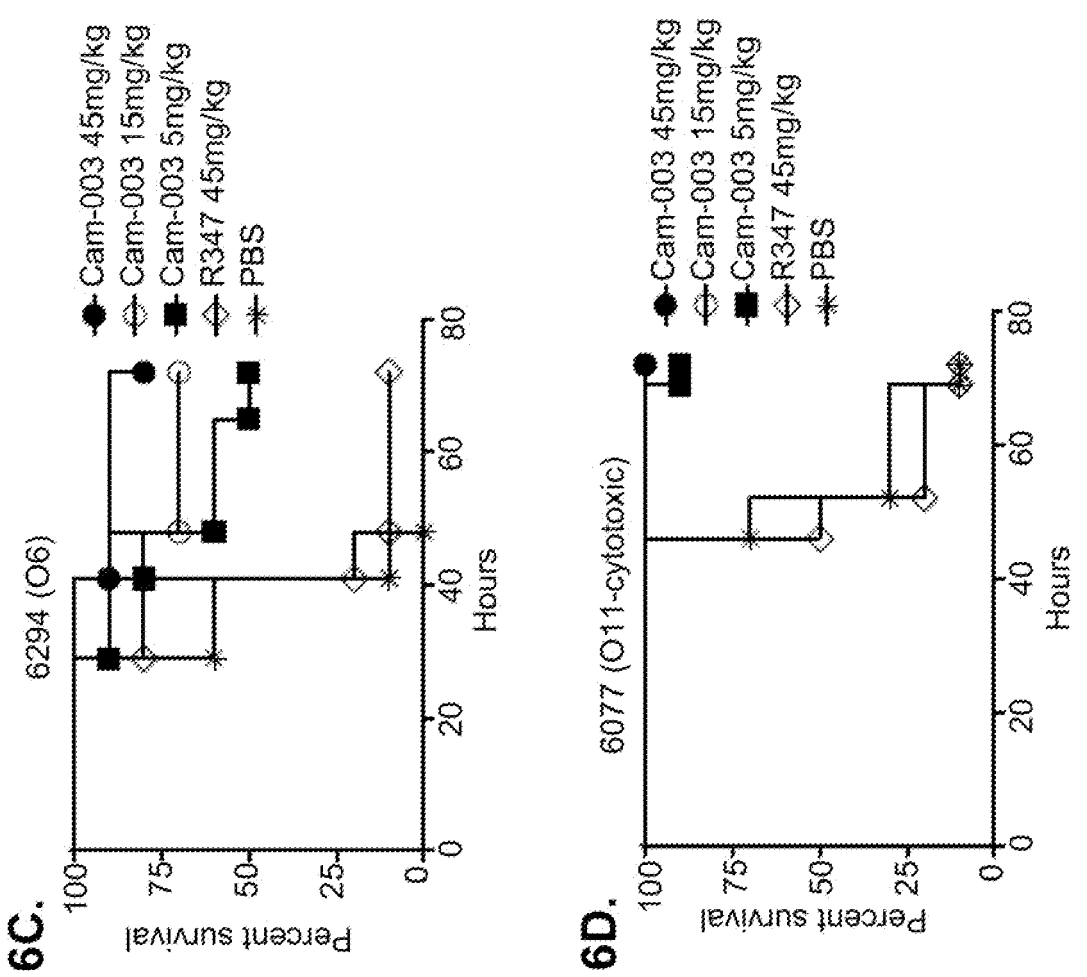

6C.
6294 (O6)
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
R347 45mg/kg
PBS
Percent survival
Hours
0
25
50
75
100
0
20
40
60
80
6D.
6077 (O11-cytotoxic)
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
R347 45mg/kg
PBS
Percent survival
Hours
0
25
50
75
100
0
20
40
60
80

FIG. 6

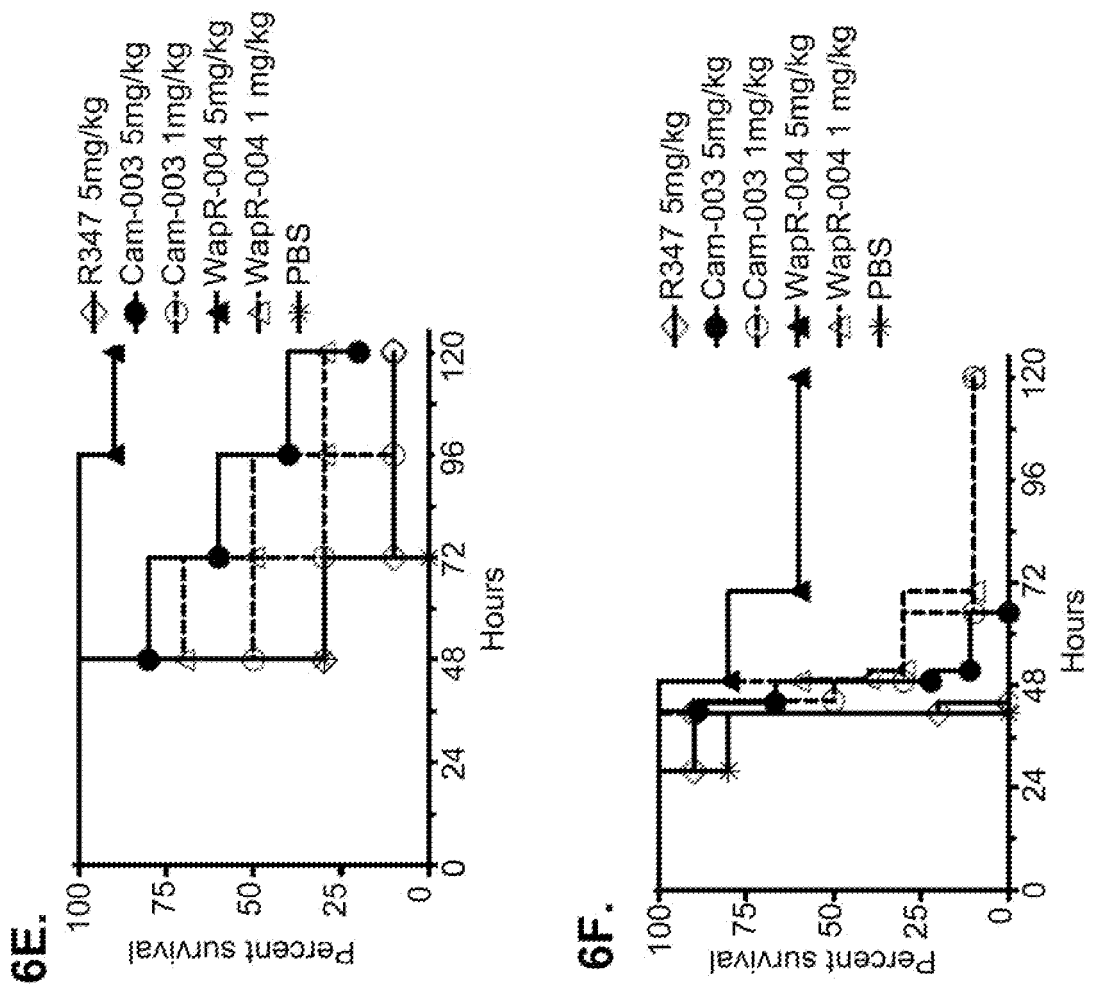

6E.
R347 5mg/kg
Cam-003 5mg/kg
Cam-003 1mg/kg
WapR-004 5mg/kg
WapR-004 1 mg/kg
PBS
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours
6F.
R347 5mg/kg
Cam-003 5mg/kg
Cam-003 1mg/kg
WapR-004 5mg/kg
WapR-004 1 mg/kg
PBS
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours

FIG. 6

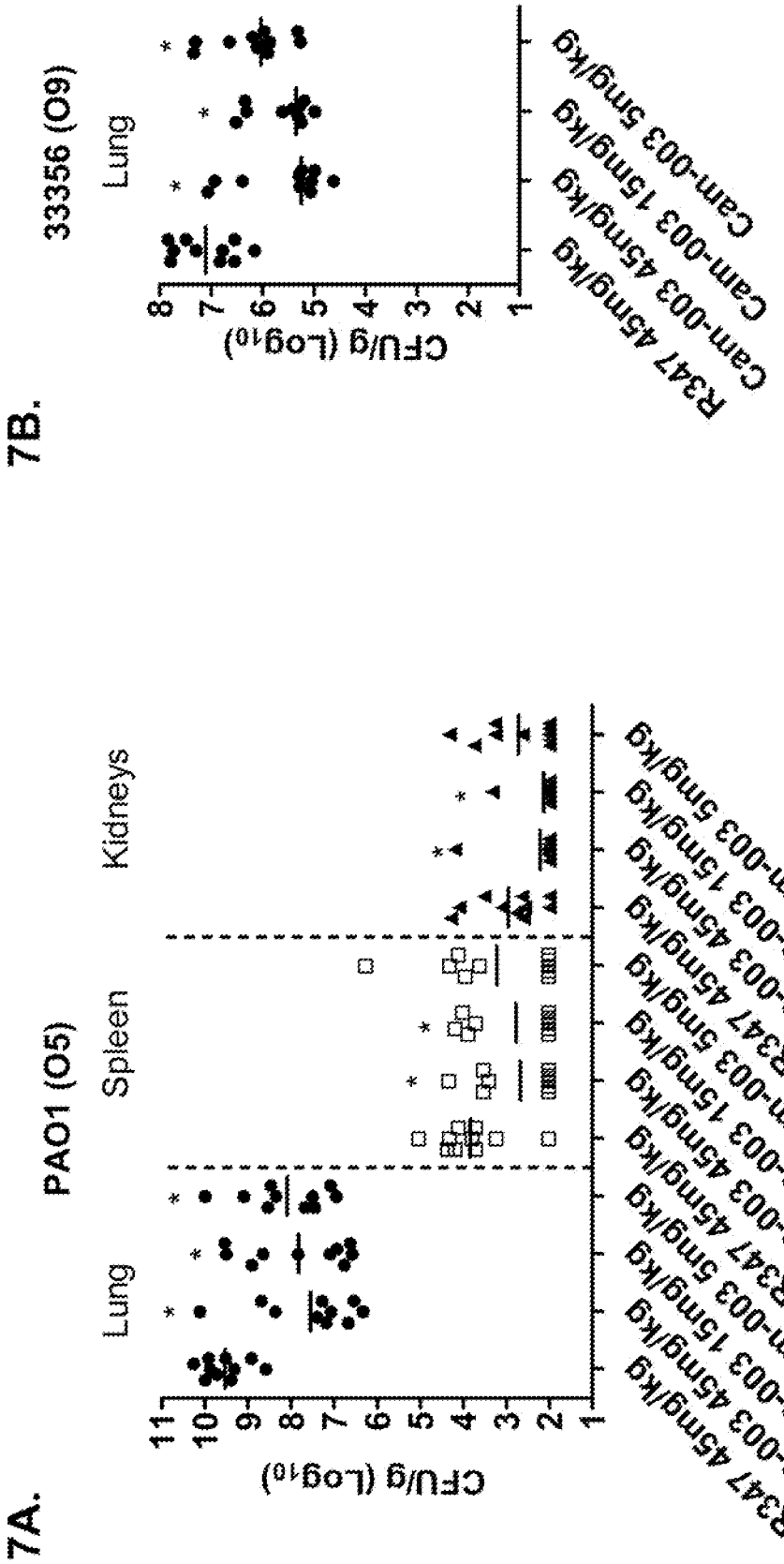

7A.
PAO1 (O5)
Lung
Spleen
Kidneys
CFU/g (Log10)
11
10
9
8
7
6
5
4
3
2
1
R347 45mg/kg
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
R347 45mg/kg
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
R347 45mg/kg
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg
7B.
33356 (O9)
Lung
CFU/g (Log10)
8
7
6
5
4
3
2
1
R347 45mg/kg
Cam-003 45mg/kg
Cam-003 15mg/kg
Cam-003 5mg/kg

FIG. 7

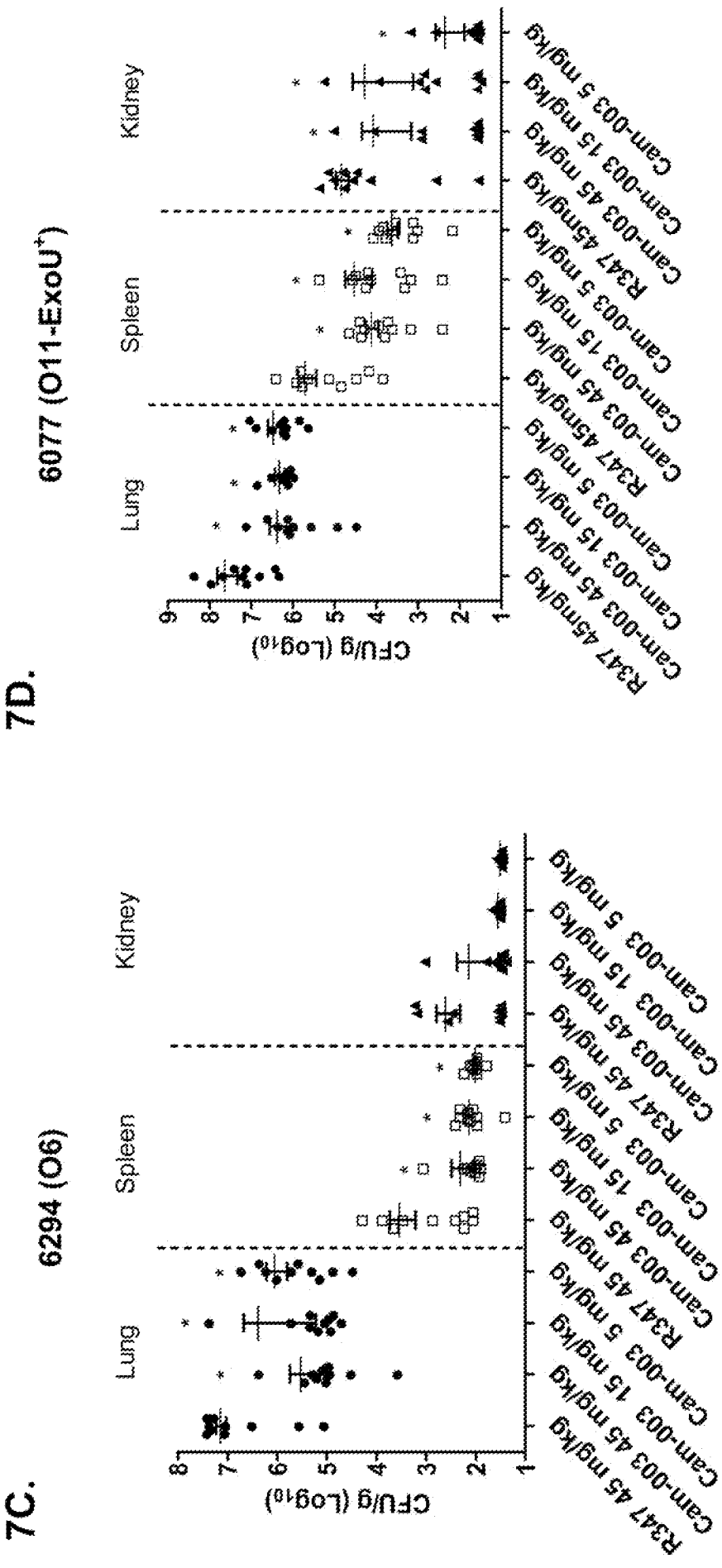
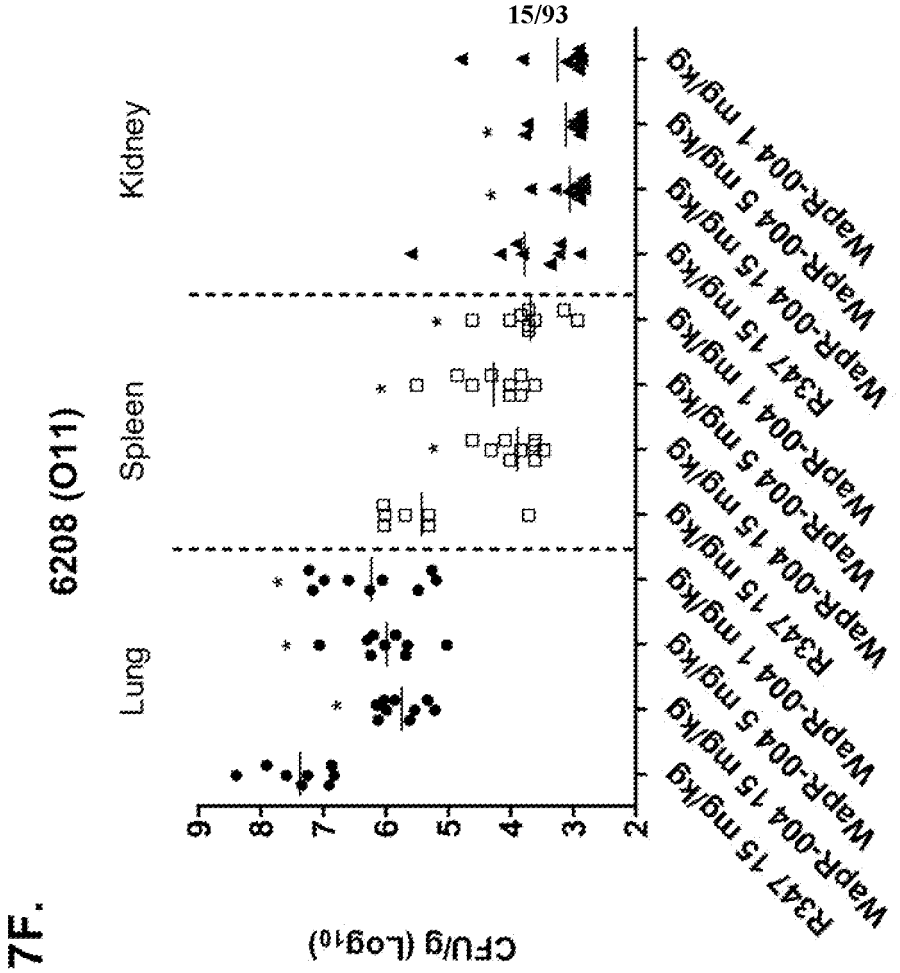

7C.
6294 (O6)
Lung
Spleen
Kidney
CFU/g (Log10)
8
7
6
5
4
3
2
1
R347 45mg/kg
Cam-003 45 mg/kg
Cam-003 15 mg/kg
Cam-003 5 mg/kg
R347 45 mg/kg
Cam-003 45 mg/kg
Cam-003 15 mg/kg
Cam-003 5 mg/kg
R347 45mg/kg
Cam-003 45 mg/kg
Cam-003 15 mg/kg
Cam-003 5 mg/kg
7D.
6077 (O11-ExoU+)
Lung
Spleen
Kidney
CFU/g (Log10)
9
8
7
6
5
4
3
2
1
R347 45mg/kg
Cam-003 45 mg/kg
Cam-003 15 mg/kg
Cam-003 5 mg/kg
R347 45mg/kg
Cam-003 45 mg/kg
Cam-003 15 mg/kg
Cam-003 5 mg/kg
R347 45mg/kg
Cam-003 45 mg/kg
Cam-003 15 mg/kg
Cam-003 5 mg/kg

FIG. 7


7F.
6208 (O11)
Kidney
Spleen
Lung
CFU/g (Log10)
9
8
7
6
5
4
3
2
WaprR-004 1 mg/kg
WaprR-004 5 mg/kg
WaprR-004 15 mg/kg
R347 15 mg/kg
WaprR-004 1 mg/kg
WaprR-004 5 mg/kg
WaprR-004 15 mg/kg
R347 15 mg/kg
WaprR-004 1 mg/kg
WaprR-004 5 mg/kg
WaprR-004 15 mg/kg
R347 15 mg/kg

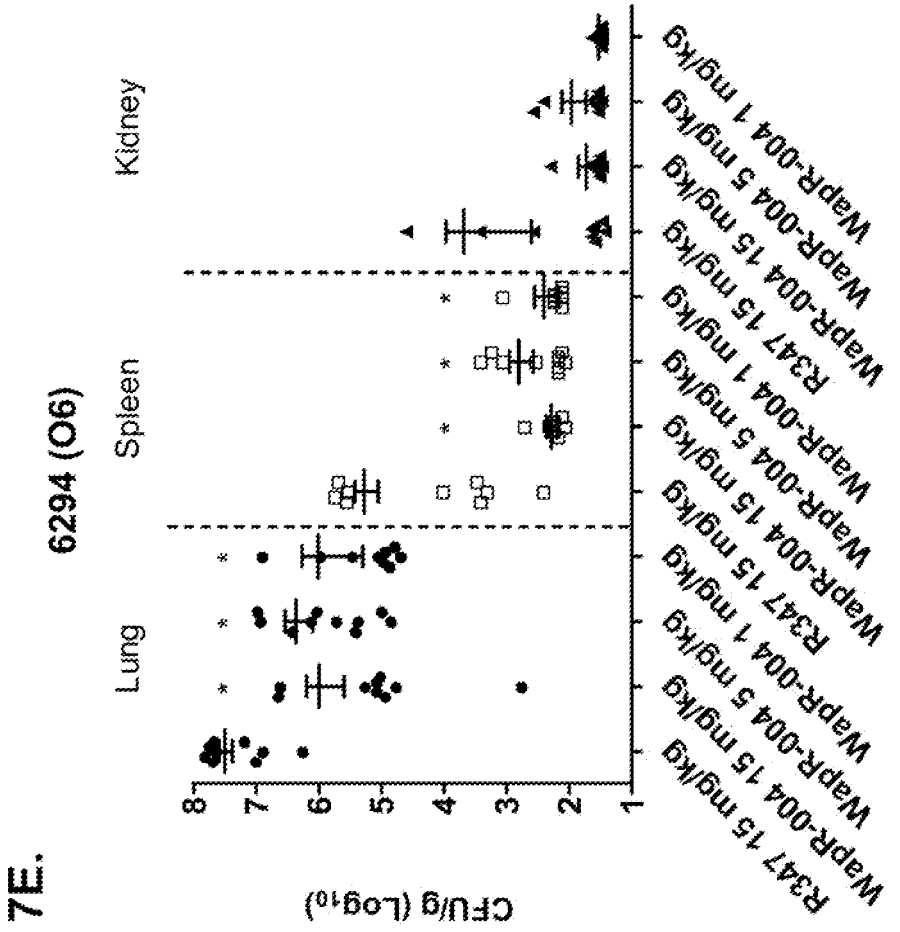

7E.
6294 (O6)
Kidney
Spleen
Lung
CFU/g (Log10)
8
7
6
5
4
3
2
1
WaprR-004 1 mg/kg
WaprR-004 5 mg/kg
WaprR-004 15 mg/kg
R347 15 mg/kg
WaprR-004 1 mg/kg
WaprR-004 5 mg/kg
WaprR-004 15 mg/kg
R347 15 mg/kg
WaprR-004 1 mg/kg
WaprR-004 5 mg/kg
WaprR-004 15 mg/kg
R347 15 mg/kg

FIG. 7

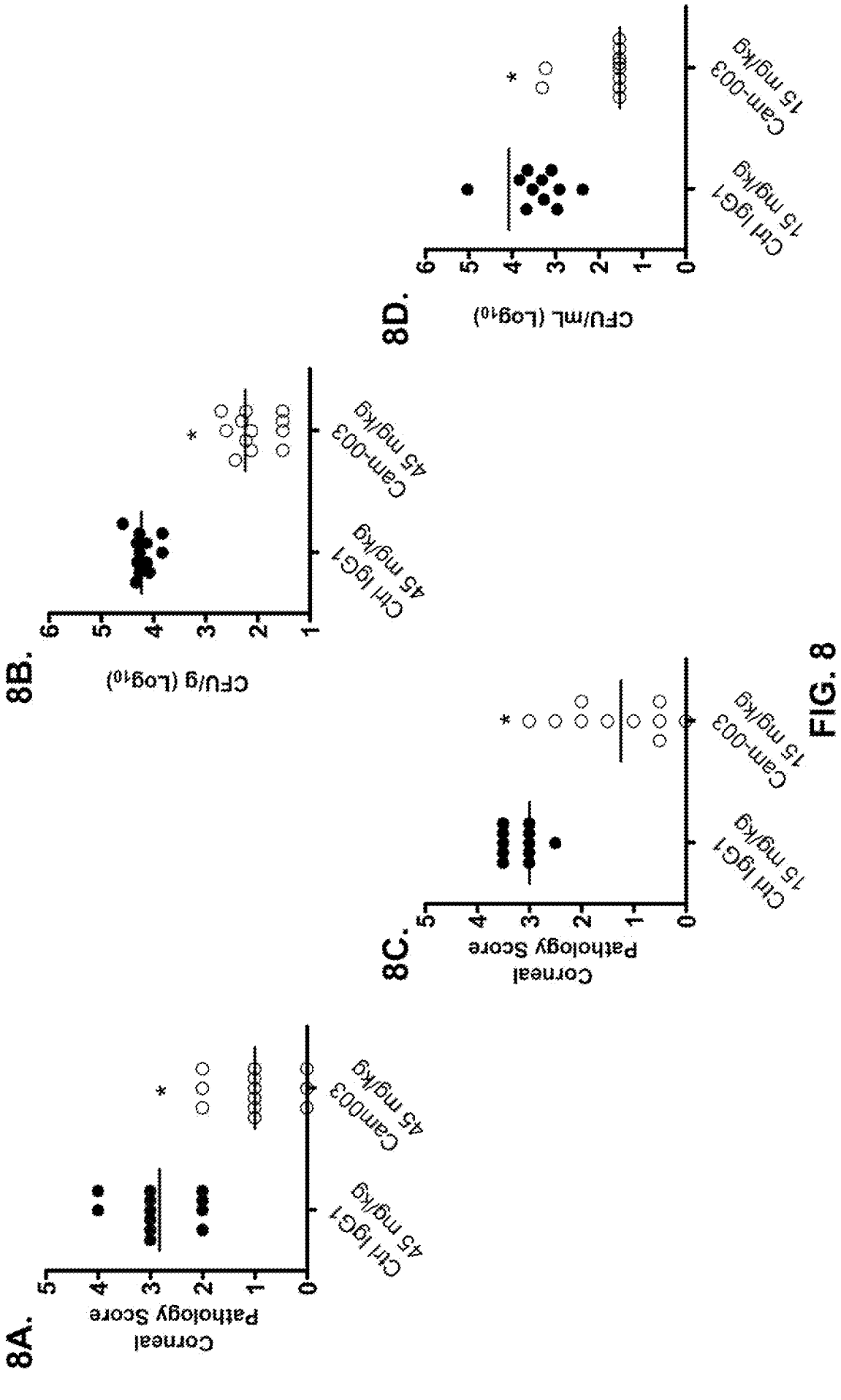

8A.
Corneal Pathology Score
Ctrl IgG1 45 mg/kg
Cam003 45 mg/kg
8B.
CFU/g (Log10)
Ctrl IgG1 45 mg/kg
Cam-003 45 mg/kg
8C.
Corneal Pathology Score
Ctrl IgG1 15 mg/kg
Cam-003 15 mg/kg
8D.
CFU/mL (Log10)
Ctrl IgG1 15 mg/kg
Cam-003 15 mg/kg

FIG. 8

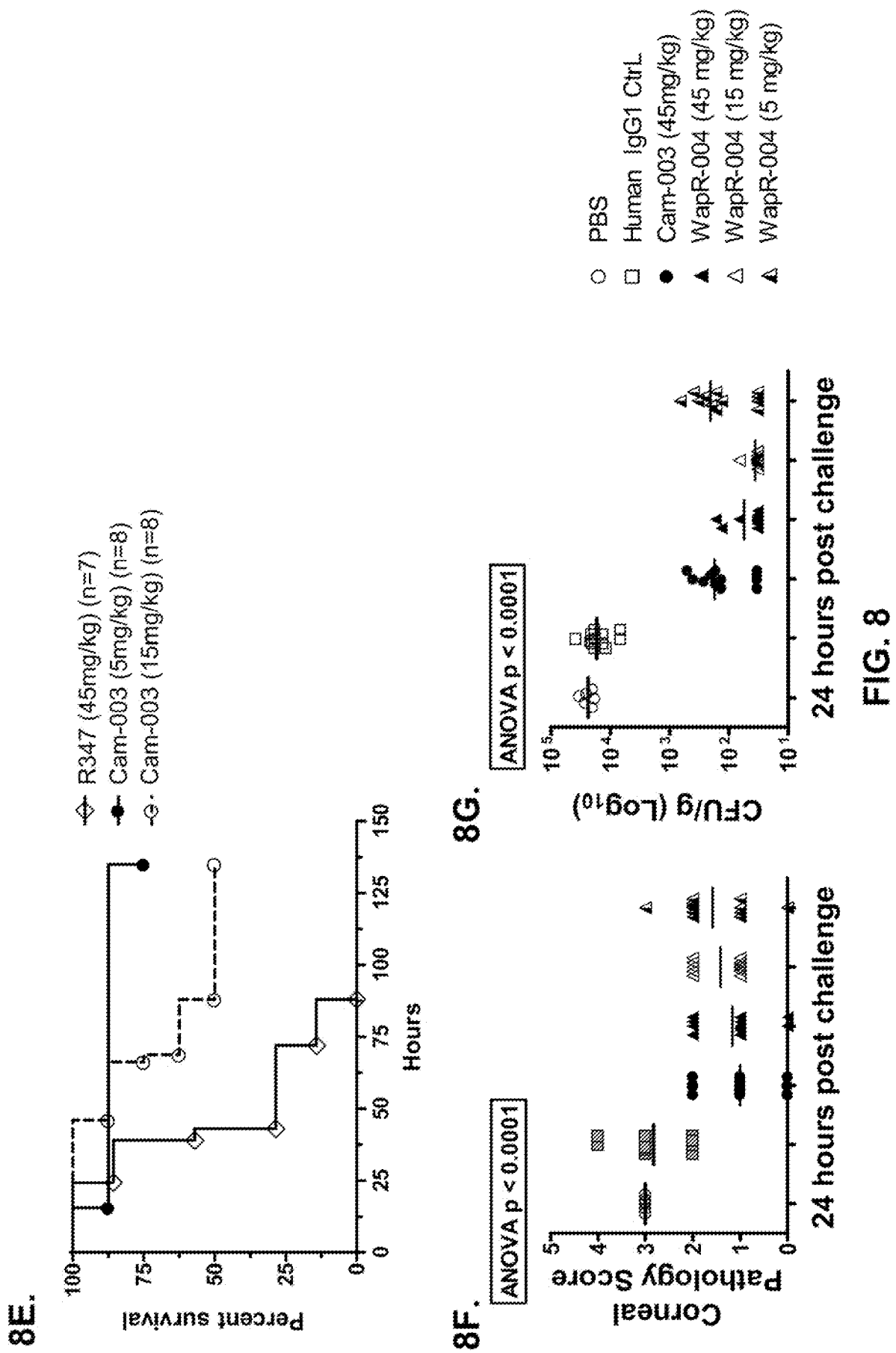

8E.
R347 (45mg/kg) (n=7)
Cam-003 (5mg/kg) (n=8)
Cam-003 (15mg/kg) (n=8)
Percent survival
100
75
50
25
0
0
25
50
75
100
125
150
Hours
8F.
ANOVA p < 0.0001
Corneal Pathology Score
5
4
3
2
1
0
24 hours post challenge
8G.
ANOVA p < 0.0001
CFU/g (Log10)
10^5
10^4
10^3
10^2
10^1
24 hours post challenge
PBS
Human IgG1 CtrL
Cam-003 (45mg/kg)
WapR-004 (45 mg/kg)
WapR-004 (15 mg/kg)
WapR-004 (5 mg/kg)

FIG. 8

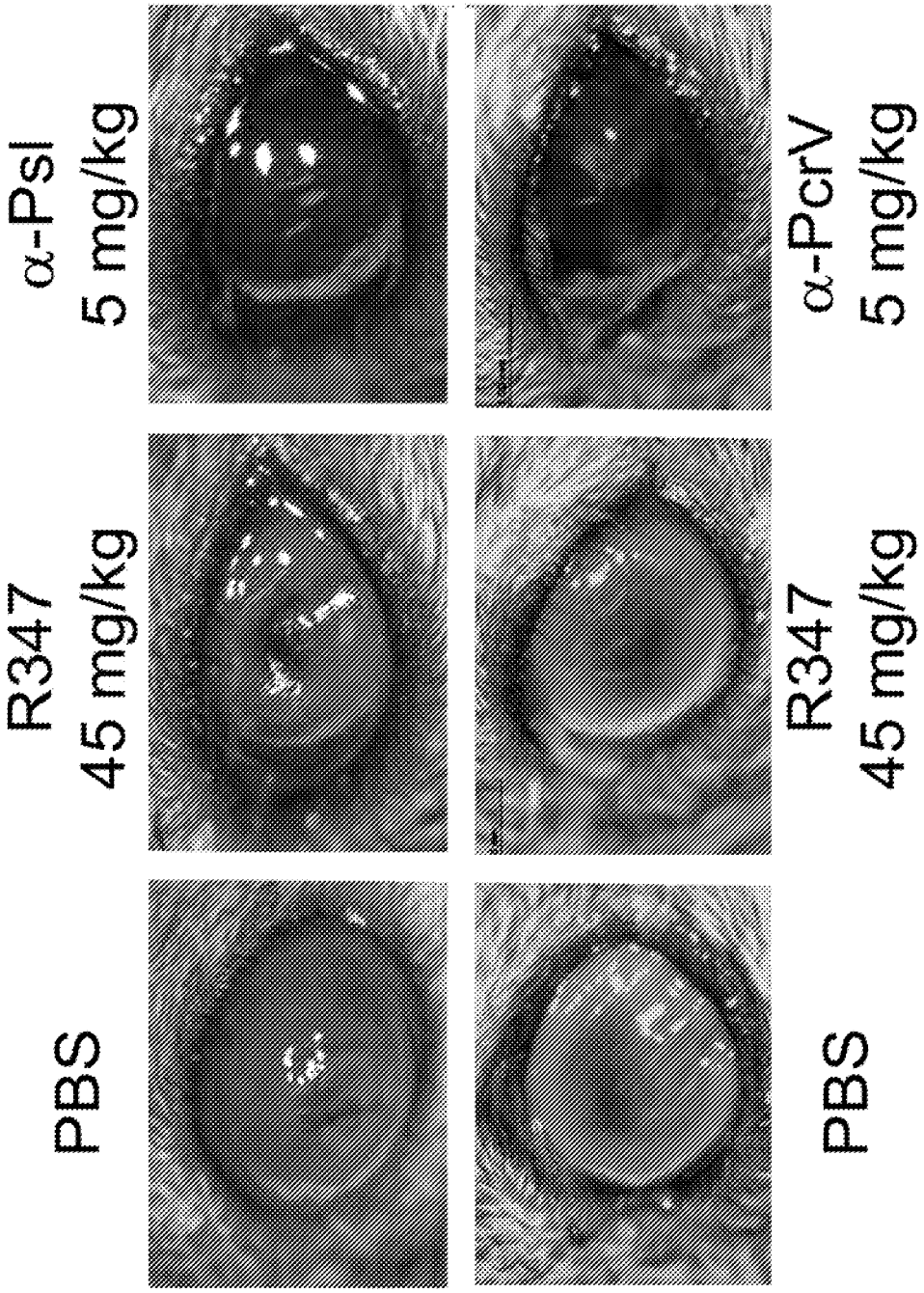


FIG. 8

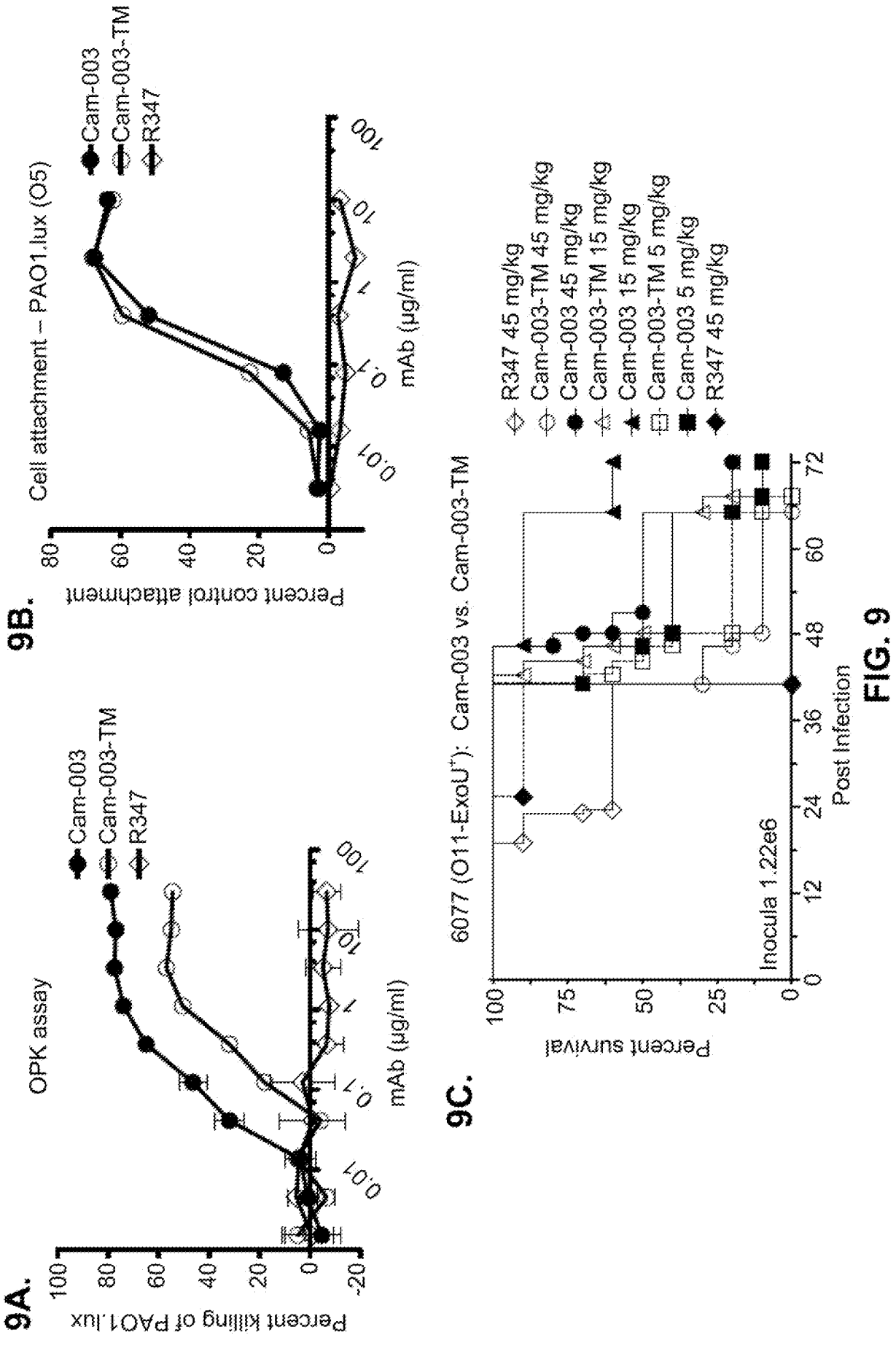

9A.
OPK assay
Cam-003
Cam-003-TM
R347
Percent killing of PAO1.lux
mAb (µg/ml)
9B.
Cell attachment – PAO1.lux (O5)
Cam-003
Cam-003-TM
R347
Percent control attachment
mAb (µg/ml)
9C.
6077 (O11-ExoU+): Cam-003 vs. Cam-003-TM
R347 45 mg/kg
Cam-003-TM 45 mg/kg
Cam-003 45 mg/kg
Cam-003-TM 15 mg/kg
Cam-003 15 mg/kg
Cam-003-TM 5 mg/kg
Cam-003 5 mg/kg
R347 45 mg/kg
Inocula 1.22e6
Percent survival
Post Infection

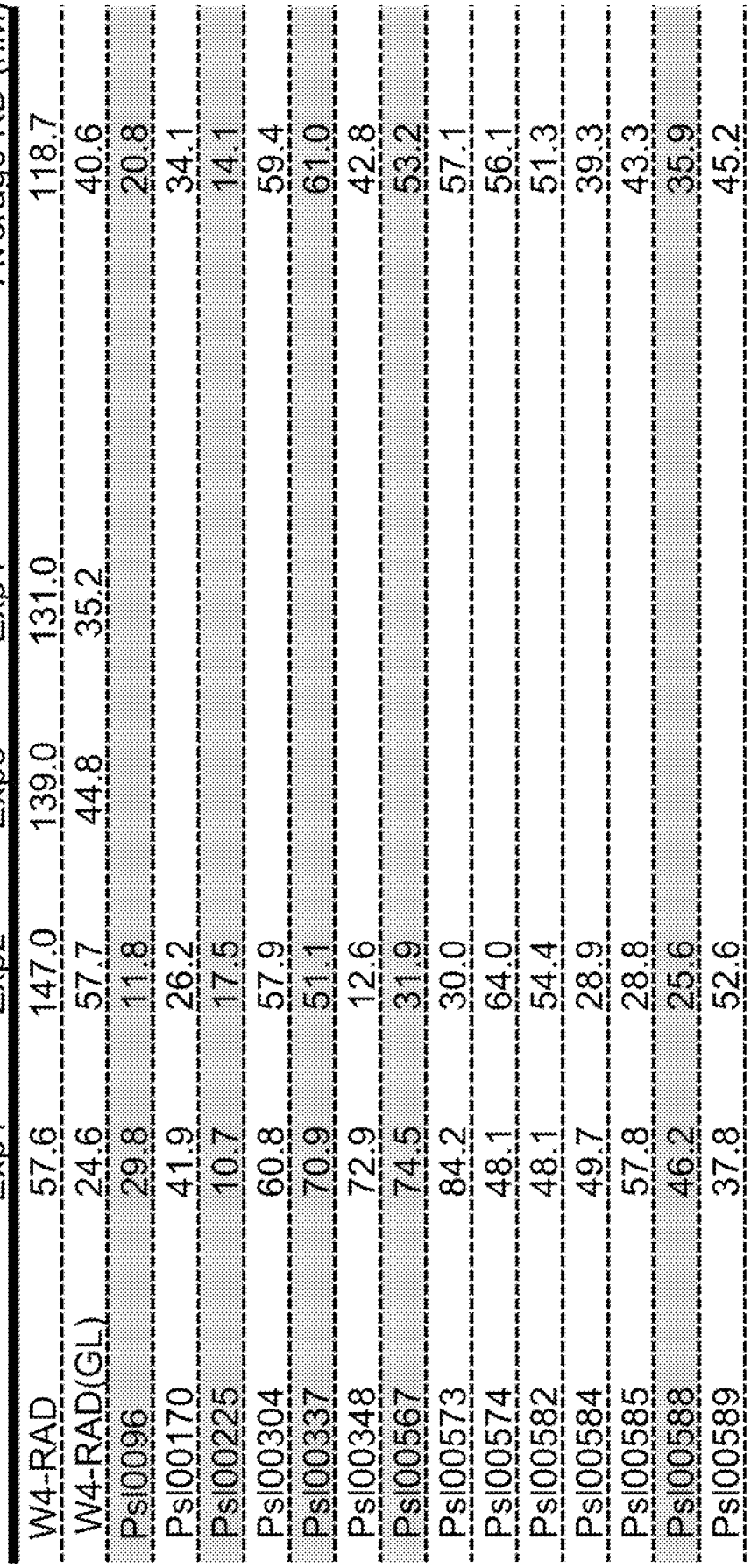
FIG. 9

Epitope	mAb	K_D(nM)	Cell attachment max. inhibition (µg/ml)	OPK EC50 (µg/ml)
Class 1	WapR-004	118.00	0.3	0.0027
	Cam-003	144.00	1.0	0.0220
	Cam-004	2100.00	>30.0	0.2771
	Cam-005	8400.00	NA	NA
Class 2	WapR-001	0.84	30.0	0.3100
	WapR-003	12.20	30.0	0.2778
	WapR-002	12.60	ND	0.3960
Class 3	WapR-016	75.00	ND	0.2417

FIG. 10A

scFV-Fc	k_{off}	k_{on}	K_D (nM)	OPK EC50
W4 RAD	1.30E-02	5.39E+04	241	0.0068
W4-M1	8.18E-02	1.69E+05	483	0.0475
W4-M7	1.28E-02	6.49E+04	196	0.0060
W4-M8	1.90E-02	1.54E+05	124	0.0056
W4-M9	1.66E-02	1.98E+05	84	0.0167
W4-M11	8.50E-03	1.25E+05	68	0.0045
W4-M12	9.10E-03	1.26E+05	72	0.0085
W4-M17	1.91E-01	9.60E+04	1990	1.3935

FIG. 10B



	Exp1	Exp2	Exp3	Exp4	Average KD (nM)
W4-RAD	57.6	147.0	139.0	131.0	118.7
W4-RAD(GL)	24.6	57.7	44.8	35.2	40.6
PsI0096	29.8	11.8			20.8
PsI00170	41.9	26.2			34.1
PsI00225	10.7	17.5			14.1
PsI00304	60.8	57.9			59.4
PsI00337	70.9	51.1			61.0
PsI00348	72.9	12.6			42.8
PsI00567	74.5	31.9			53.2
PsI00573	84.2	30.0			57.1
PsI00574	48.1	64.0			56.1
PsI00582	48.1	54.4			51.3
PsI00584	49.7	28.9			39.3
PsI00585	57.8	28.8			43.3
PsI00588	46.2	25.6			35.9
PsI00589	37.8	52.6			45.2

FIG. 10C

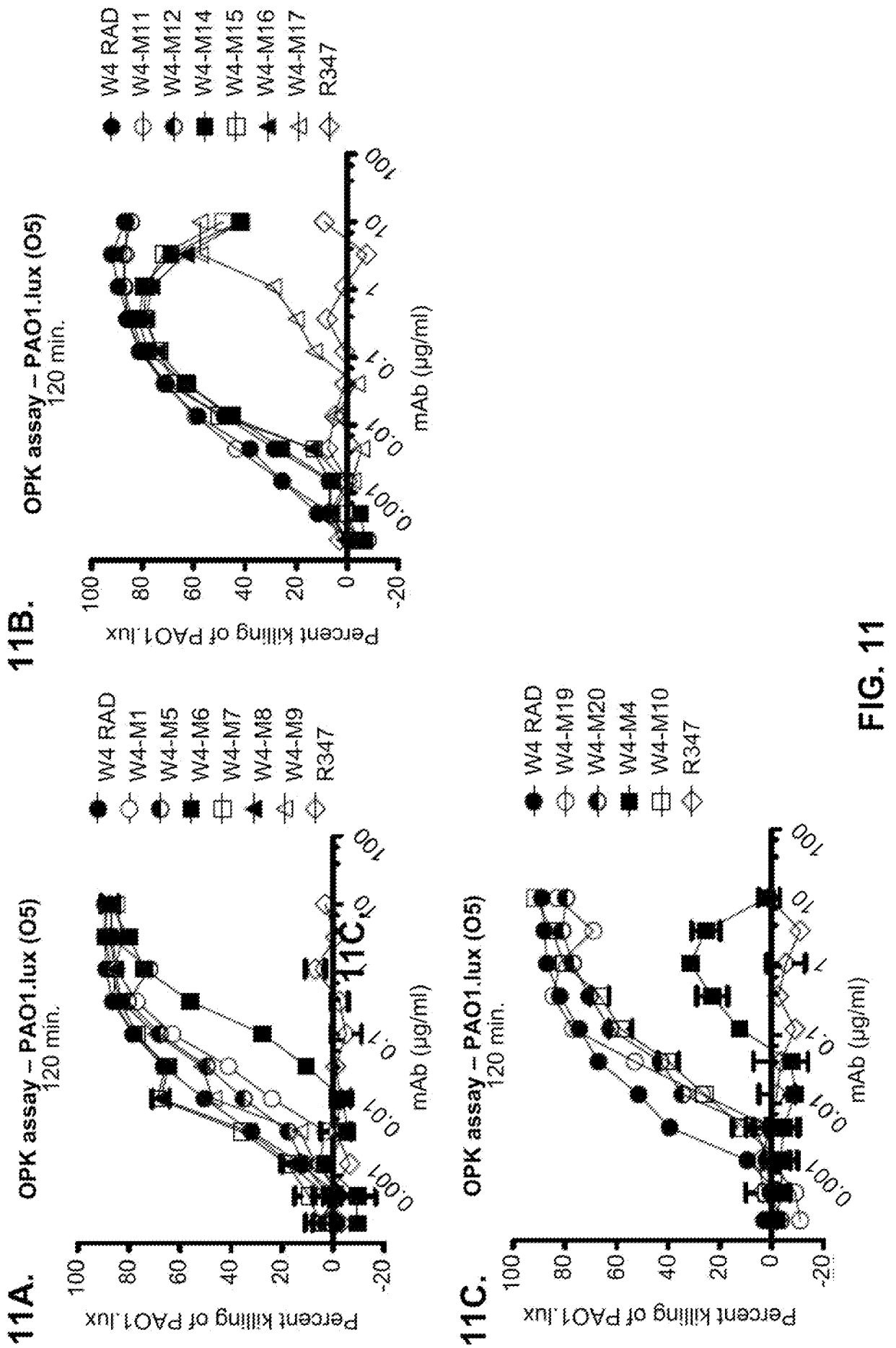

11A.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD
W4-M1
W4-M5
W4-M6
W4-M7
W4-M8
W4-M9
R347
Percent killing of PAO1.lux
mAb (µg/ml)
11B.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD
W4-M11
W4-M12
W4-M14
W4-M15
W4-M16
W4-M17
R347
Percent killing of PAO1.lux
mAb (µg/ml)
11C.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD
W4-M19
W4-M20
W4-M4
W4-M10
R347
Percent killing of PAO1.lux
mAb (µg/ml)

FIG. 11

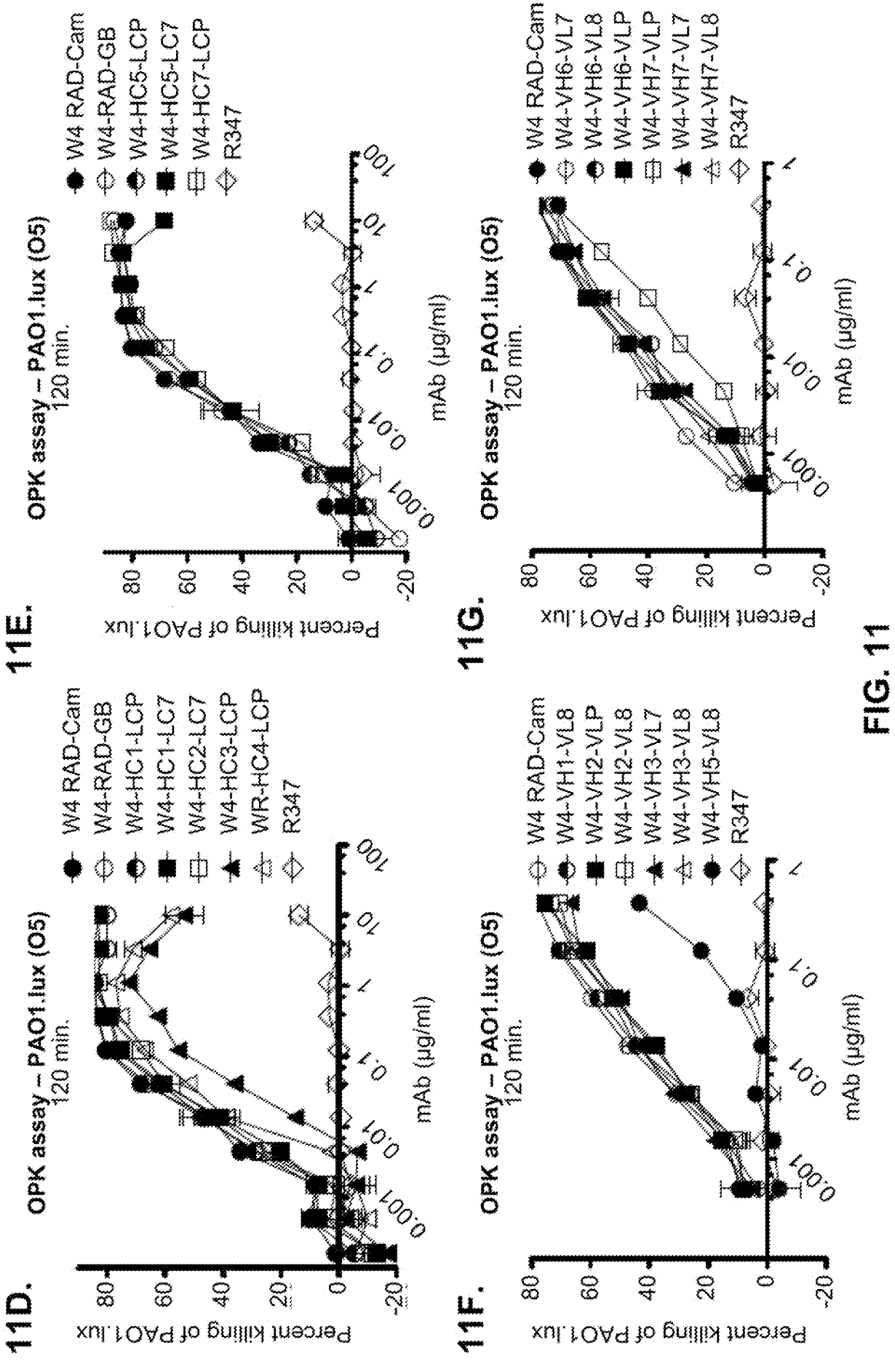

11D.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD-Cam
W4-RAD-GB
W4-HC1-LCP
W4-HC1-LC7
W4-HC2-LC7
W4-HC3-LCP
WR-HC4-LCP
R347
Percent killing of PAO1.lux
mAb (µg/ml)
11E.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD-Cam
W4-RAD-GB
W4-HC5-LCP
W4-HC5-LC7
W4-HC7-LCP
R347
Percent killing of PAO1.lux
mAb (µg/ml)
11F.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD-Cam
W4-VH1-VL8
W4-VH2-VLP
W4-VH2-VL8
W4-VH3-VL7
W4-VH3-VL8
W4-VH5-VL8
R347
Percent killing of PAO1.lux
mAb (µg/ml)
11G.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD-Cam
W4-VH6-VL7
W4-VH6-VL8
W4-VH6-VLP
W4-VH7-VLP
W4-VH7-VL7
W4-VH7-VL8
R347
Percent killing of PAO1.lux
mAb (µg/ml)

FIG. 11

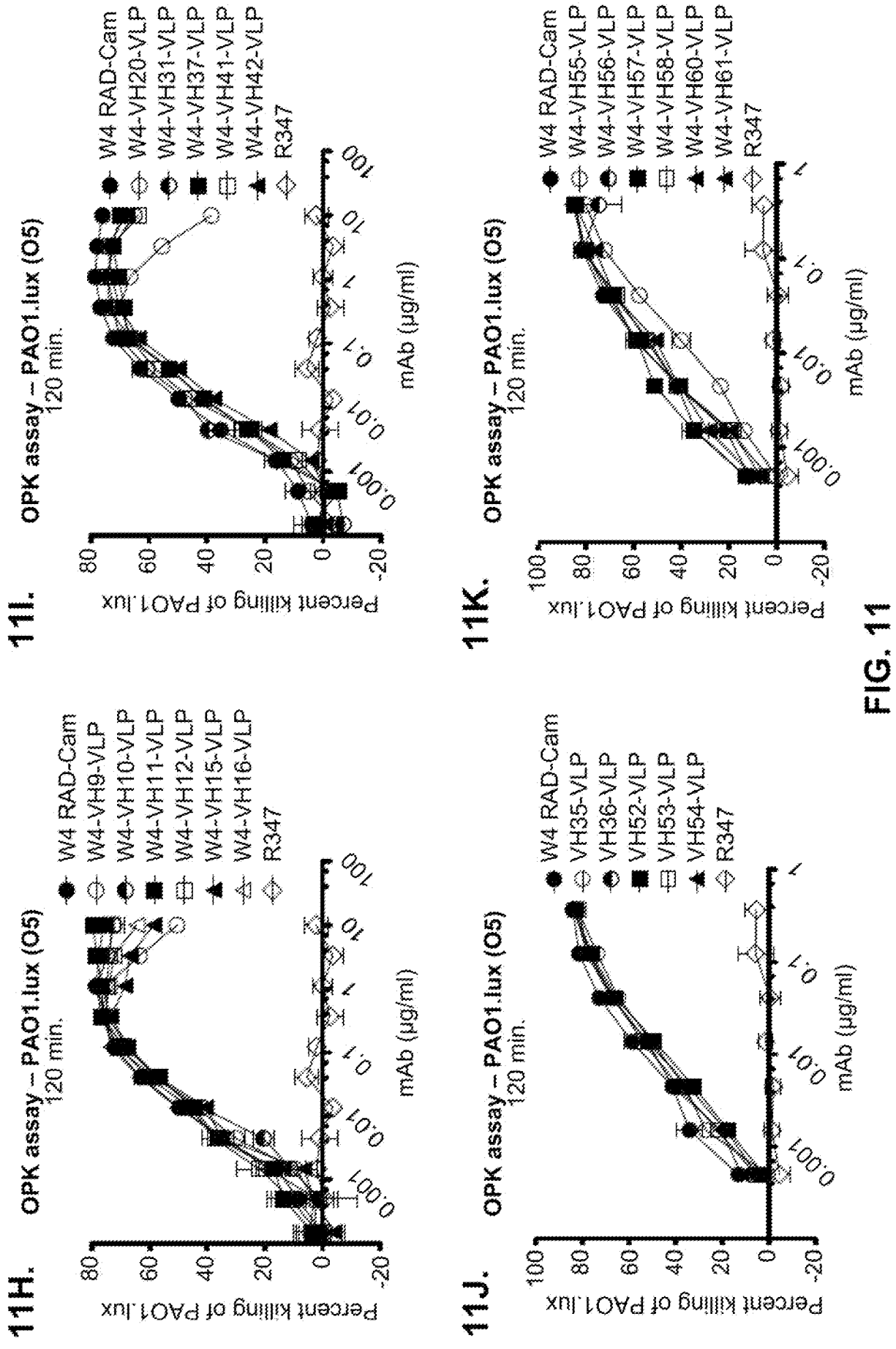
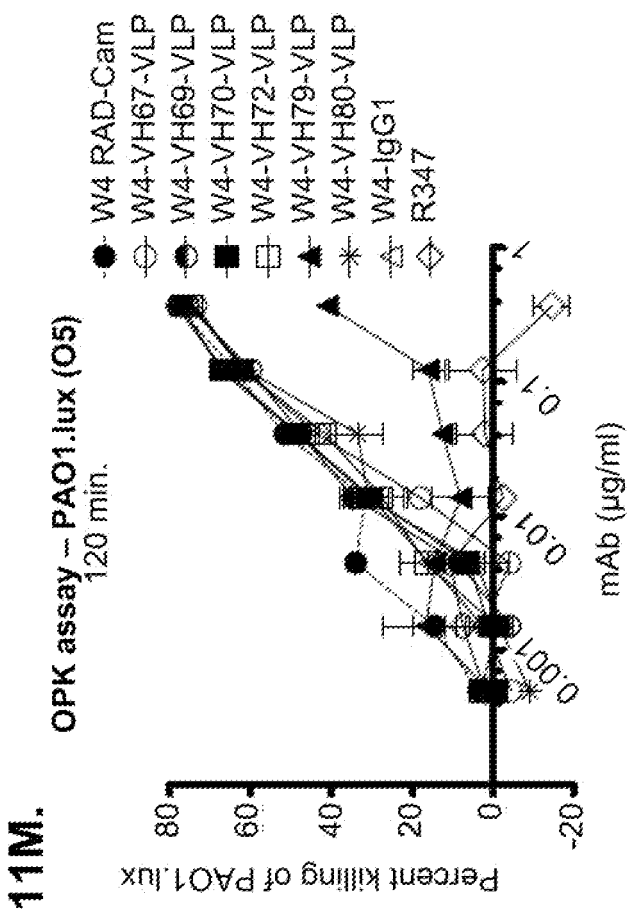

11H.
OPK assay – PAO1.lux (O5)
120 min.
Percent killing of PAO1.lux
mAb (µg/ml)
W4 RAD-Cam
W4-VH9-VLP
W4-VH10-VLP
W4-VH11-VLP
W4-VH12-VLP
W4-VH15-VLP
W4-VH16-VLP
R347
11I.
OPK assay – PAO1.lux (O5)
120 min.
Percent killing of PAO1.lux
mAb (µg/ml)
W4 RAD-Cam
W4-VH20-VLP
W4-VH31-VLP
W4-VH37-VLP
W4-VH41-VLP
W4-VH42-VLP
R347
11J.
OPK assay – PAO1.lux (O5)
120 min.
Percent killing of PAO1.lux
mAb (µg/ml)
W4 RAD-Cam
VH35-VLP
VH36-VLP
VH52-VLP
VH53-VLP
VH54-VLP
R347
11K.
OPK assay – PAO1.lux (O5)
120 min.
Percent killing of PAO1.lux
mAb (µg/ml)
W4 RAD-Cam
W4-VH55-VLP
W4-VH56-VLP
W4-VH57-VLP
W4-VH58-VLP
W4-VH60-VLP
W4-VH61-VLP
R347

FIG. 11


11M.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD-Cam
W4-VH67-VLP
W4-VH69-VLP
W4-VH70-VLP
W4-VH72-VLP
W4-VH79-VLP
W4-VH80-VLP
W4-IgG1
R347
Percent killing of PAO1.lux
80
60
40
20
0
-20
1
0.1
0.01
0.001
mAb (µg/ml)

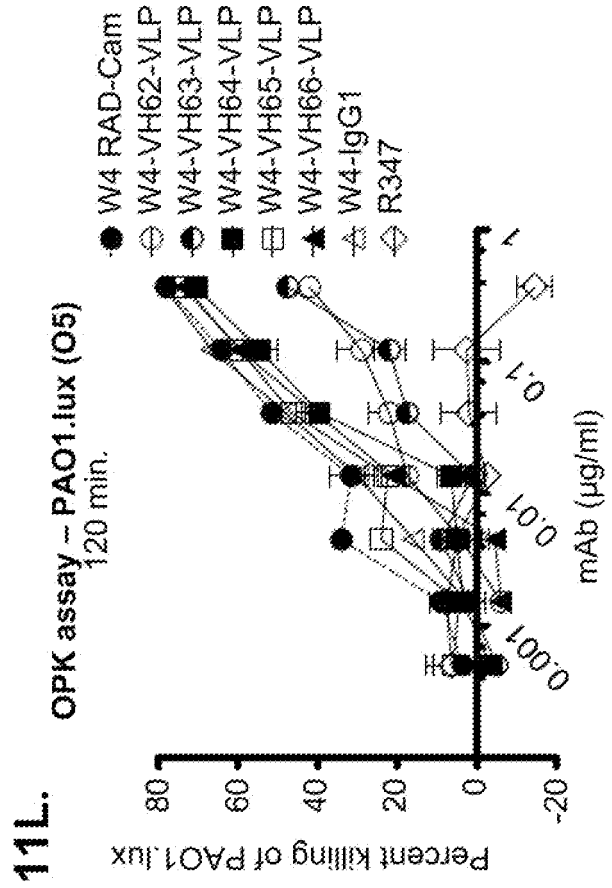

11L.
OPK assay – PAO1.lux (O5)
120 min.
W4 RAD-Cam
W4-VH62-VLP
W4-VH63-VLP
W4-VH64-VLP
W4-VH65-VLP
W4-VH66-VLP
W4-IgG1
R347
Percent killing of PAO1.lux
80
60
40
20
0
-20
1
0.1
0.01
0.001
mAb (µg/ml)

FIG. 11

11N.

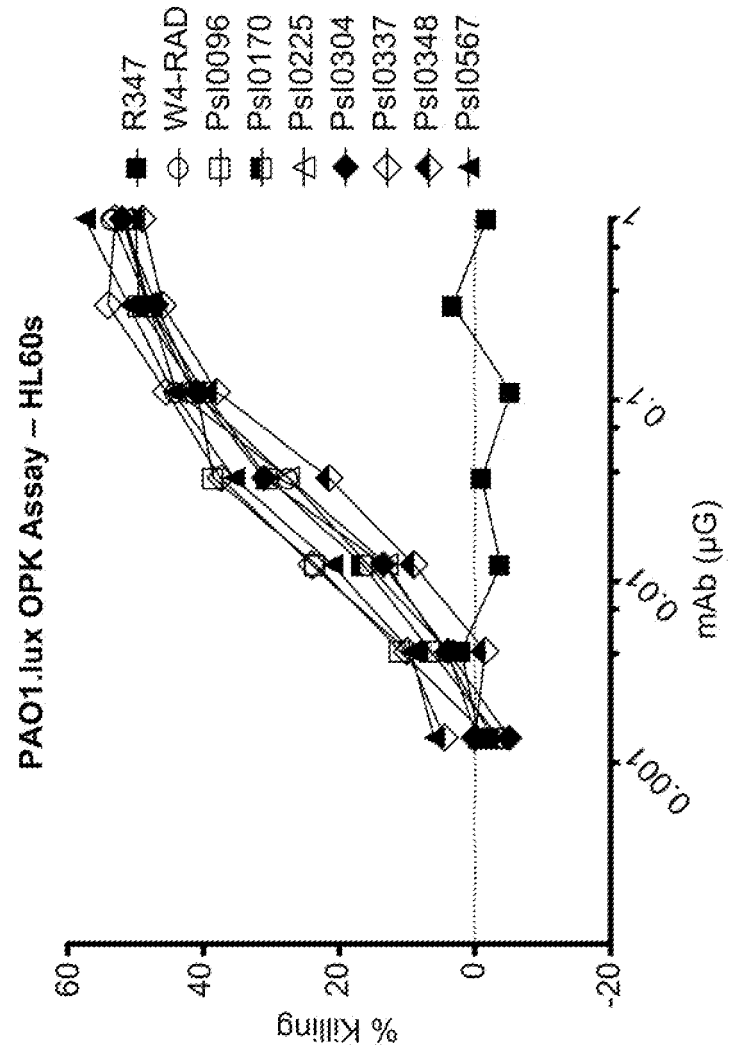
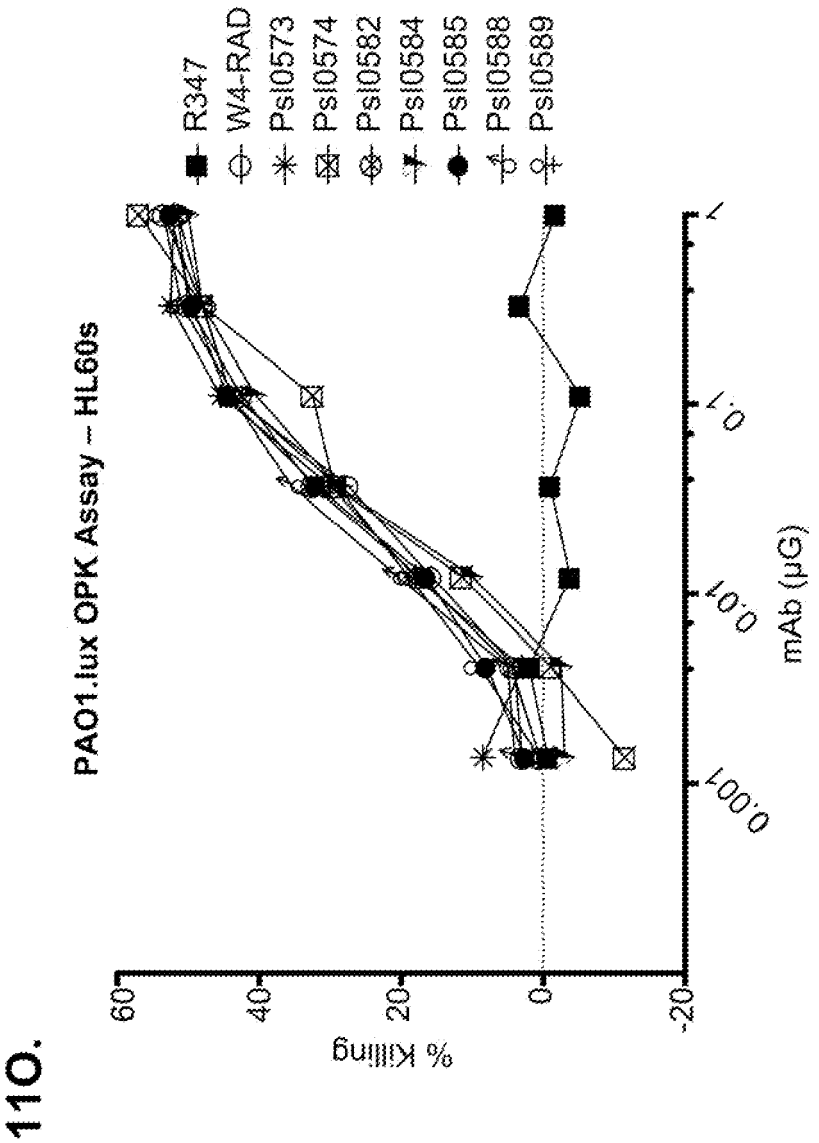

PAO1.lux OPK Assay – HL60s
R347
W4-RAD
Psl0096
Psl0170
Psl0225
Psl0304
Psl0337
Psl0348
Psl0567
% Killing
60
40
20
0
-20
0.001
0.01
0.1
1
mAb (µG)

FIG. 11


PAO1.lux OPK Assay – HL60s
R347
W4-RAD
PsI0573
PsI0574
PsI0582
PsI0584
PsI0585
PsI0588
PsI0589
% Killing
60
40
20
0
-20
0.001
0.01
0.1
1
mAb (µG)

11O.

FIG. 11

11P.

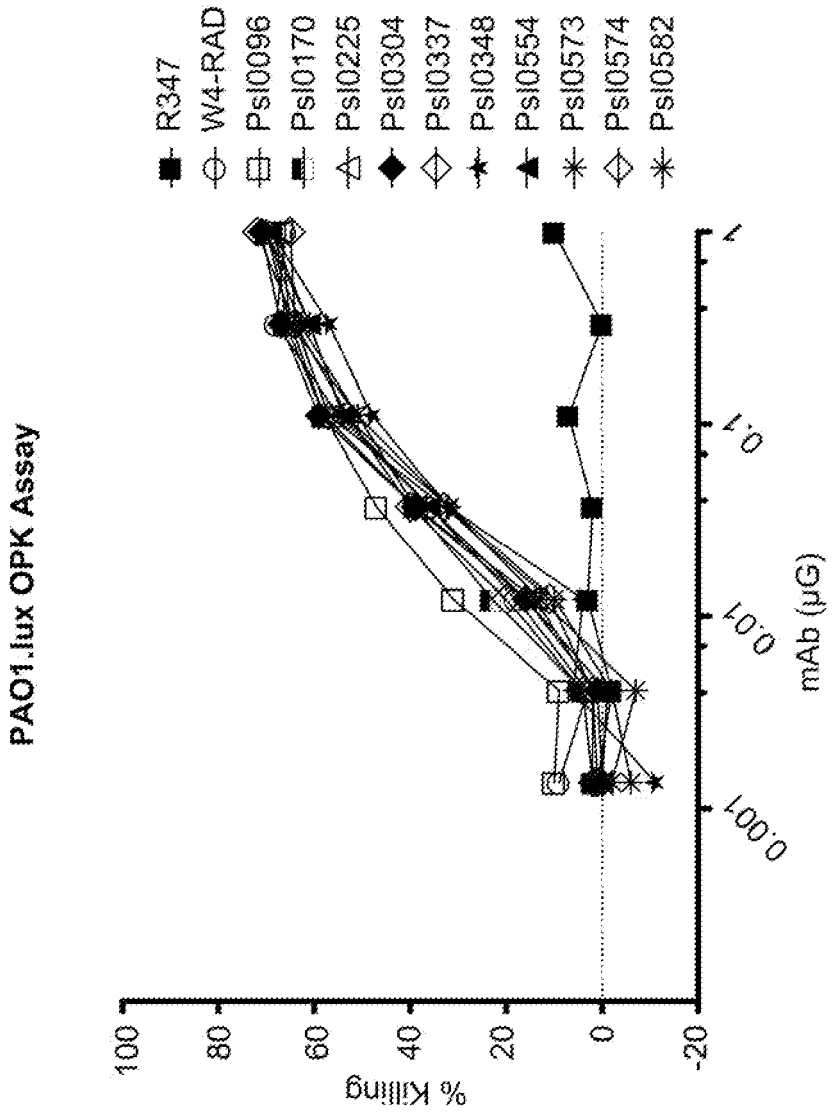

PAO1.lux OPK Assay
R347
W4-RAD
PsI0096
PsI0170
PsI0225
PsI0304
PsI0337
PsI0348
PsI0554
PsI0573
PsI0574
PsI0582
% Killing
100
80
60
40
20
0
-20
mAb (µG)
0.001
0.01
0.1
1

FIG. 11

11Q.

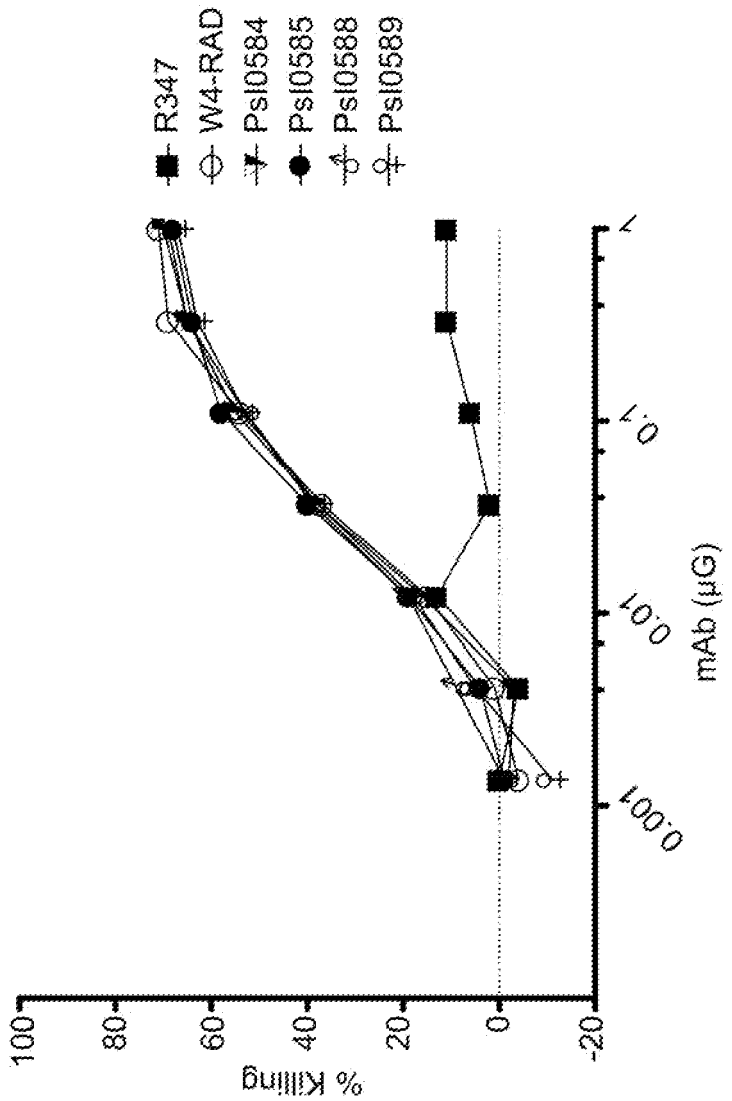

PAO1.lux OPK Assay
R347
W4-RAD
PsI0584
PsI0585
PsI0588
PsI0589
% Killing
100
80
60
40
20
0
-20
0.001
0.01
0.1
1
mAb (µG)

FIG. 11

12A.

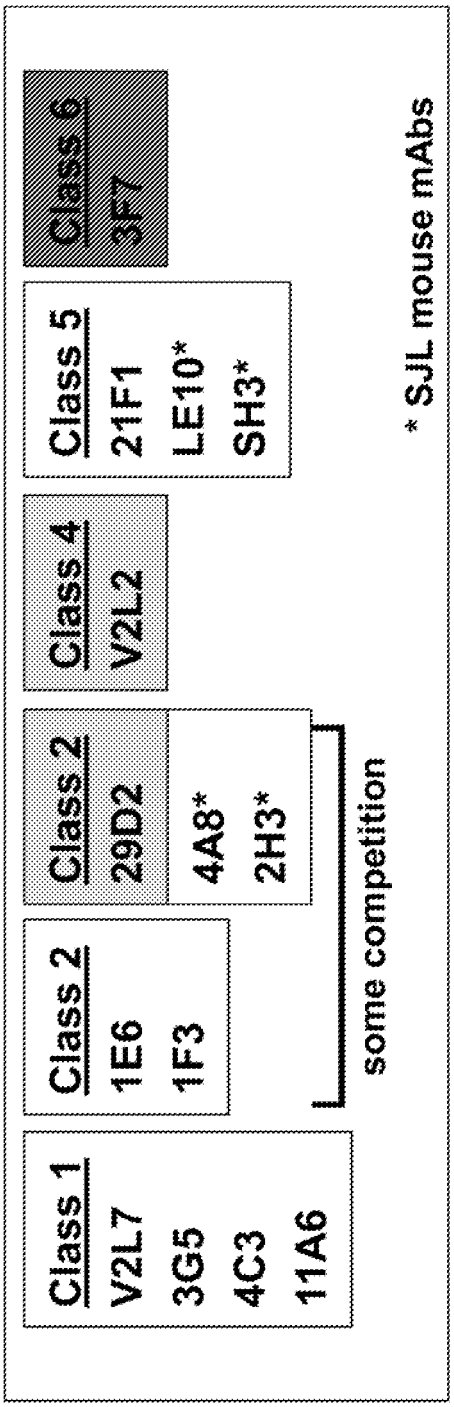

Class 1
V2L7
3G5
4C3
11A6
Class 2
1E6
1F3
Class 2
29D2
4A8*
2H3*
some competition
Class 4
V2L2
Class 5
21F1
LE10*
SH3*
Class 6
3F7
* SJL mouse mAbs
In vivo:
protective
not protective
ND

FIG. 12

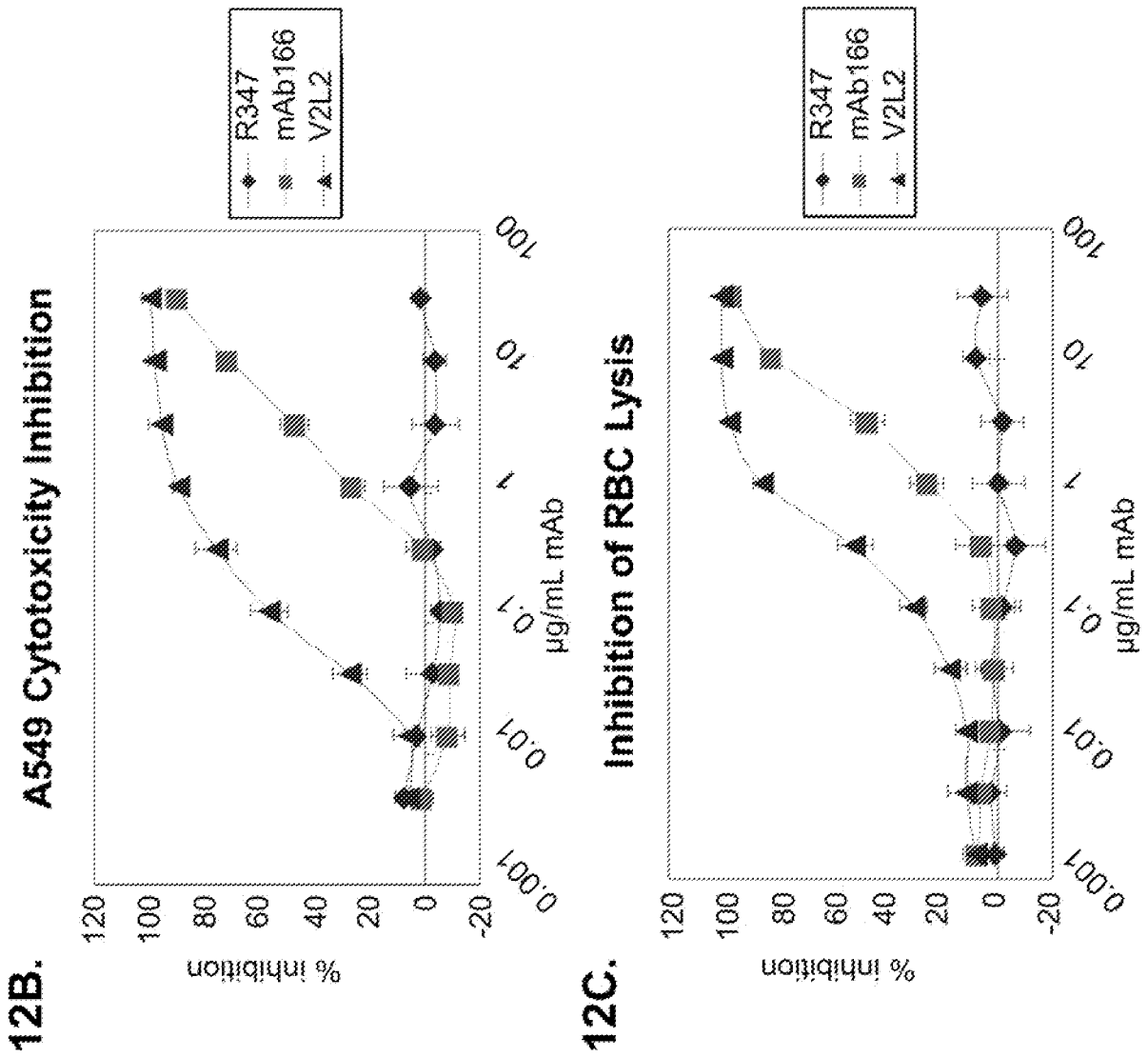

12B.
A549 Cytotoxicity Inhibition
R347
mAb166
V2L2
% inhibition
120
100
80
60
40
20
0
-20
100
10
1
0.1
0.01
0.001
µg/mL mAb
12C.
Inhibition of RBC Lysis
R347
mAb166
V2L2
% inhibition
120
100
80
60
40
20
0
-20
100
10
1
0.1
0.01
0.001
µg/mL mAb

FIG. 12

12D.

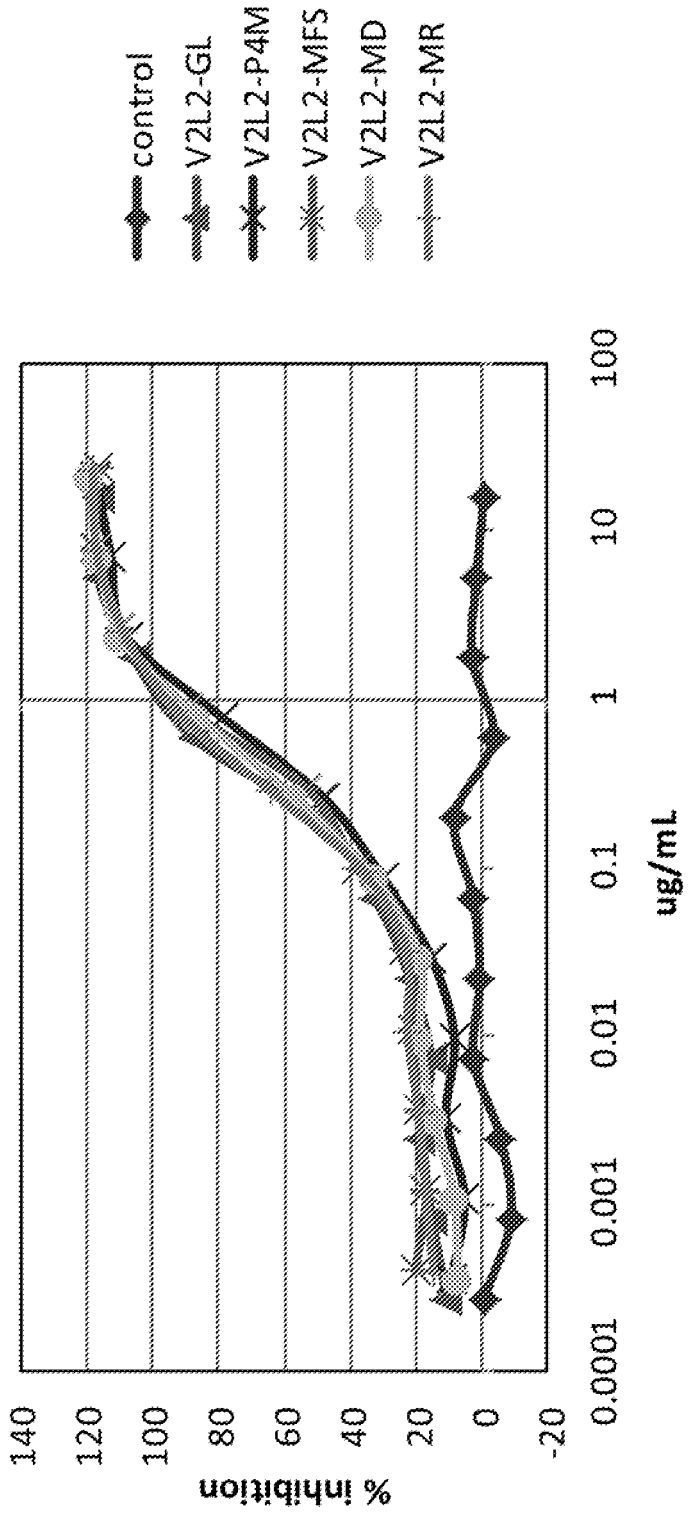

RBC Lysis Inhibition 2012_01_18-plate1A
control
V2L2-GL
V2L2-P4M
V2L2-MFS
V2L2-MD
V2L2-MR
% inhibition
140
120
100
80
60
40
20
0
-20
0.0001
0.001
0.01
0.1
1
10
100
ug/mL

FIG. 12

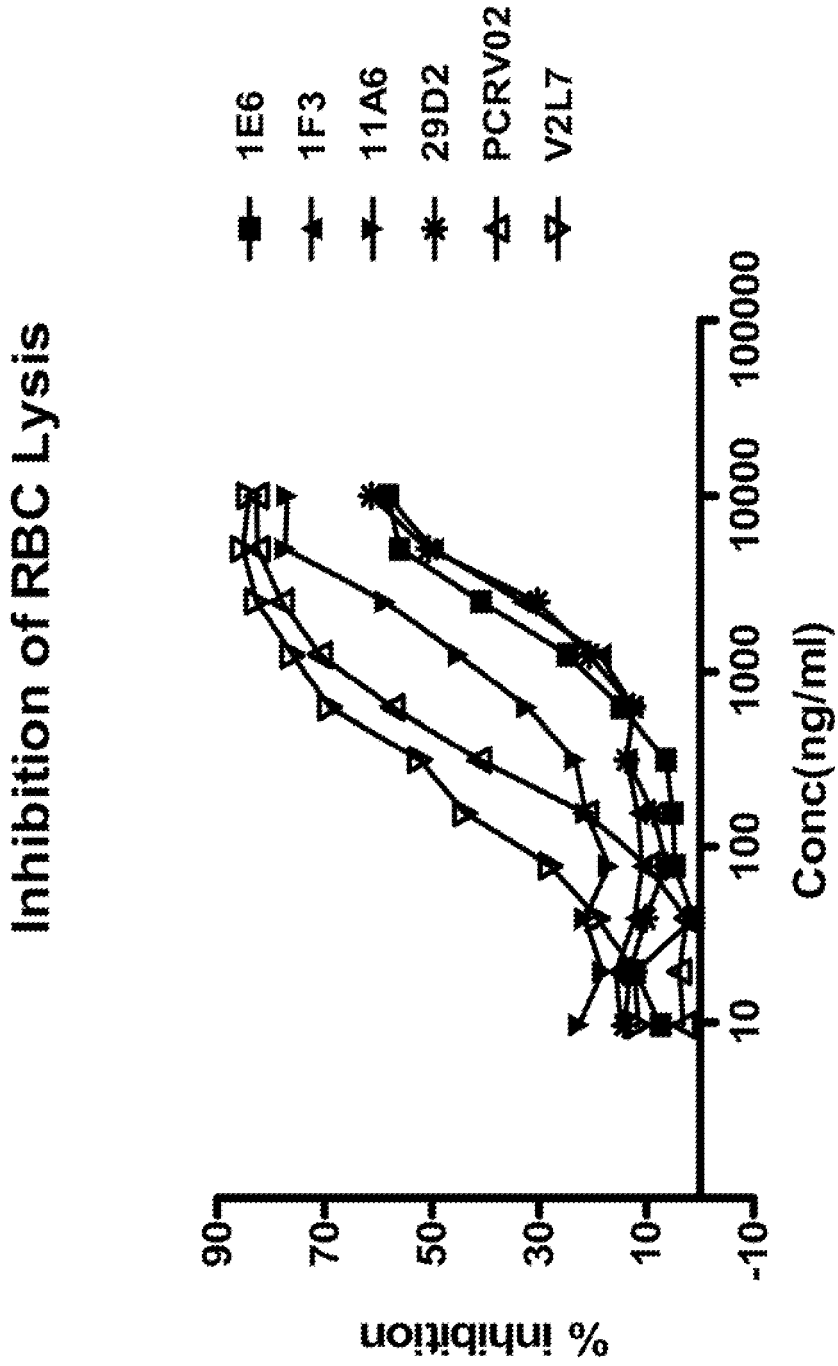
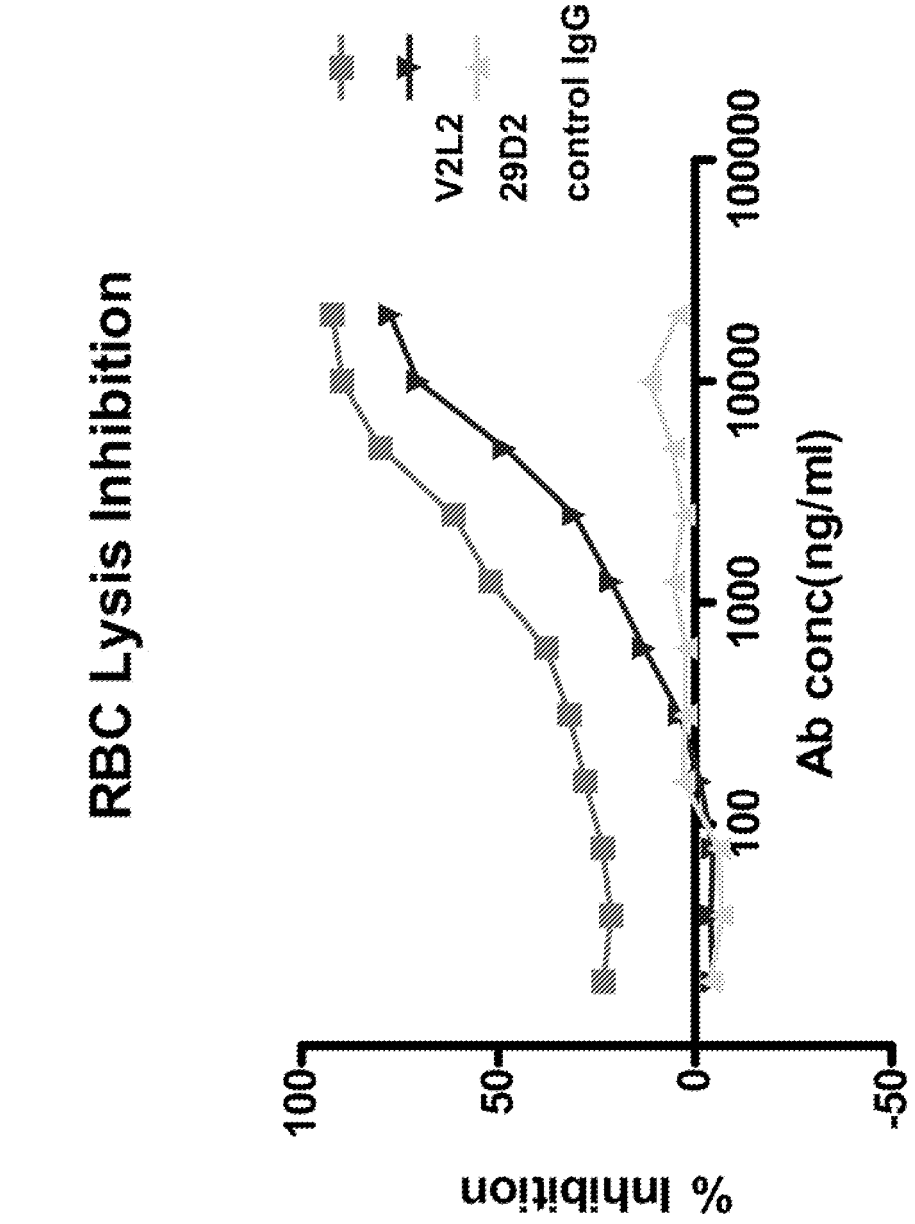

Inhibition of RBC Lysis
1E6
1F3
11A6
29D2
PCRV02
V2L7
% inhibition
90
70
50
30
10
-10
Conc(ng/ml)
10
100
1000
10000
100000

FIG. 12

12E.


RBC Lysis Inhibition
V2L2
29D2
control IgG
% Inhibition
100
50
0
-50
100
1000
10000
100000
Ab conc(ng/ml)

12F.

FIG. 12

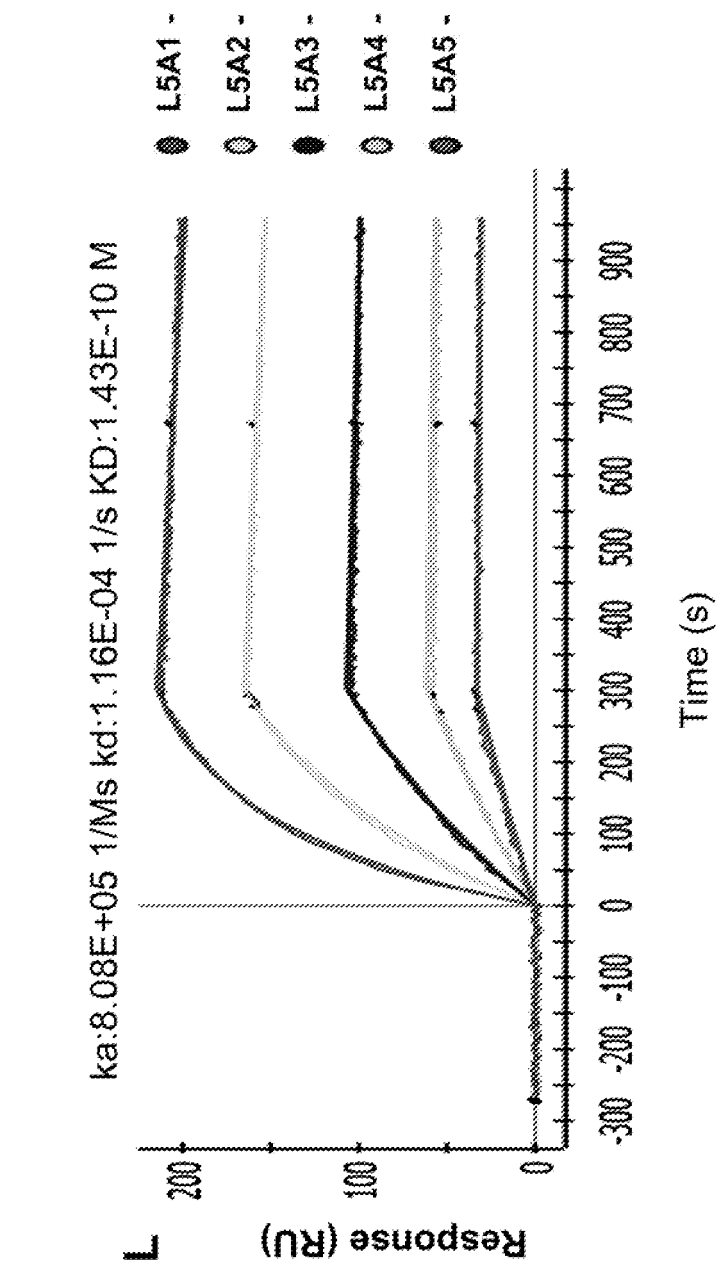
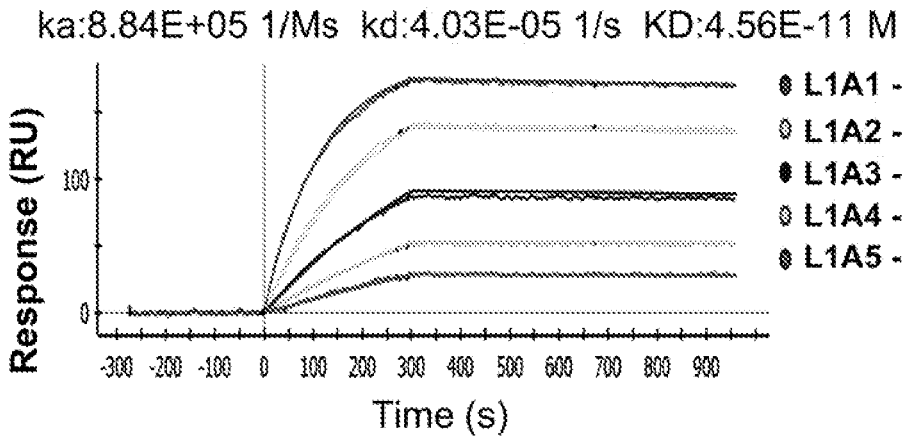

12G.
V2L2-GL
ka:8.08E+05 1/Ms kd:1.16E-04 1/s KD:1.43E-10 M
L5A1
L5A2
L5A3
L5A4
L5A5
Response (RU)
200
100
0
-300 -200 -100 0 100 200 300 400 500 600 700 800 900
Time (s)

FIG. 12

12H.

V2L2-MD



Clone	Association rate (*kon*) ($\times 10^5$ M^{-1} s^{-1})	Dissociation rate (*koff*) ($\times 10^{-5}$ s^{-1})	K_D (pM)
V2L2GL	8.08	11.6	143
V2L2MD	8.84	4.03	46

FIG. 12

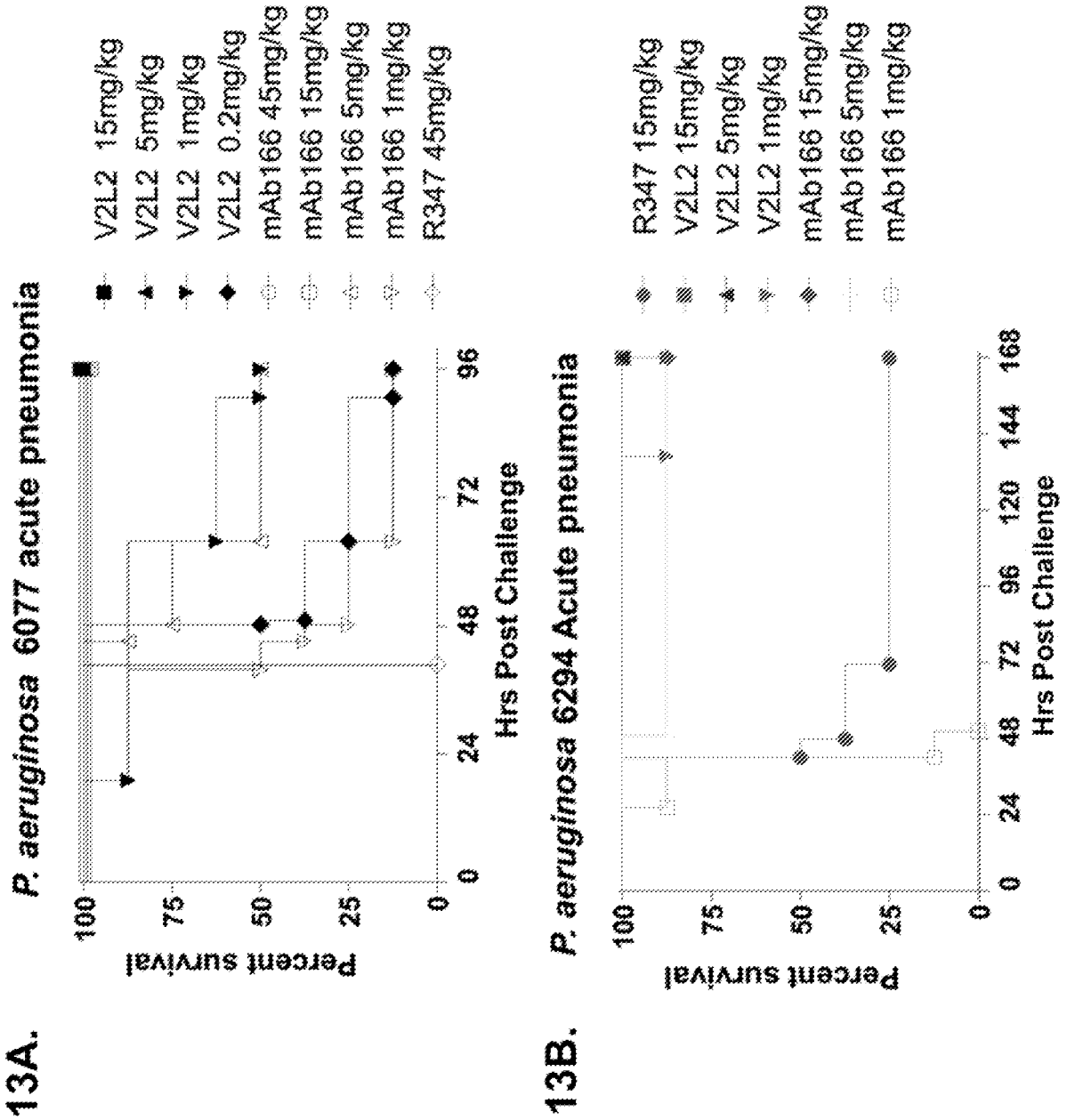
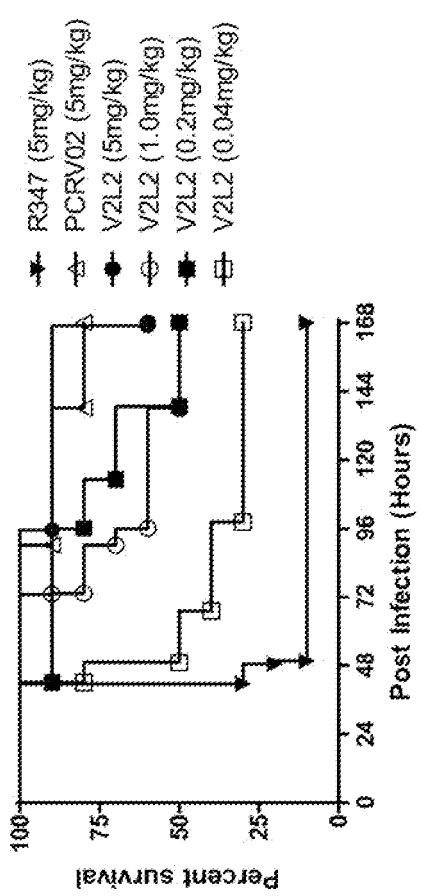

13A.
P. aeruginosa 6077 acute pneumonia
Percent survival
100
75
50
25
0
0
24
48
72
96
Hrs Post Challenge
V2L2 15mg/kg
V2L2 5mg/kg
V2L2 1mg/kg
V2L2 0.2mg/kg
mAb166 45mg/kg
mAb166 15mg/kg
mAb166 5mg/kg
mAb166 1mg/kg
R347 45mg/kg
13B.
P. aeruginosa 6294 Acute pneumonia
Percent survival
100
75
50
25
0
0
24
48
72
96
120
144
168
Hrs Post Challenge
R347 15mg/kg
V2L2 15mg/kg
V2L2 5mg/kg
V2L2 1mg/kg
mAb166 15mg/kg
mAb166 5mg/kg
mAb166 1mg/kg

FIG. 13

13C.



13D.

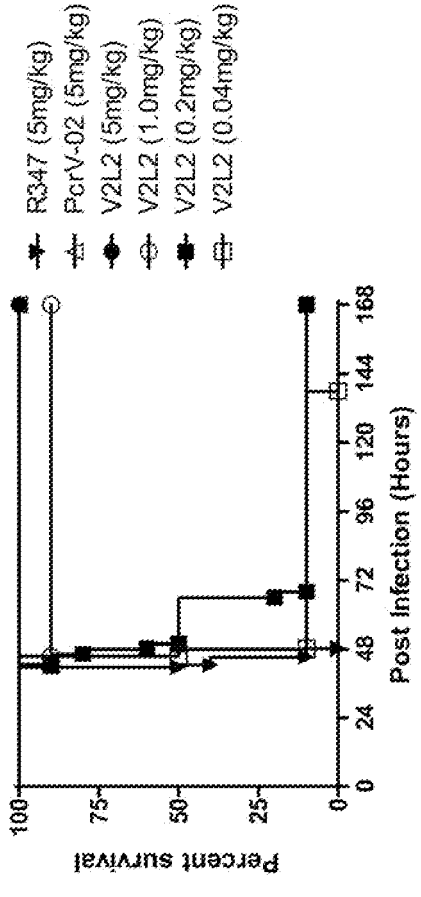


FIG. 13

13E.

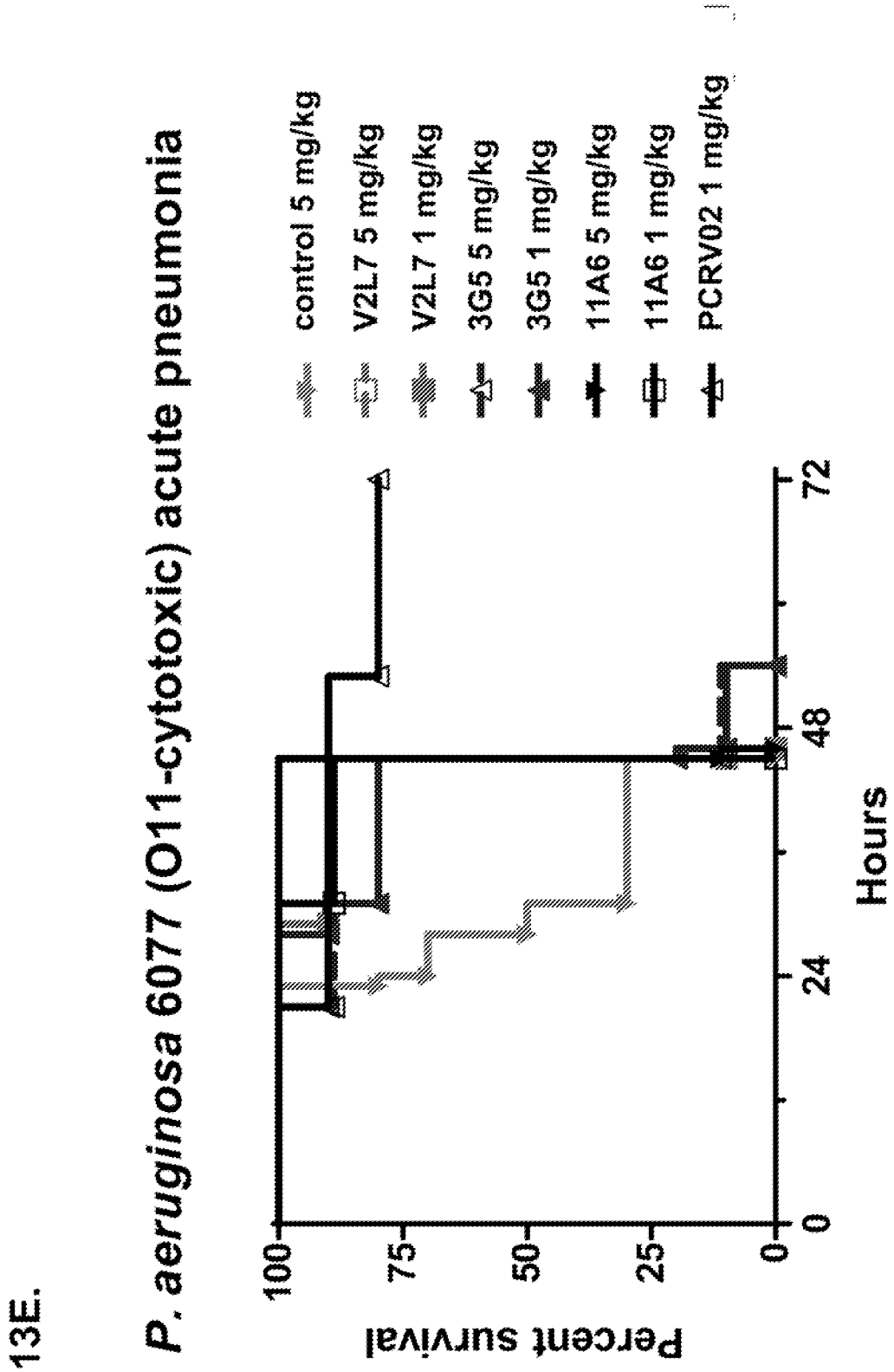

P. aeruginosa 6077 (O11-cytotoxic) acute pneumonia
control 5 mg/kg
V2L7 5 mg/kg
V2L7 1 mg/kg
3G5 5 mg/kg
3G5 1 mg/kg
11A6 5 mg/kg
11A6 1 mg/kg
PCRV02 1 mg/kg
Percent survival
100
75
50
25
0
0
24
48
72
Hours

FIG. 13

13F.

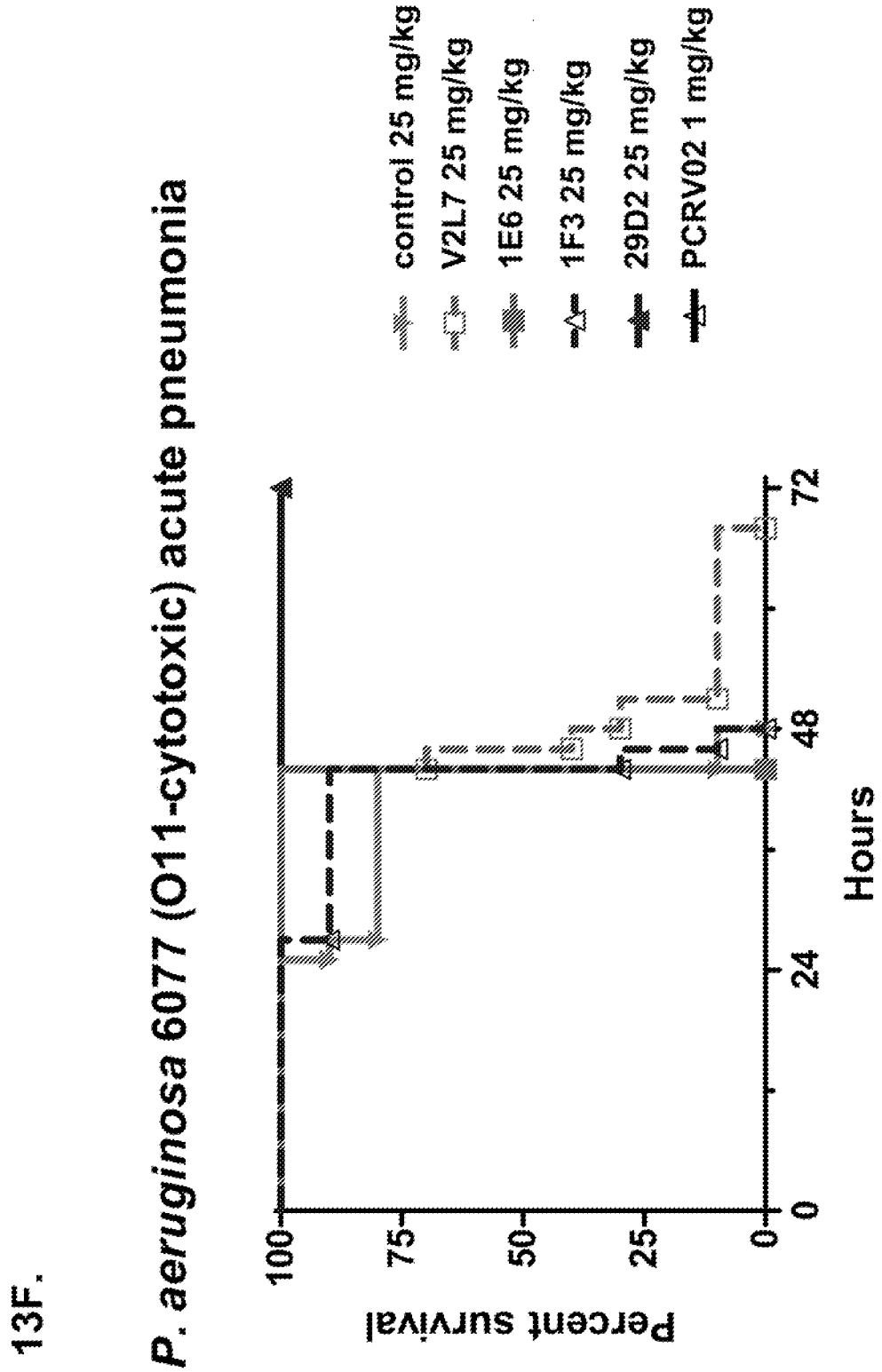

P. aeruginosa 6077 (O11-cytotoxic) acute pneumonia
control 25 mg/kg
V2L7 25 mg/kg
1E6 25 mg/kg
1F3 25 mg/kg
29D2 25 mg/kg
PCRV02 1 mg/kg
Percent survival
100
75
50
25
0
0
24
48
72
Hours

FIG. 13

13G.

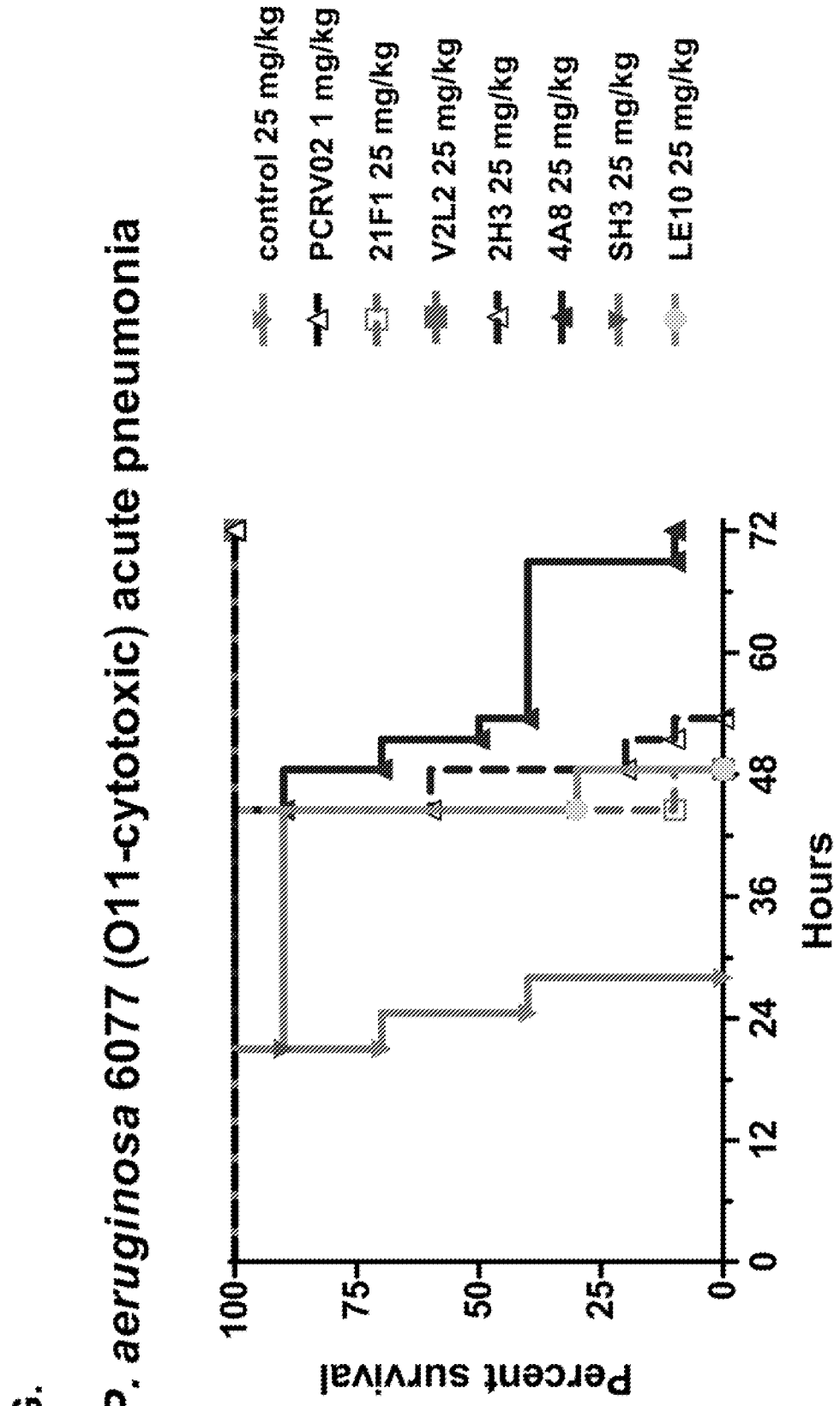

P. aeruginosa 6077 (O11-cytotoxic) acute pneumonia
control 25 mg/kg
PCRV02 1 mg/kg
21F1 25 mg/kg
V2L2 25 mg/kg
2H3 25 mg/kg
4A8 25 mg/kg
SH3 25 mg/kg
LE10 25 mg/kg
Percent survival
100
75
50
25
0
0
12
24
36
48
60
72
Hours

FIG. 13

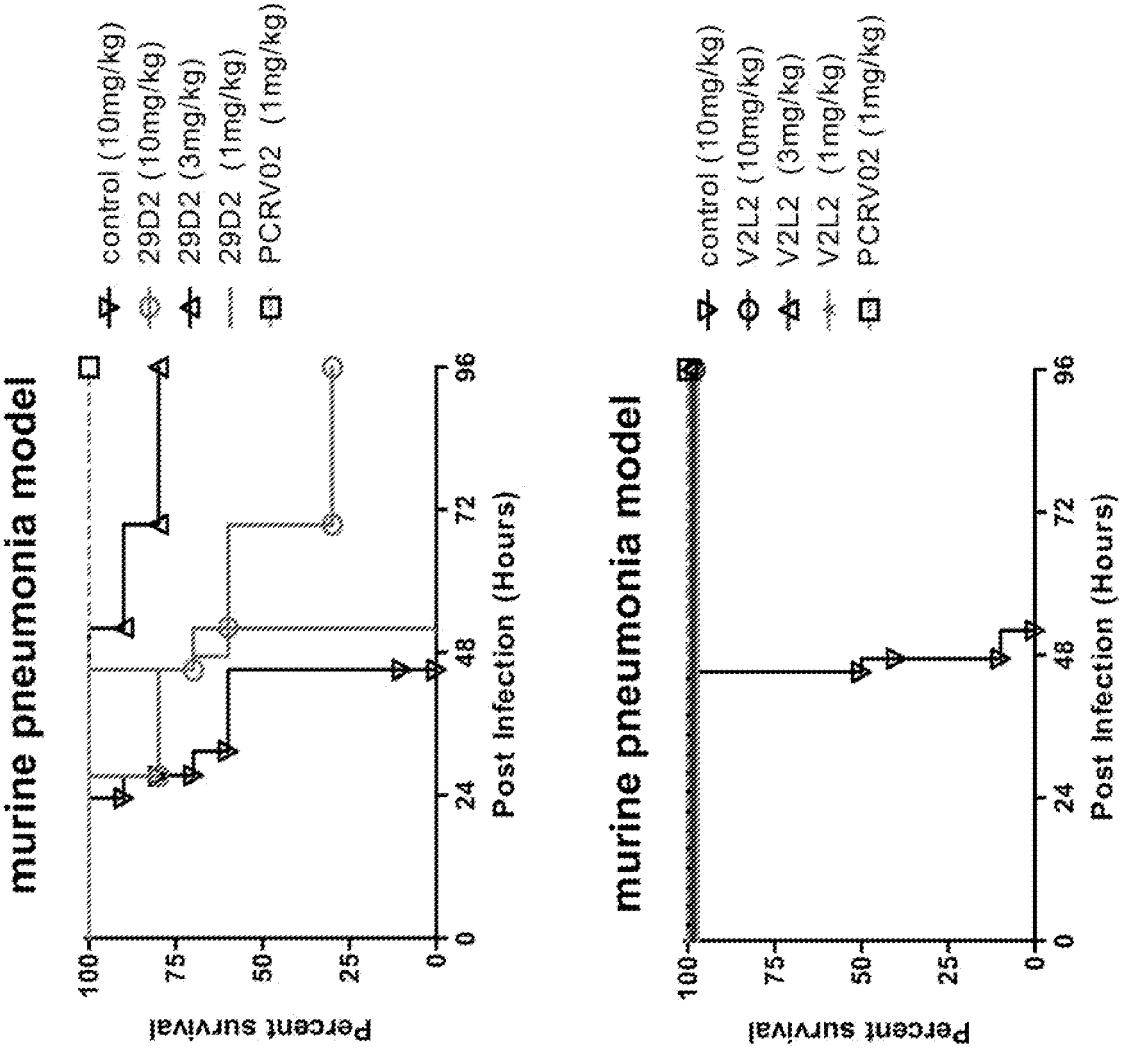

13H.
29D2
murine pneumonia model
control (10mg/kg)
29D2 (10mg/kg)
29D2 (3mg/kg)
29D2 (1mg/kg)
PCRV02 (1mg/kg)
Percent survival
Post Infection (Hours)
0
25
50
75
100
0
24
48
72
96
V2L2
murine pneumonia model
control (10mg/kg)
V2L2 (10mg/kg)
V2L2 (3mg/kg)
V2L2 (1mg/kg)
PCRV02 (1mg/kg)
Percent survival
Post Infection (Hours)

FIG. 13

13I.

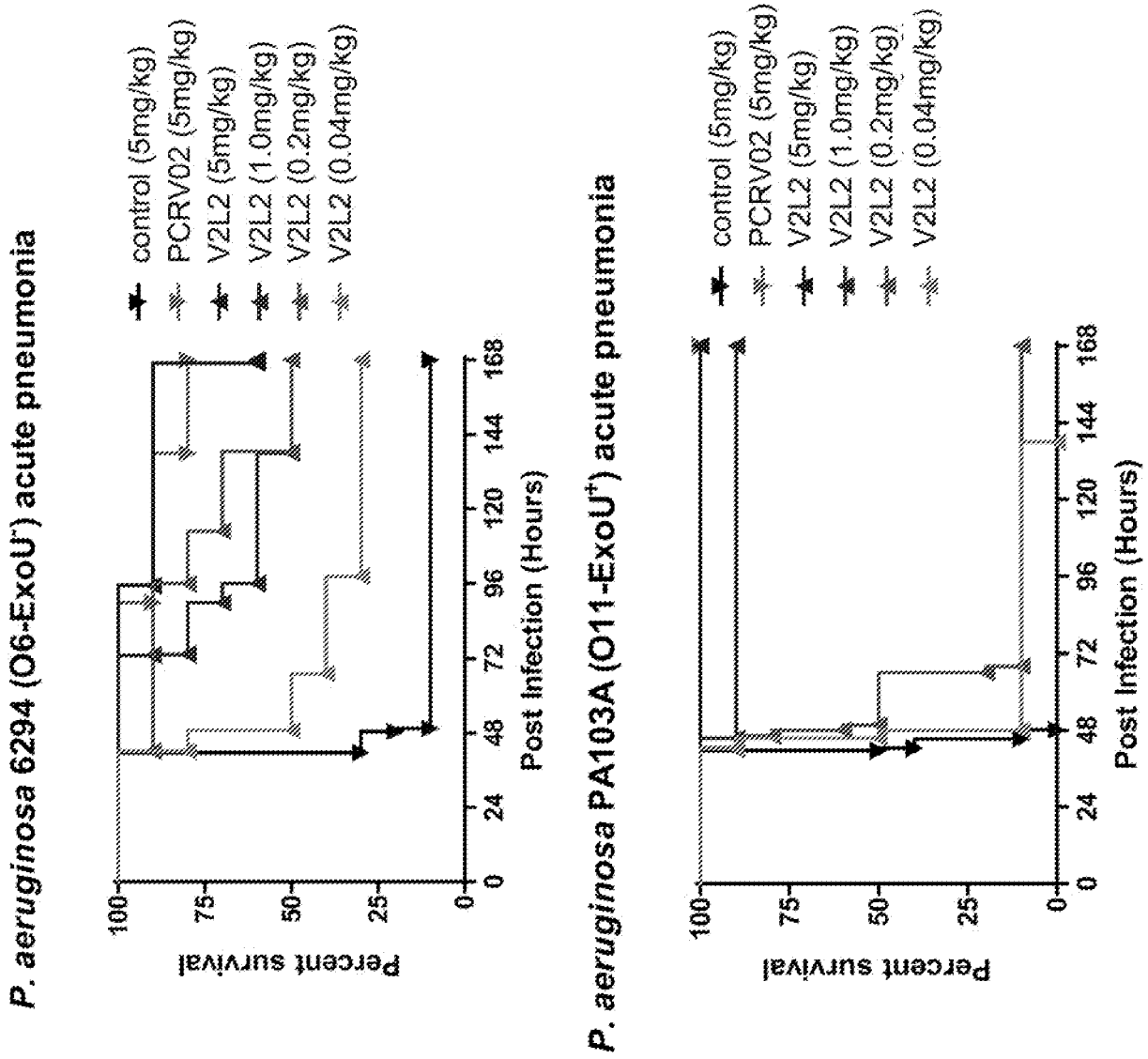
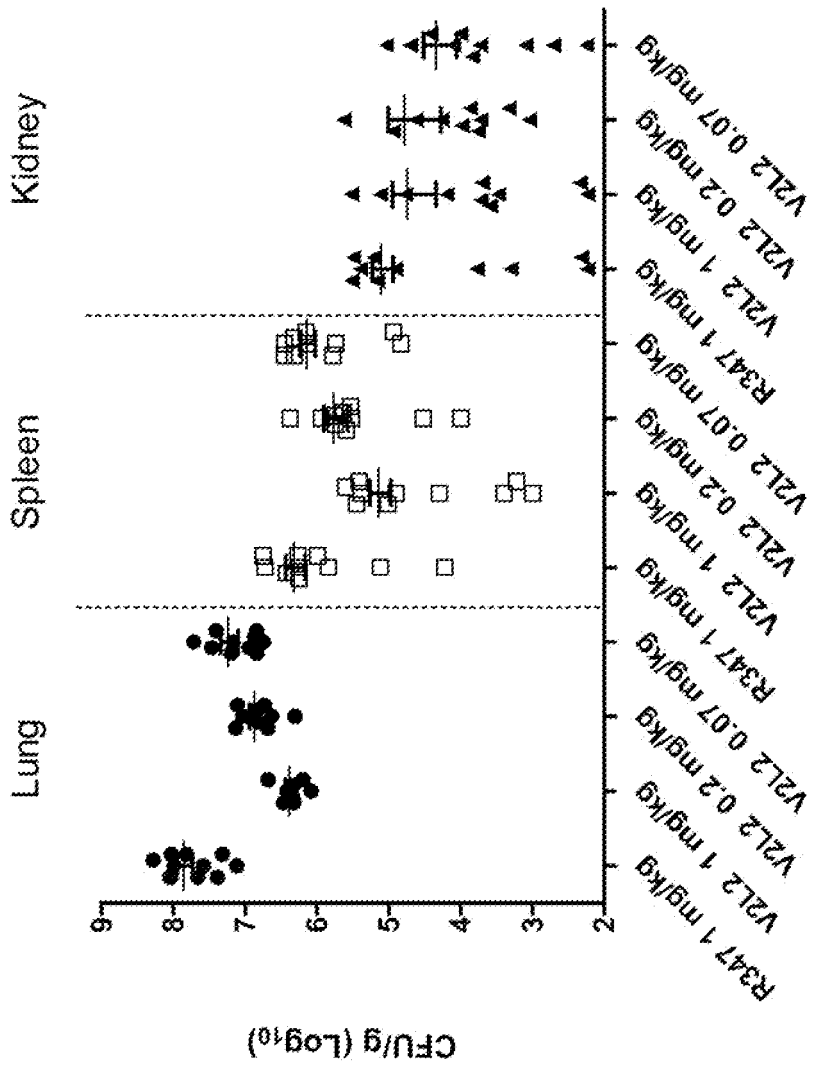
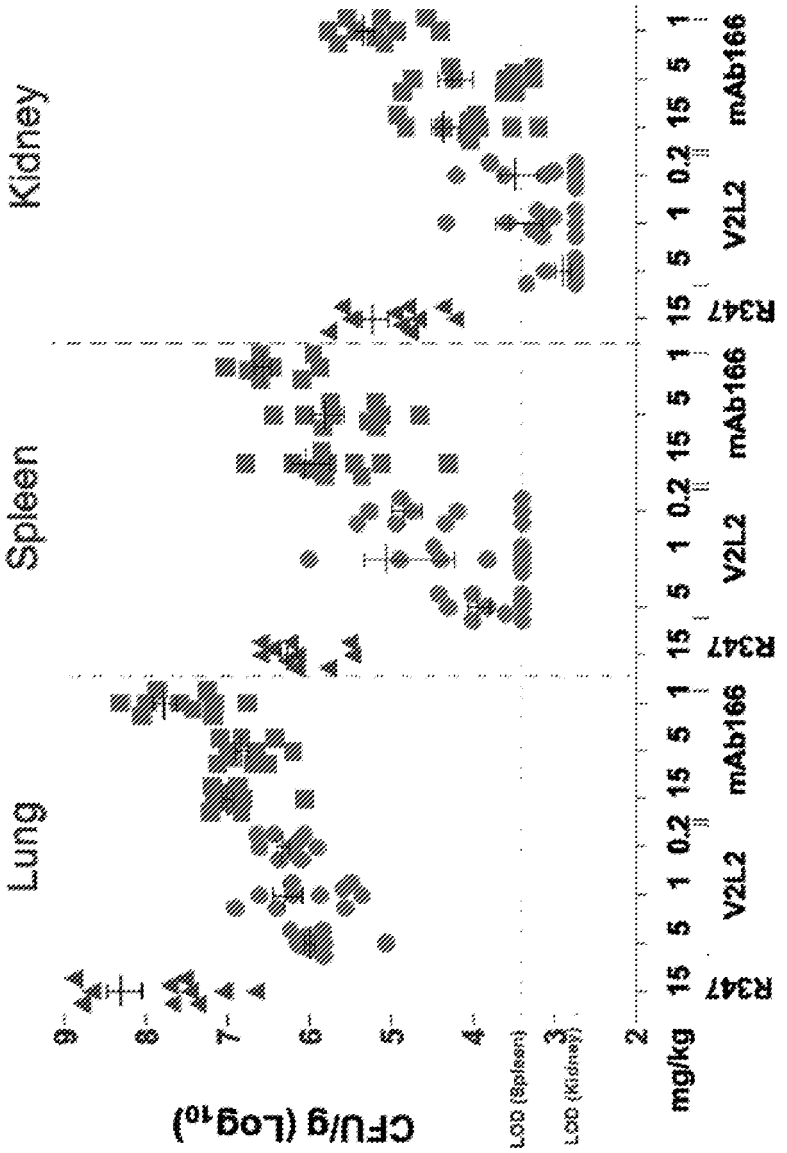

P. aeruginosa 6294 (O6-ExoU-) acute pneumonia
control (5mg/kg)
PCRV02 (5mg/kg)
V2L2 (5mg/kg)
V2L2 (1.0mg/kg)
V2L2 (0.2mg/kg)
V2L2 (0.04mg/kg)
Percent survival
100
75
50
25
0
0
24
48
72
96
120
144
168
Post Infection (Hours)
P. aeruginosa PA103A (O11-ExoU+) acute pneumonia
control (5mg/kg)
PCRV02 (5mg/kg)
V2L2 (5mg/kg)
V2L2 (1.0mg/kg)
V2L2 (0.2mg/kg)
V2L2 (0.04mg/kg)
Percent survival
100
75
50
25
0
0
24
48
72
96
120
144
168
Post Infection (Hours)

FIG. 13


Kidney
Spleen
Lung
9
8
7
6
5
4
3
2
CFU/g (Log10)
R347 1 mg/kg
V2L2 1 mg/kg
V2L2 0.2 mg/kg
V2L2 0.07 mg/kg
R347 1 mg/kg
V2L2 1 mg/kg
V2L2 0.2 mg/kg
V2L2 0.07 mg/kg
R347 1 mg/kg
V2L2 1 mg/kg
V2L2 0.2 mg/kg
V2L2 0.07 mg/kg

14A.

FIG. 14


Lung
Spleen
Kidney
CFU/g (Log10)
9
8
7
6
5
4
3
2
LOD (Spleen)
LOD (Kidney)
mg/kg
15 5 1 0.2 15 5 1 0.2 15 5 1
R347 V2L2 mAb166 R347 V2L2 mAb166 R347 V2L2 mAb166

14B.

FIG. 14

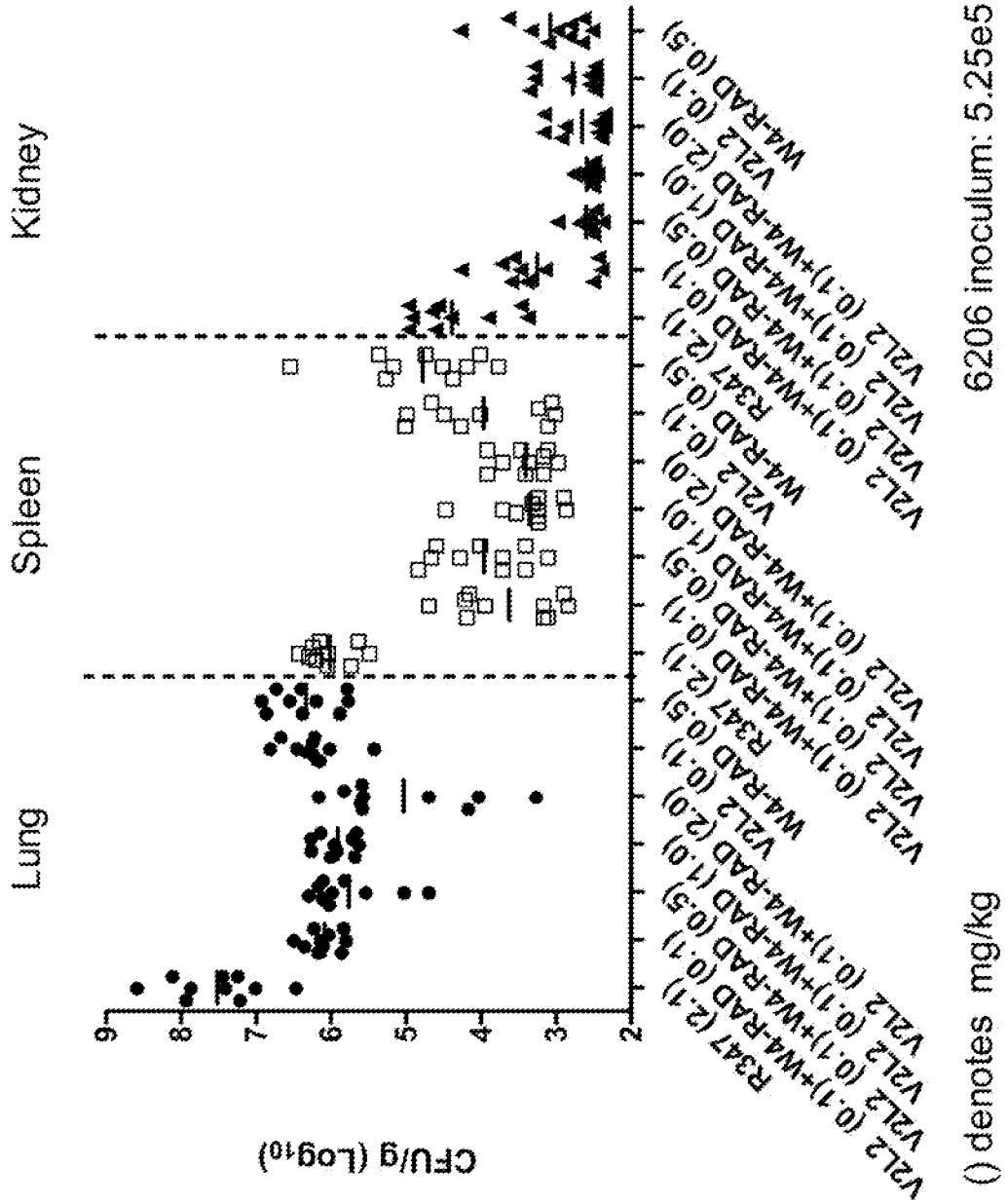
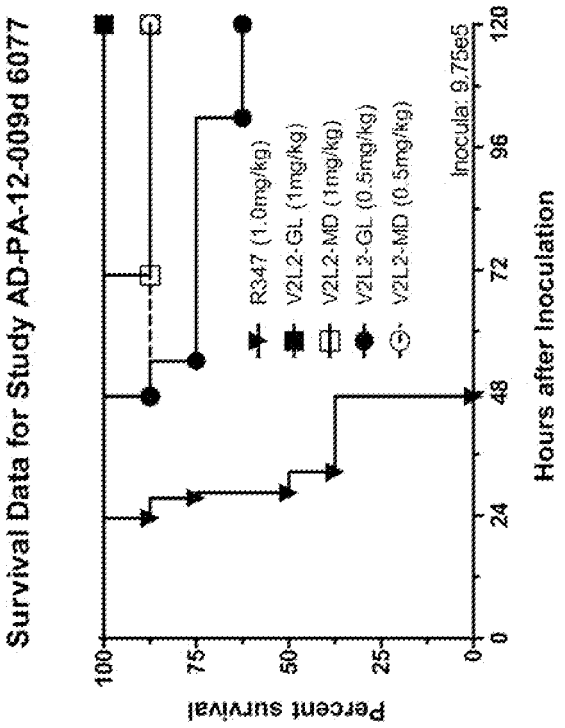

Lung
Spleen
Kidney
CFU/g (Log10)
9
8
7
6
5
4
3
2
W4-RAD (0.5)
V2L2 (0.1)
V2L2 (2.0)
W4-RAD (1.0)
W4-RAD (0.5)
V2L2 (0.1)+W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.5)
V2L2 (0.1)+W4-RAD (1.0)
R347 (2.1)
W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.5)
V2L2 (0.1)+W4-RAD (1.0)
V2L2 (2.0)
W4-RAD (0.5)
R347 (2.1)
W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.5)
V2L2 (0.1)+W4-RAD (1.0)
V2L2 (2.0)
W4-RAD (0.5)
R347 (2.1)
W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.1)
V2L2 (0.1)+W4-RAD (0.5)
V2L2 (0.1)+W4-RAD (1.0)
V2L2 (2.0)
() denotes mg/kg
6206 inoculum: 5.25e5

FIG. 15

16A.



16B.

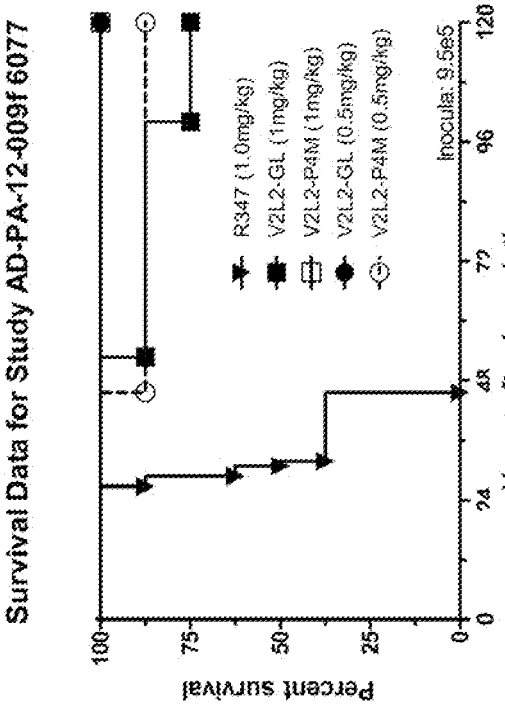
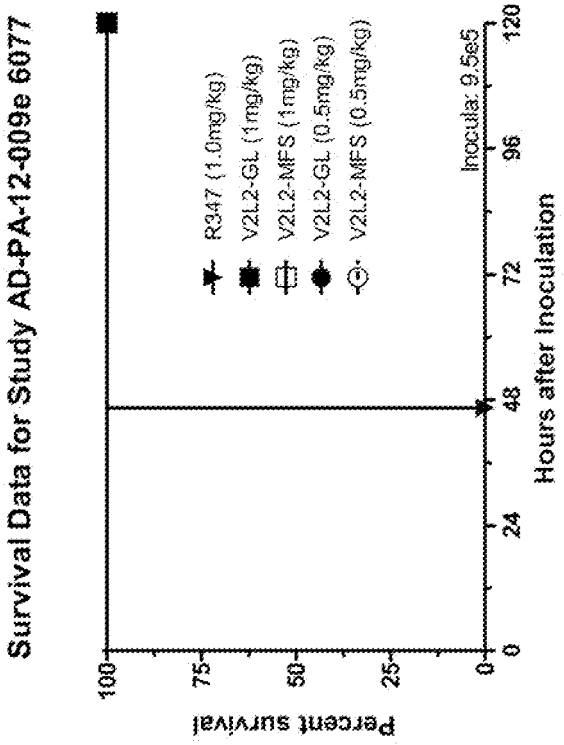


FIG. 16

16C.



16D.

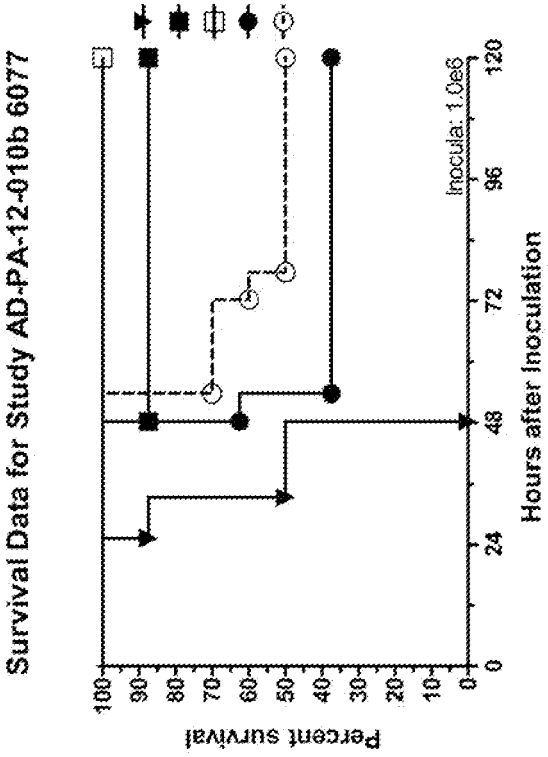
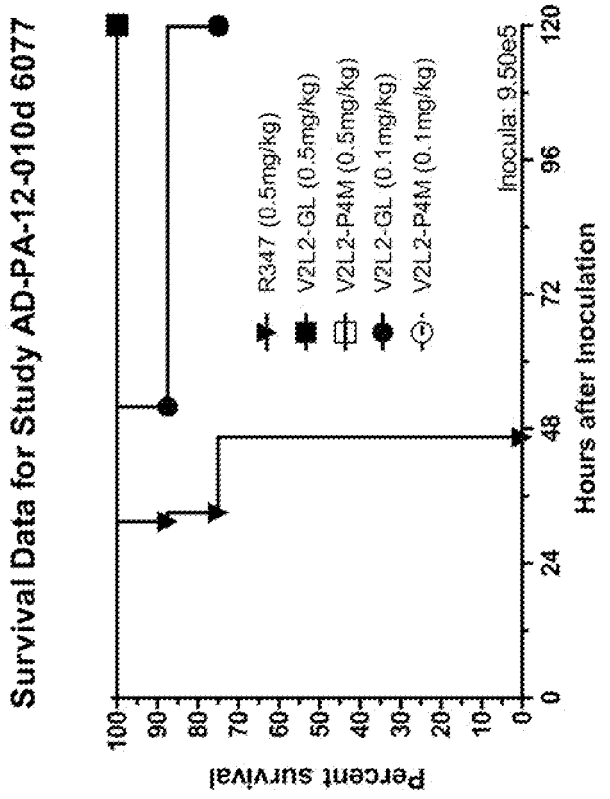


FIG. 16

16E.



16F.

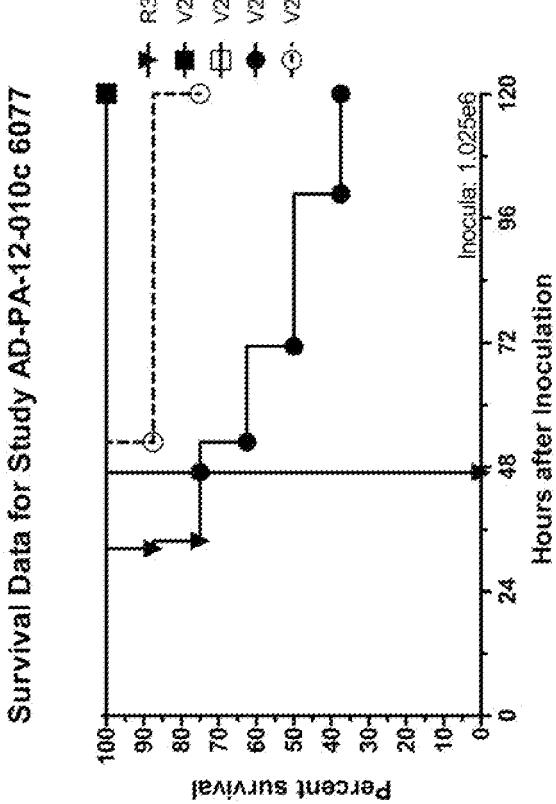


FIG. 16

16G.

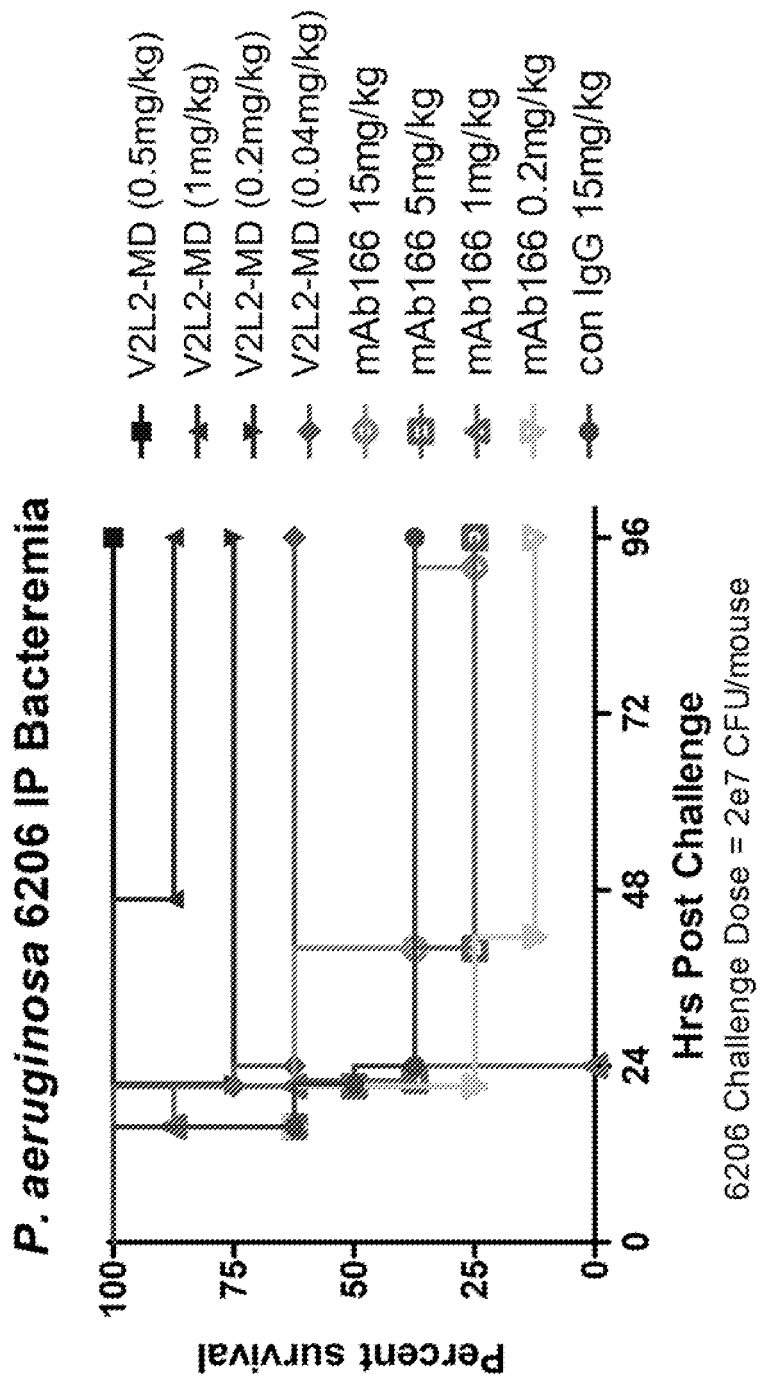

P. aeruginosa 6206 IP Bacteremia
Percent survival
100
75
50
25
0
0
24
48
72
96
Hrs Post Challenge
6206 Challenge Dose = 2e7 CFU/mouse
V2L2-MD (0.5mg/kg)
V2L2-MD (1mg/kg)
V2L2-MD (0.2mg/kg)
V2L2-MD (0.04mg/kg)
mAb166 15mg/kg
mAb166 5mg/kg
mAb166 1mg/kg
mAb166 0.2mg/kg
con IgG 15mg/kg

FIG. 16

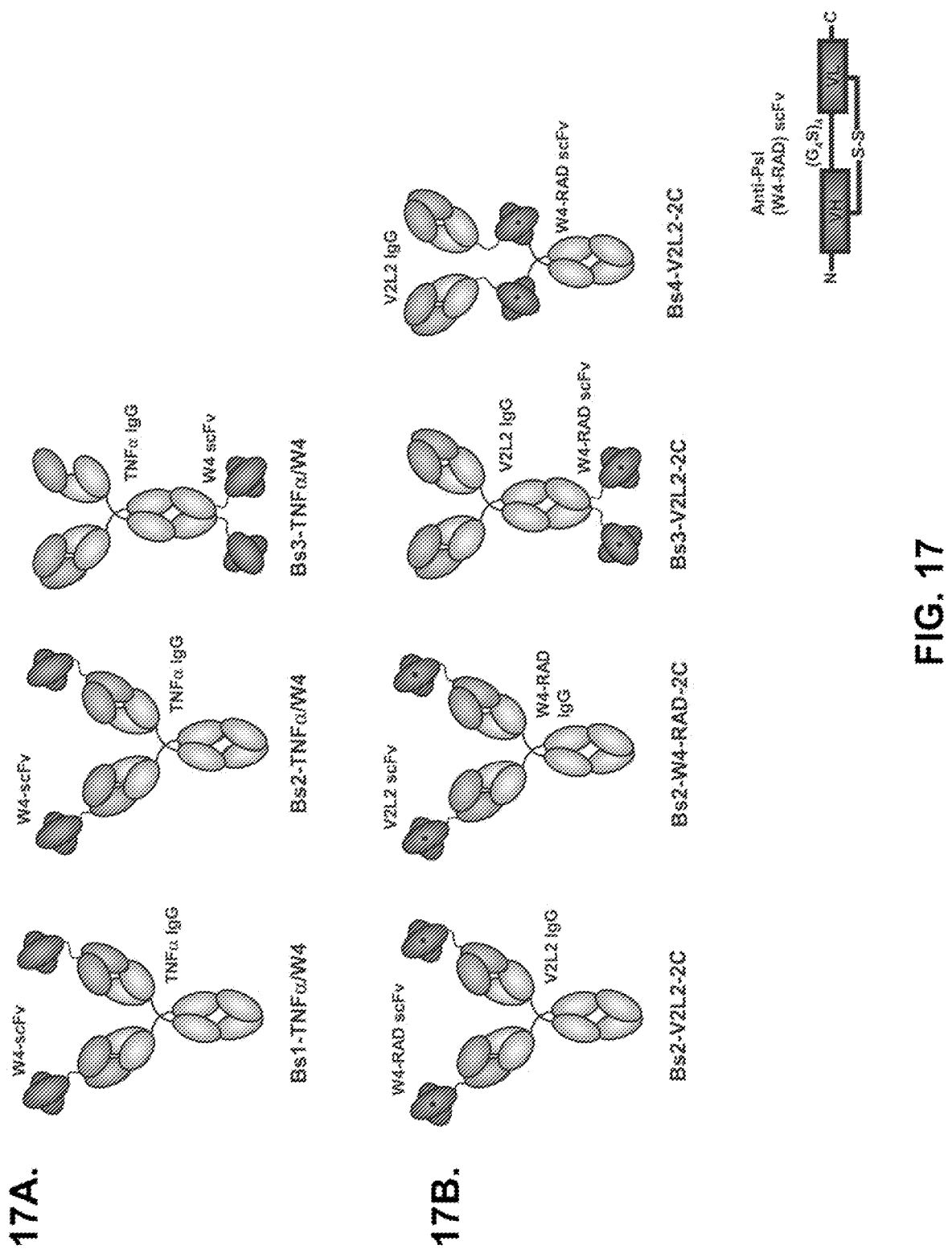

17A.
W4-scFv
TNFα IgG
Bs1-TNFα/W4
W4-scFv
TNFα IgG
Bs2-TNFα/W4
TNFα IgG
W4 scFv
Bs3-TNFα/W4
17B.
W4-RAD scFv
V2L2 IgG
Bs2-V2L2-2C
V2L2 scFv
W4-RAD IgG
Bs2-W4-RAD-2C
V2L2 IgG
W4-RAD scFv
Bs3-V2L2-2C
V2L2 IgG
W4-RAD scFv
Bs4-V2L2-2C
Anti-Psl (W4-RAD) scFv
(G4S)3
S-S
N
C

FIG. 17

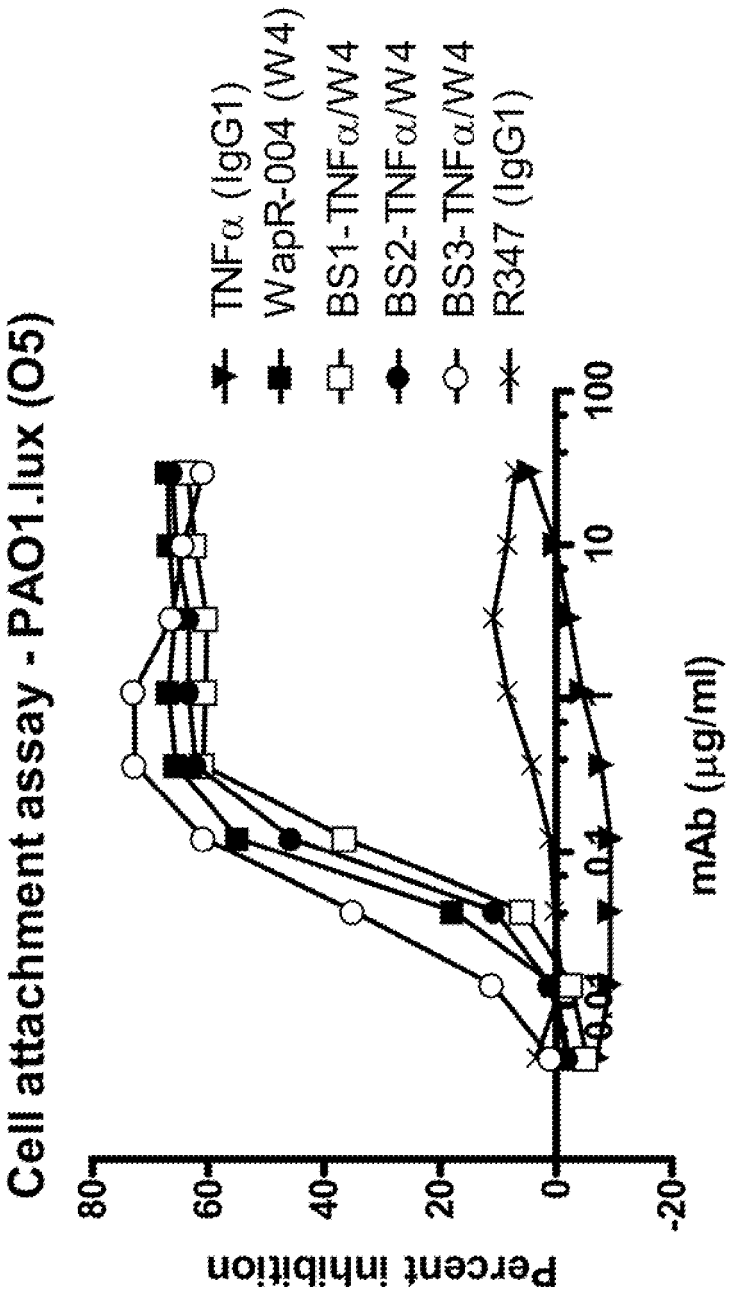

Cell attachment assay - PAO1.lux (O5)
TNFα (IgG1)
WapR-004 (W4)
BS1-TNFα/W4
BS2-TNFα/W4
BS3-TNFα/W4
R347 (IgG1)
Percent inhibition
80
60
40
20
0
-20
0.01
0.1
1
10
100
mAb (μg/ml)

FIG. 18

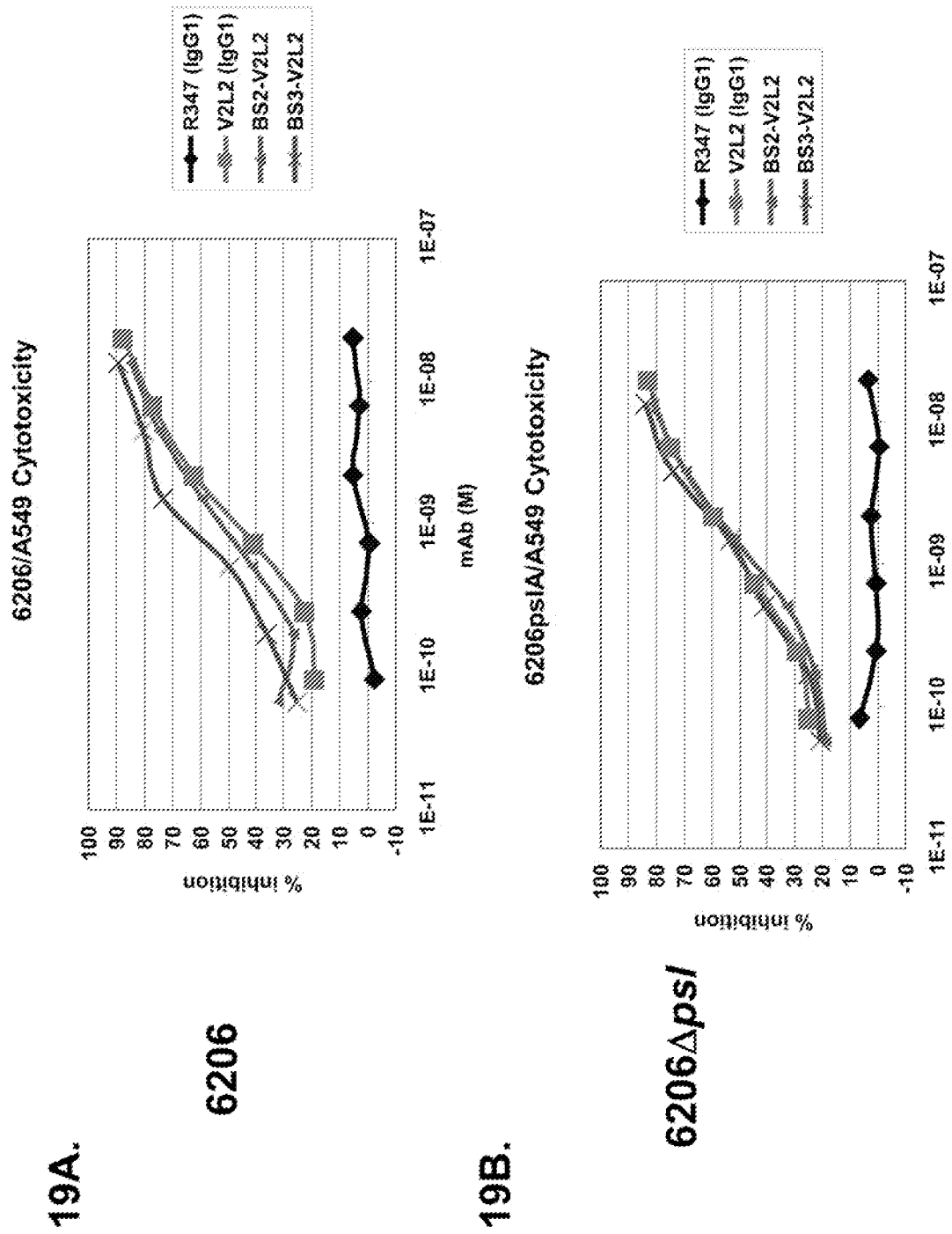

19A.
6206
6206/A549 Cytotoxicity
R347 (IgG1)
V2L2 (IgG1)
BS2-V2L2
BS3-V2L2
% inhibition
100
90
80
70
60
50
40
30
20
10
0
-10
1E-11
1E-10
1E-09
1E-08
1E-07
mAb (M)
19B.
6206Δpsl
6206pslA/A549 Cytotoxicity
R347 (IgG1)
V2L2 (IgG1)
BS2-V2L2
BS3-V2L2
% inhibition
100
90
80
70
60
50
40
30
20
10
0
-10
1E-11
1E-10
1E-09
1E-08
1E-07
mAb (M)

FIG. 19

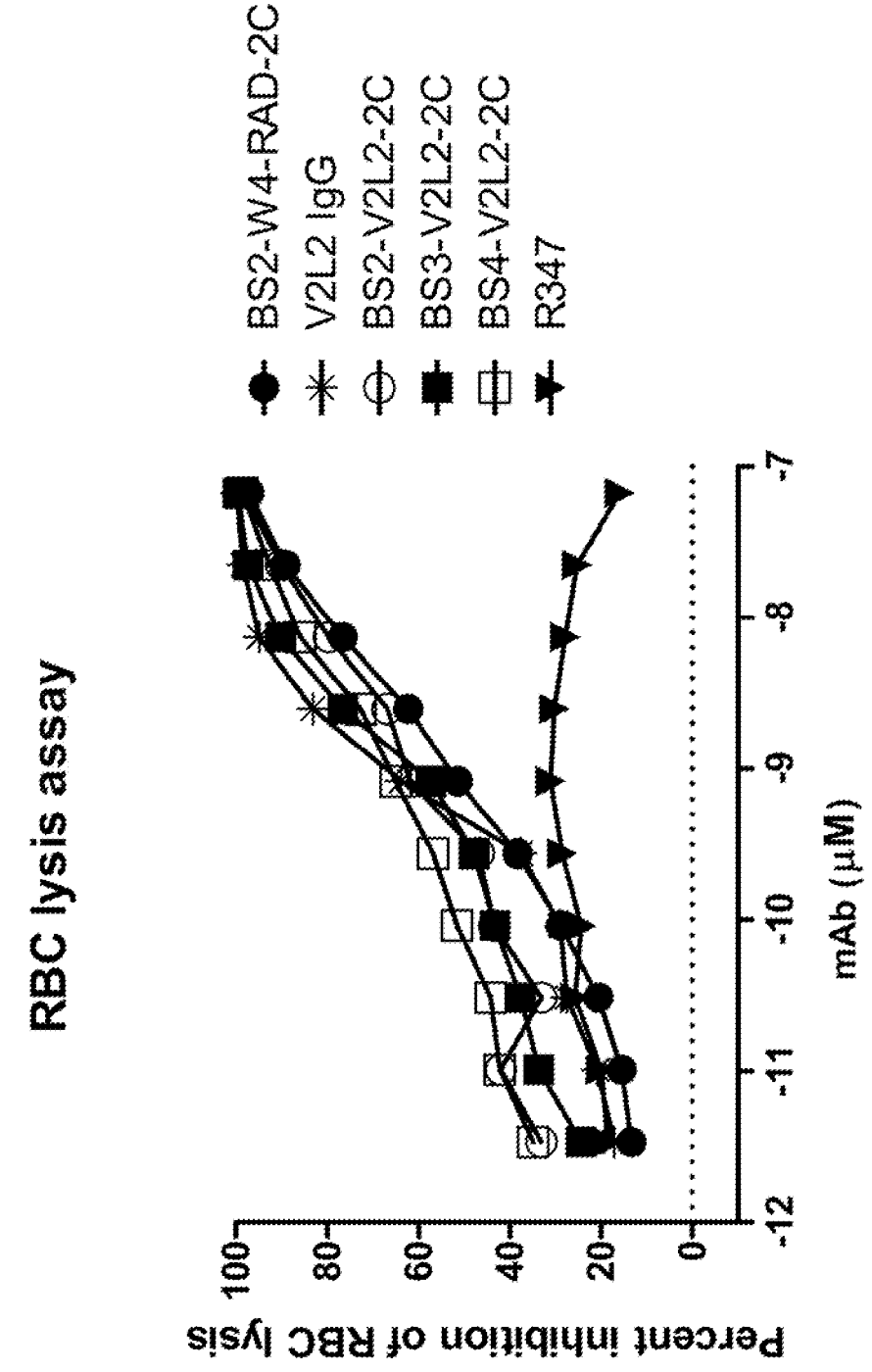

19C.
RBC lysis assay
BS2-W4-RAD-2C
V2L2 IgG
BS2-V2L2-2C
BS3-V2L2-2C
BS4-V2L2-2C
R347
Percent inhibition of RBC lysis
100
80
60
40
20
0
-12
-11
-10
-9
-8
-7
mAb (μM)

FIG. 19

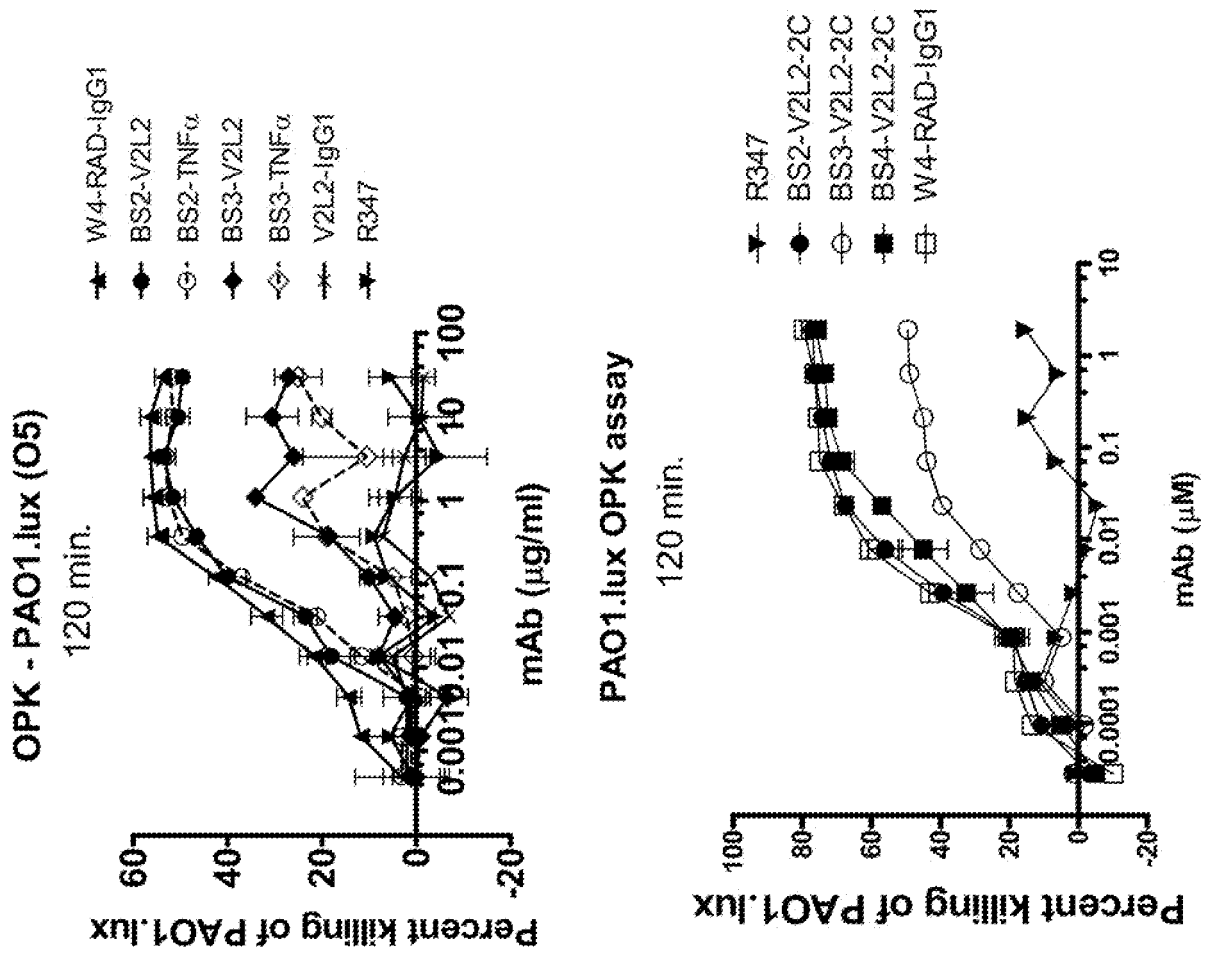
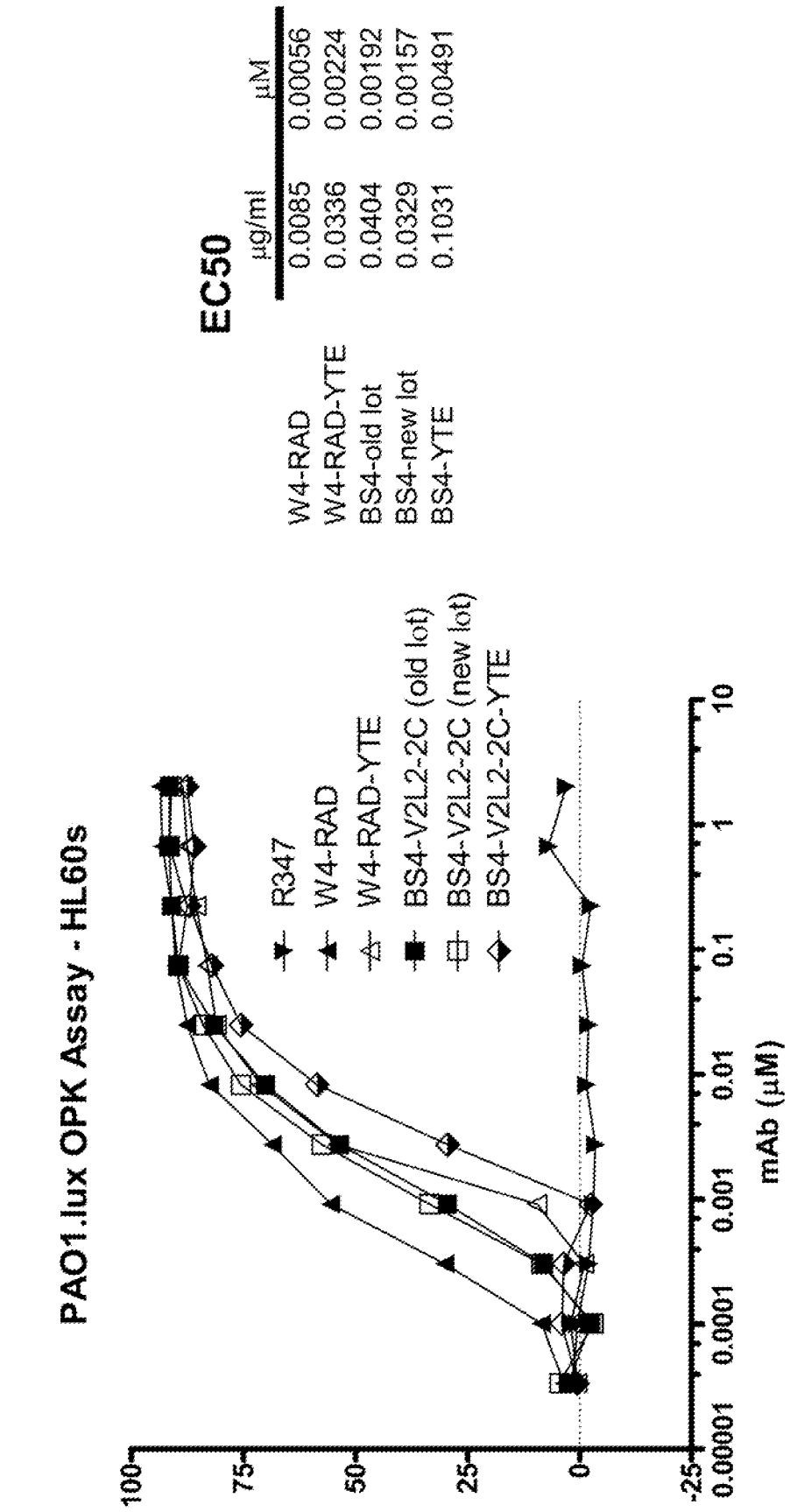

20A.
OPK - PAO1.lux (O5)
120 min.
W4-RAD-IgG1
BS2-V2L2
BS2-TNFα
BS3-V2L2
BS3-TNFα
V2L2-IgG1
R347
Percent killing of PAO1.lux
mAb (µg/ml)
20B.
PAO1.lux OPK assay
120 min.
R347
BS2-V2L2-2C
BS3-V2L2-2C
BS4-V2L2-2C
W4-RAD-IgG1
Percent killing of PAO1.lux
mAb (µM)

FIG. 20

20C.



EC50

	μg/ml	μM
W4-RAD	0.0085	0.00056
W4-RAD-YTE	0.0336	0.00224
BS4-old lot	0.0404	0.00192
BS4-new lot	0.0329	0.00157
BS4-YTE	0.1031	0.00491

FIG. 20

21A.

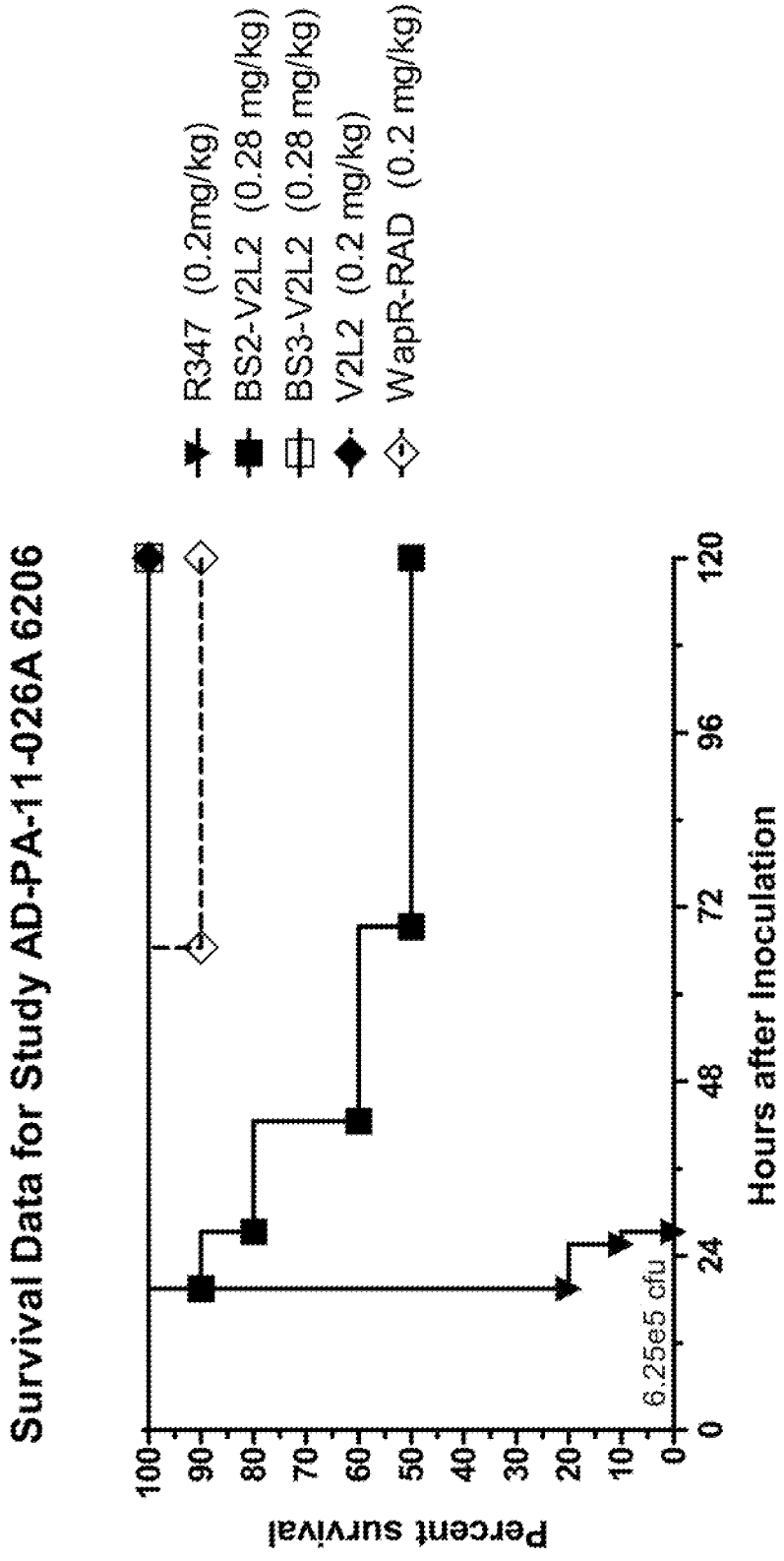

Survival Data for Study AD-PA-11-026A 6206
R347 (0.2mg/kg)
BS2-V2L2 (0.28 mg/kg)
BS3-V2L2 (0.28 mg/kg)
V2L2 (0.2 mg/kg)
WapR-RAD (0.2 mg/kg)
Percent survival
100
90
80
70
60
50
40
30
20
10
0
6.25e5 cfu
0
24
48
72
96
120
Hours after Inoculation

FIG. 21

21B.

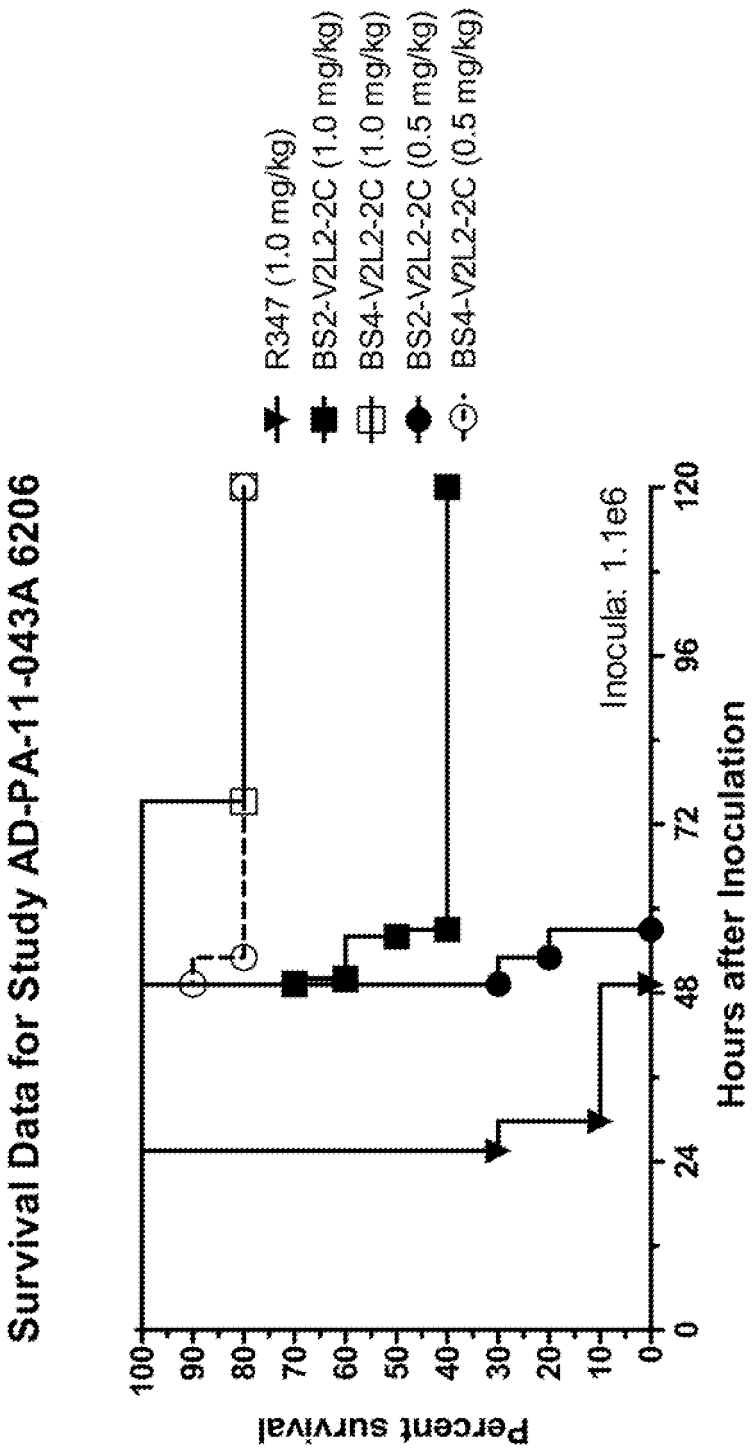
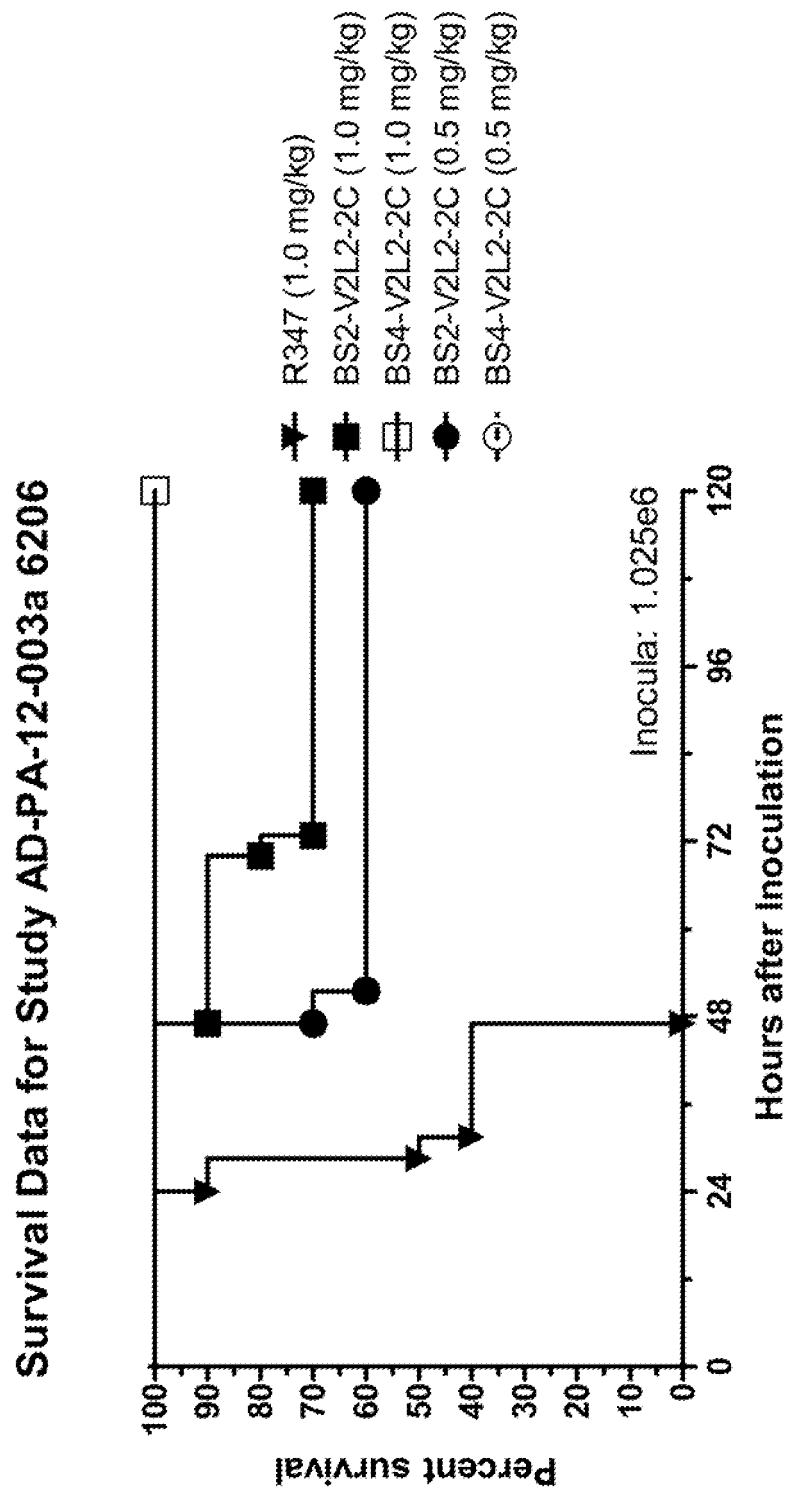

Survival Data for Study AD-PA-11-043A 6206
R347 (1.0 mg/kg)
BS2-V2L2-2C (1.0 mg/kg)
BS4-V2L2-2C (1.0 mg/kg)
BS2-V2L2-2C (0.5 mg/kg)
BS4-V2L2-2C (0.5 mg/kg)
Inocula: 1.1e6
Percent survival
Hours after Inoculation
100
90
80
70
60
50
40
30
20
10
0
0
24
48
72
96
120

FIG. 21


Survival Data for Study AD-PA-12-003a 6206
Percent survival
Hours after inoculation
Inocula: 1.025e6
R347 (1.0 mg/kg)
BS2-V2L2-2C (1.0 mg/kg)
BS4-V2L2-2C (1.0 mg/kg)
BS2-V2L2-2C (0.5 mg/kg)
BS4-V2L2-2C (0.5 mg/kg)
0
10
20
30
40
50
60
70
80
90
100
0
24
48
72
96
120

21C.

FIG. 21

21D.

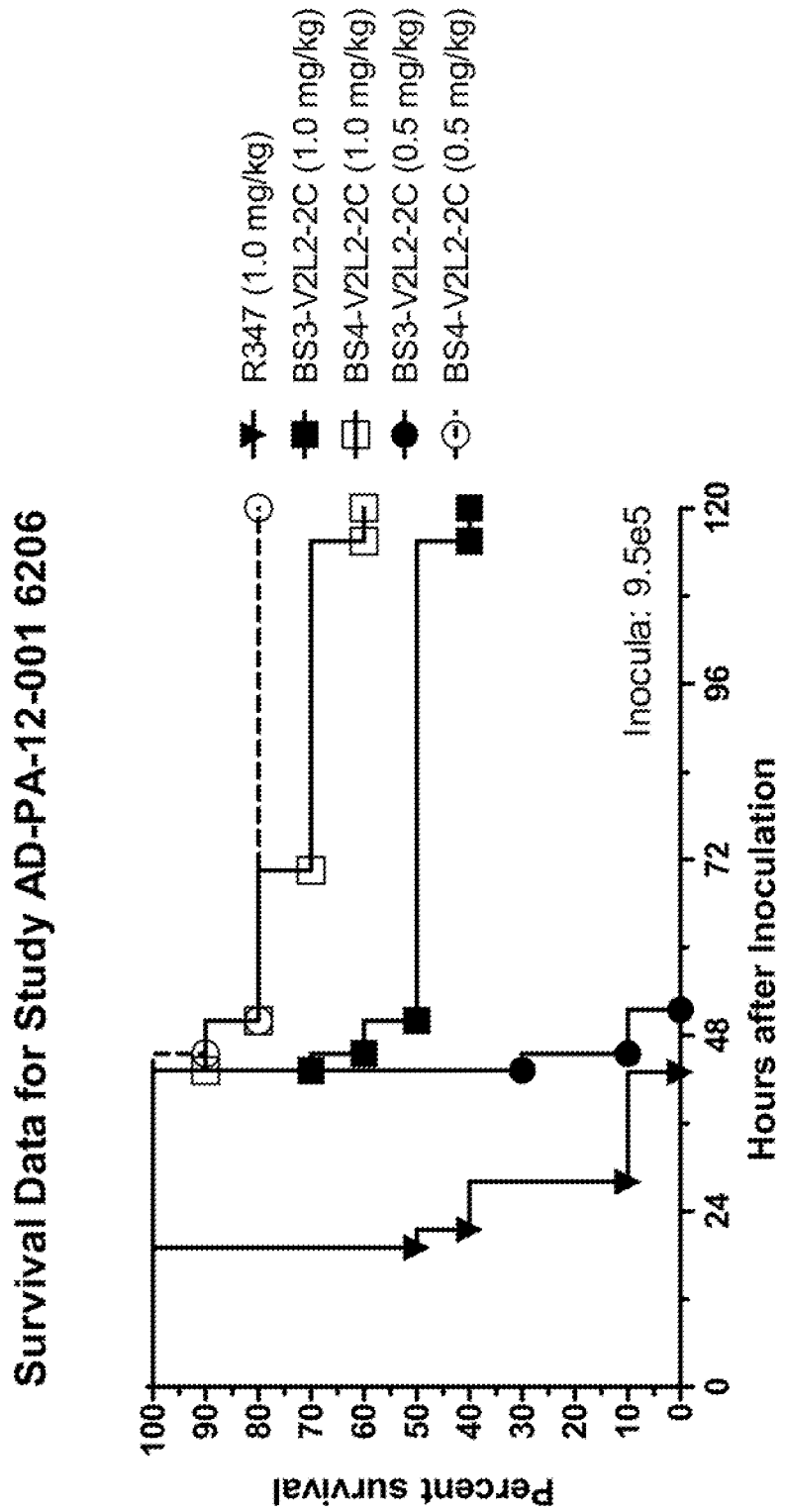
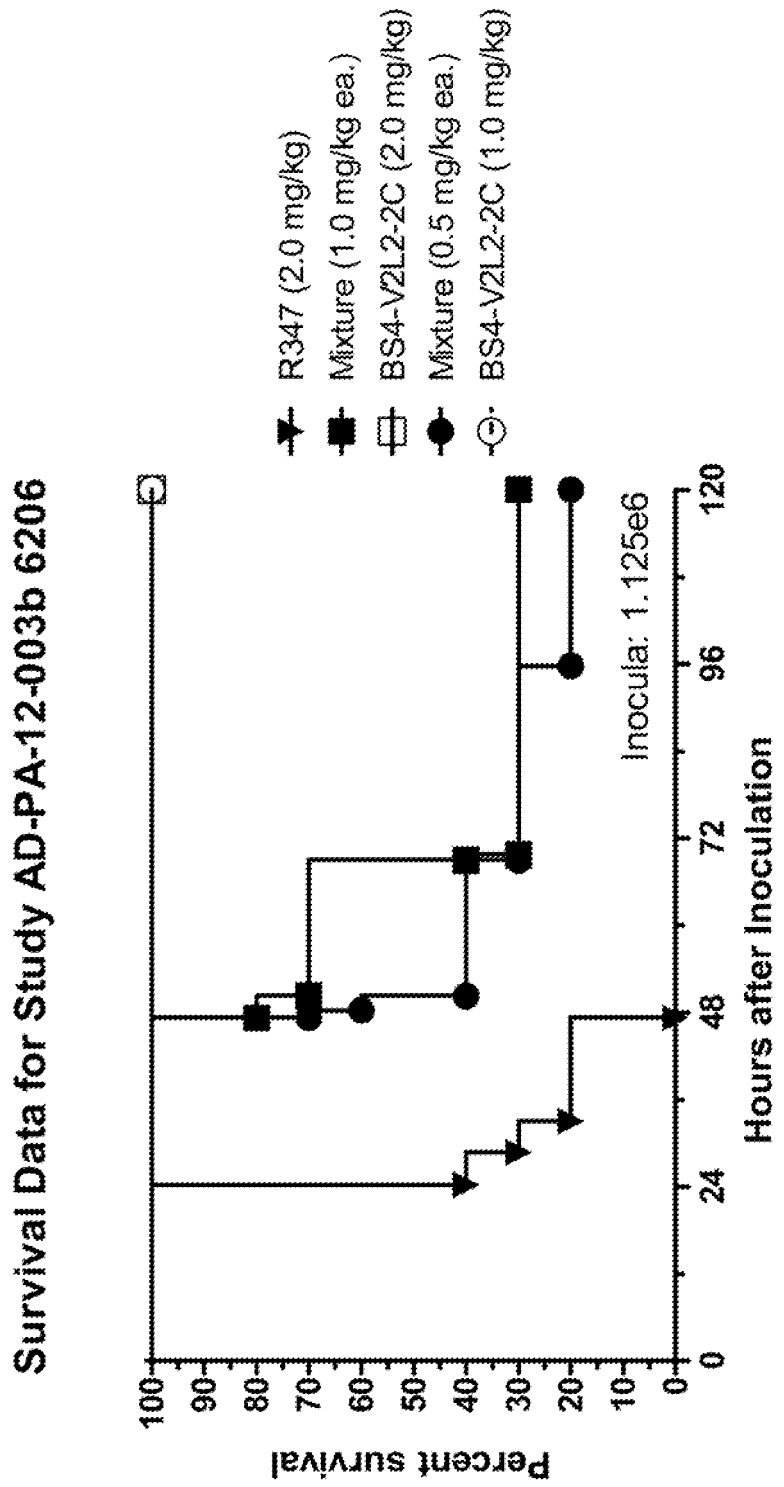

Survival Data for Study AD-PA-12-001 6206
R347 (1.0 mg/kg)
BS3-V2L2-2C (1.0 mg/kg)
BS4-V2L2-2C (1.0 mg/kg)
BS3-V2L2-2C (0.5 mg/kg)
BS4-V2L2-2C (0.5 mg/kg)
Inocula: 9.5e5
Percent survival
Hours after Inoculation
100
90
80
70
60
50
40
30
20
10
0
0
24
48
72
96
120

FIG. 21


Survival Data for Study AD-PA-12-003b 6206
R347 (2.0 mg/kg)
Mixture (1.0 mg/kg ea.)
BS4-V2L2-2C (2.0 mg/kg)
Mixture (0.5 mg/kg ea.)
BS4-V2L2-2C (1.0 mg/kg)
Inocula: 1.125e6
Percent survival
Hours after Inoculation
0
10
20
30
40
50
60
70
80
90
100
0
24
48
72
96
120

21E.

FIG. 21

21F.

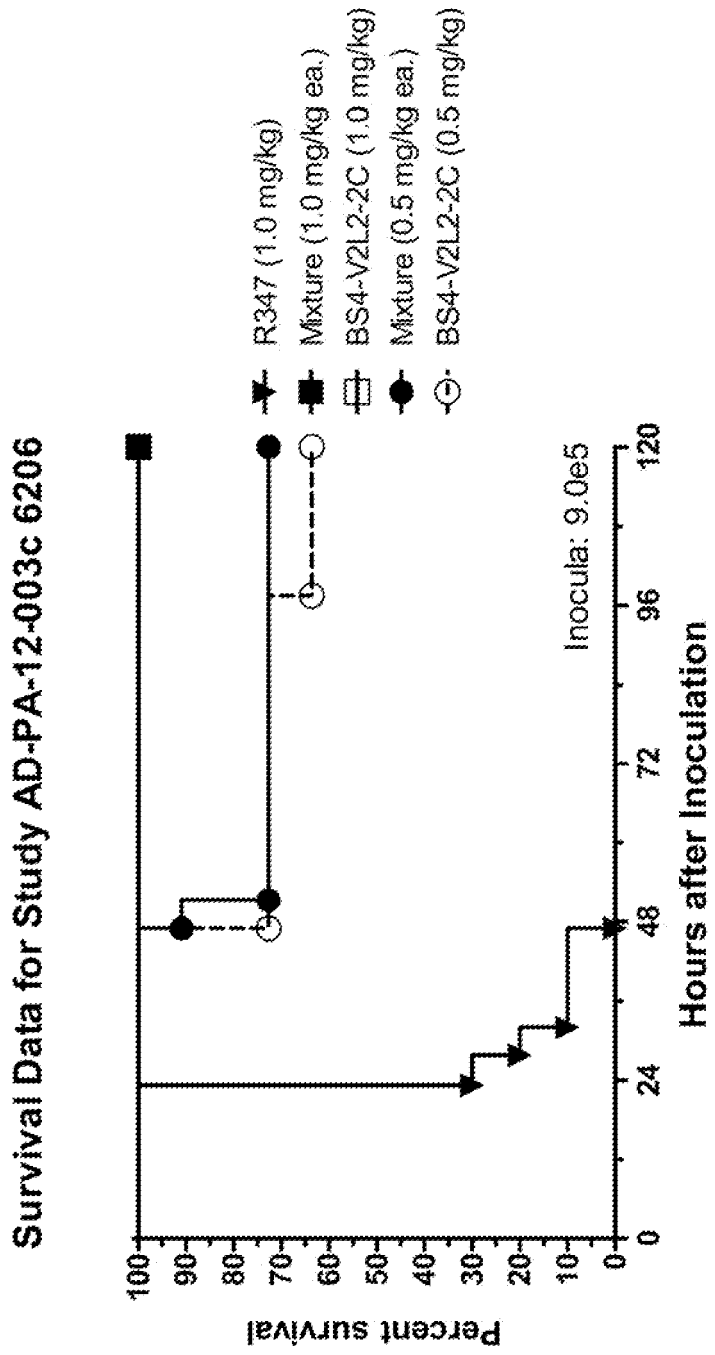

Survival Data for Study AD-PA-12-003c 6206
R347 (1.0 mg/kg)
Mixture (1.0 mg/kg ea.)
BS4-V2L2-2C (1.0 mg/kg)
Mixture (0.5 mg/kg ea.)
BS4-V2L2-2C (0.5 mg/kg)
Inocula: 9.0e5
Percent survival
100
90
80
70
60
50
40
30
20
10
0
0
24
48
72
96
120
Hours after Inoculation

FIG. 21

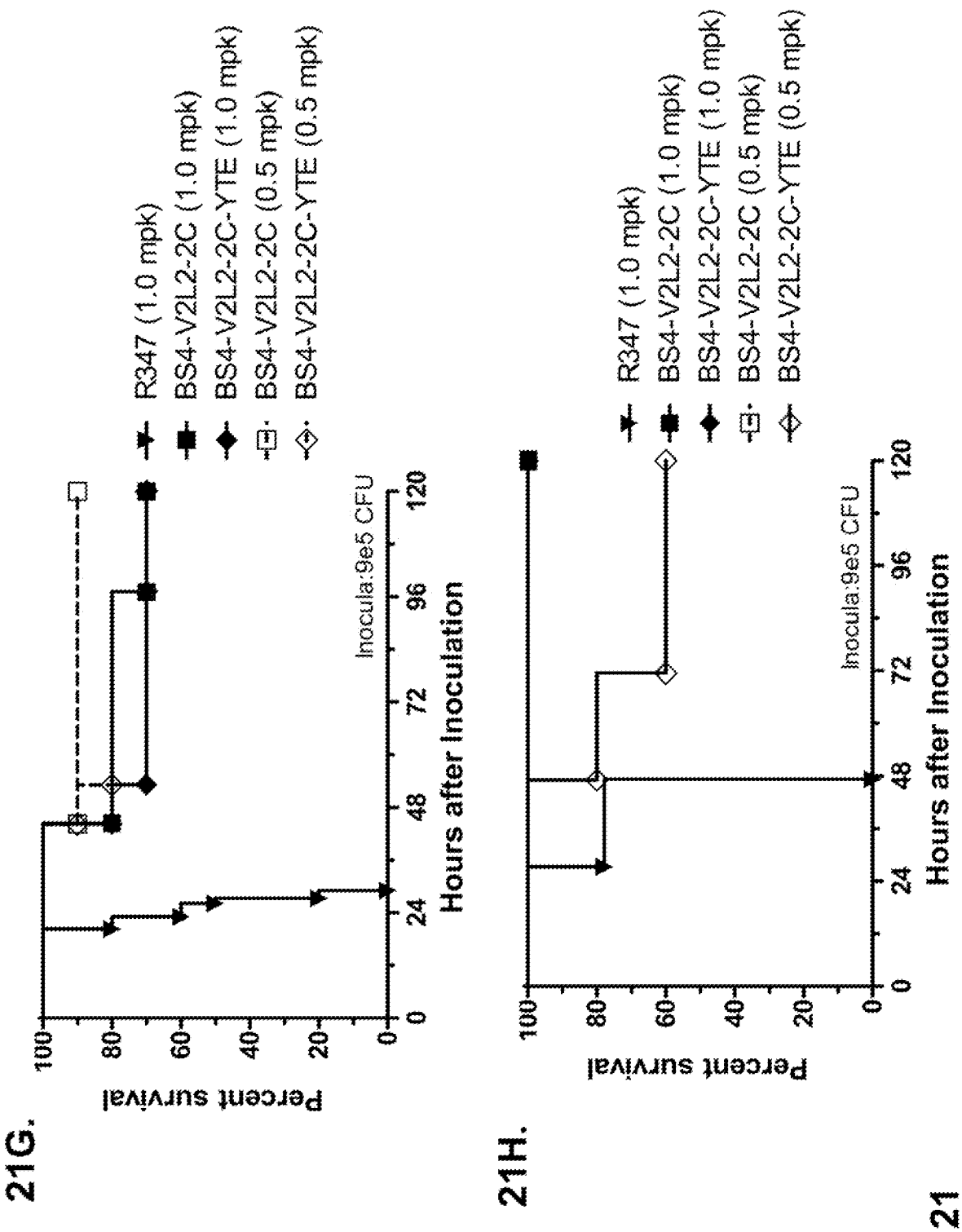

21G.
Percent survival
100
80
60
40
20
0
0
24
48
72
96
120
Hours after Inoculation
Inocula:9e5 CFU
R347 (1.0 mpk)
BS4-V2L2-2C (1.0 mpk)
BS4-V2L2-2C-YTE (1.0 mpk)
BS4-V2L2-2C (0.5 mpk)
BS4-V2L2-2C-YTE (0.5 mpk)
21H.
Percent survival
100
80
60
40
20
0
0
24
48
72
96
120
Hours after Inoculation
Inocula:9e5 CFU
R347 (1.0 mpk)
BS4-V2L2-2C (1.0 mpk)
BS4-V2L2-2C-YTE (1.0 mpk)
BS4-V2L2-2C (0.5 mpk)
BS4-V2L2-2C-YTE (0.5 mpk)

FIG. 21

21I.

Percent protection against lethal pneumonia in mice challenged with *P. aeruginosa* strain 6206 (O11-ExoU$^+$)

	Antibody concentration (mg/kg)							
Antibody	15	10	5	2	1	0.5	0.2	0.1
BS2-V2L2[&]	100 (10)	-	100 (10)	-	67 (30)	40 (30)	-	-
BS2-V2L2-2C			90 (20)		25 (20)	0 (20)	0 (10)	
BS2-W4-RAD-2C			70 (10)		10 (10)	0 (10)	0 (10)	
BS3-V2L2-2C	-	80 (10)	40 (20)	-	10 (20)	0 (20)	0 (20)	-
BS4-V2L2-2C	-	-	100 (60)	-	88 (60)	60 (60)	10 (60)	-
V2L2	-	-	80 (10)	-	20 (10)	10 (10)	0 (10)	-
W4-RAD	0 (10)	-	0 (10)	-	0 (10)	-	-	-
	Antibody concentration (mg/kg for each mAb)							
Mixture			5	2	1	0.5	0.2	0.1
W4-RAD + V2L2	-	-	100 (10)	100 (40)	78 (40)	15 (40)	-	3 (40)

120 hr post-infection (inocula ~1.0e6 CFU/animal)
Parentheses indicate total number of animals
[&]1mg/kg and 0.5mg/kg includes studies where animals were treated with 1.7 and 0.55mg/kg, respectively

FIG. 21

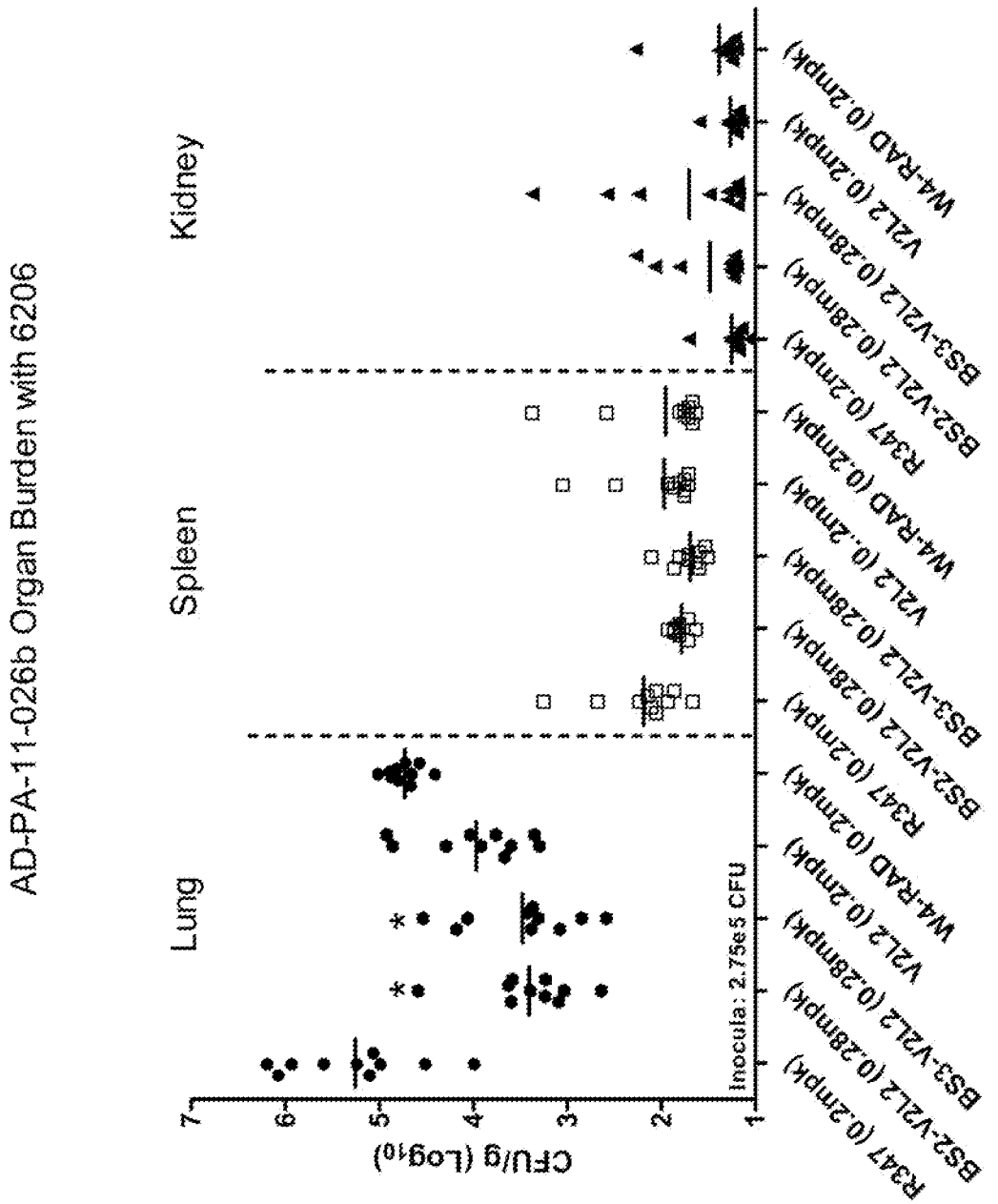
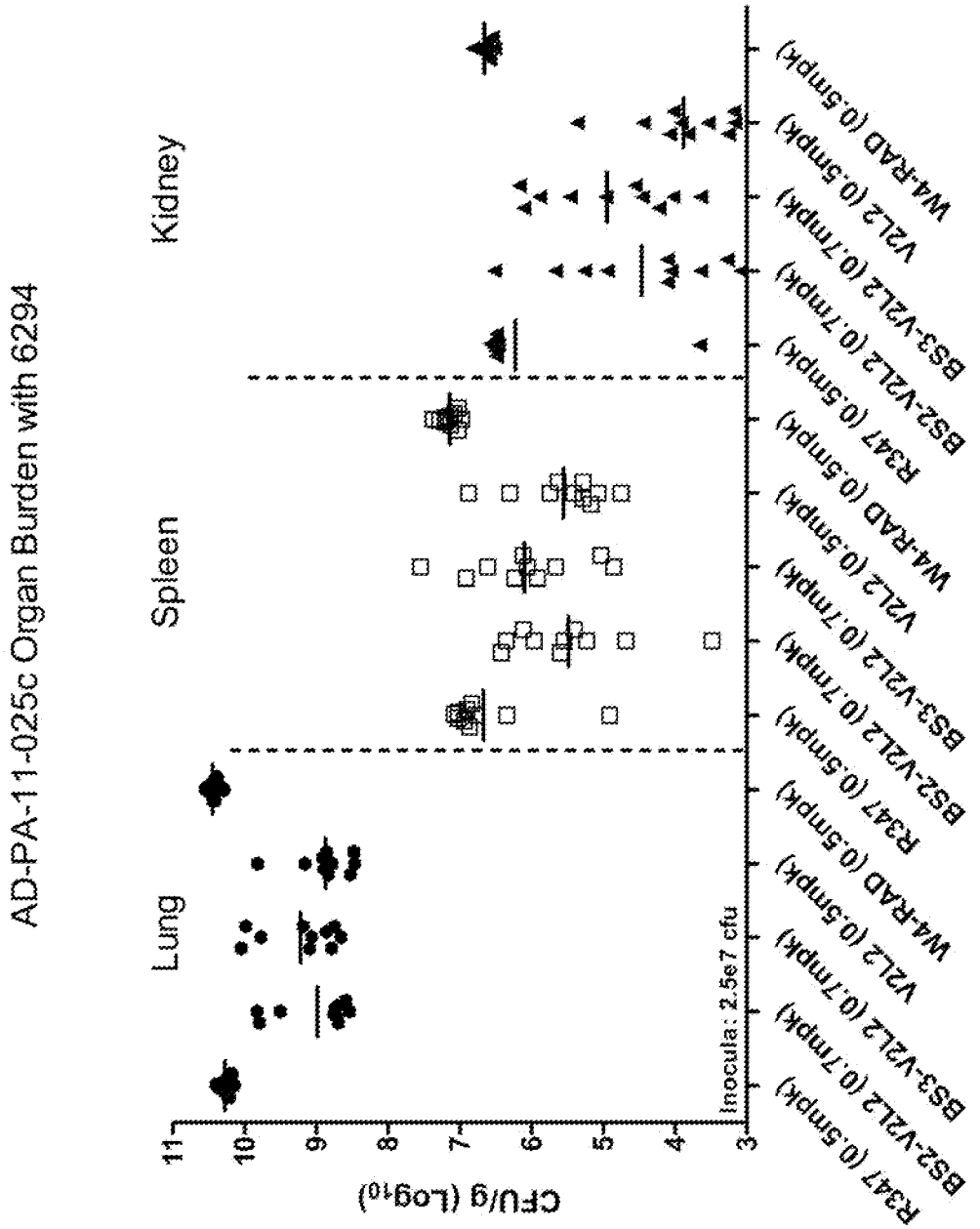

AD-PA-11-026b Organ Burden with 6206
Lung
Spleen
Kidney
CFU/g (Log10)
7
6
5
4
3
2
1
Inocula: 2.75e5 CFU
R347 (0.2mpk)
BS2-V2L2 (0.28mpk)
BS3-V2L2 (0.28mpk)
V2L2 (0.28mpk)
WA-RAD (0.2mpk)
R347 (0.2mpk)
BS2-V2L2 (0.28mpk)
BS3-V2L2 (0.28mpk)
V2L2 (0..2mpk)
WA-RAD (0.2mpk)
R347 (0.2mpk)
BS2-V2L2 (0.28mpk)
BS3-V2L2 (0.28mpk)
V2L2 (0.28mpk)
WA-RAD (0.2mpk)

FIG. 22


AD-PA-11-025c Organ Burden with 6294
Lung
Spleen
Kidney
CFU/g (Log10)
11
10
9
8
7
6
5
4
3
Inocula: 2.5e7 cfu
R347 (0.5mpk)
BS2-V2L2 (0.7mpk)
BS3-V2L2 (0.7mpk)
V2L2 (0.5mpk)
WA-RAD (0.5mpk)
R347 (0.5mpk)
BS2-V2L2 (0.7mpk)
BS3-V2L2 (0.7mpk)
V2L2 (0.5mpk)
WA-RAD (0.5mpk)
R347 (0.5mpk)
BS2-V2L2 (0.7mpk)
BS3-V2L2 (0.7mpk)
V2L2 (0.5mpk)
WA-RAD (0.5mpk)

23A.

FIG. 23

23B.

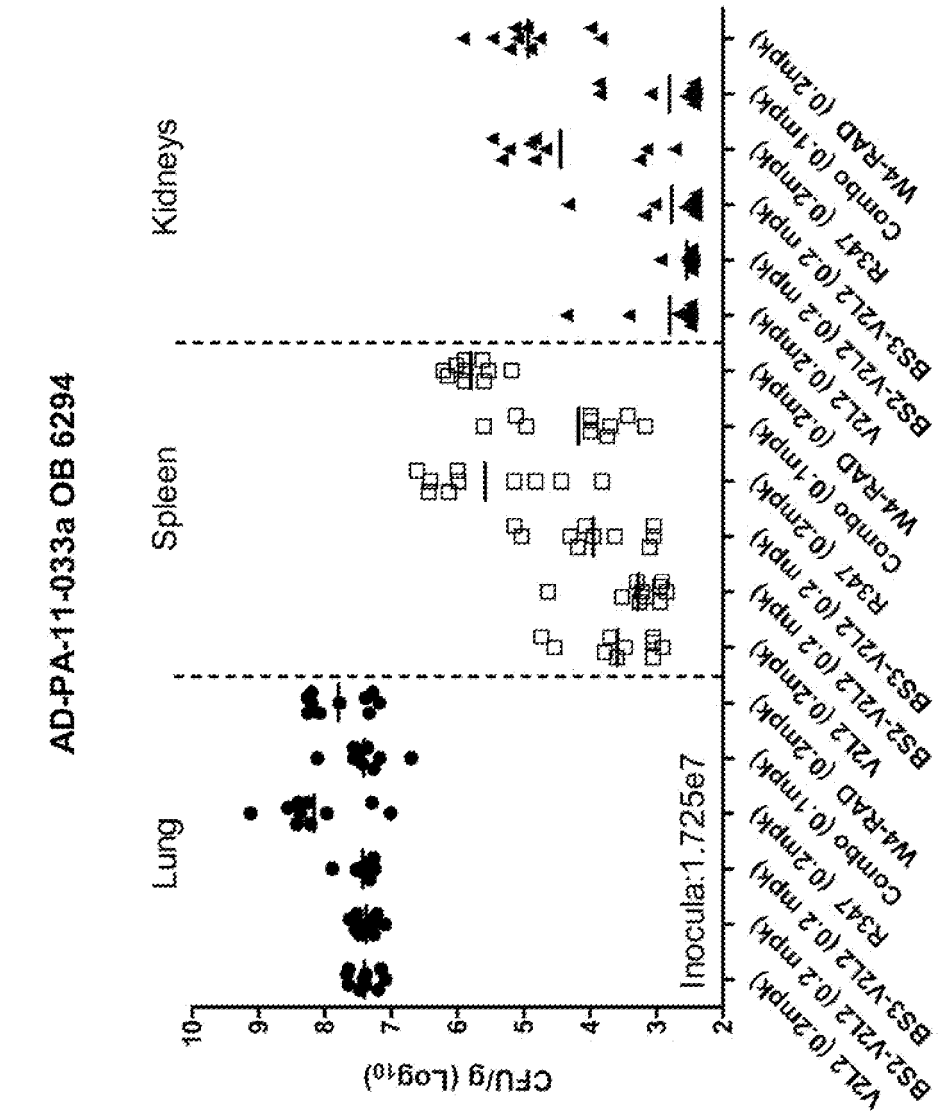

AD-PA-11-033a OB 6294
Lung
Spleen
Kidneys
CFU/g (Log10)
10
9
8
7
6
5
4
3
2
Inocula:1.725e7
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2mpk)
Combo (0.1mpk)
W4-RAD (0.2mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2mpk)
Combo (0.1mpk)
W4-RAD (0.2mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2mpk)
Combo (0.1mpk)
W4-RAD (0.2mpk)

FIG. 23

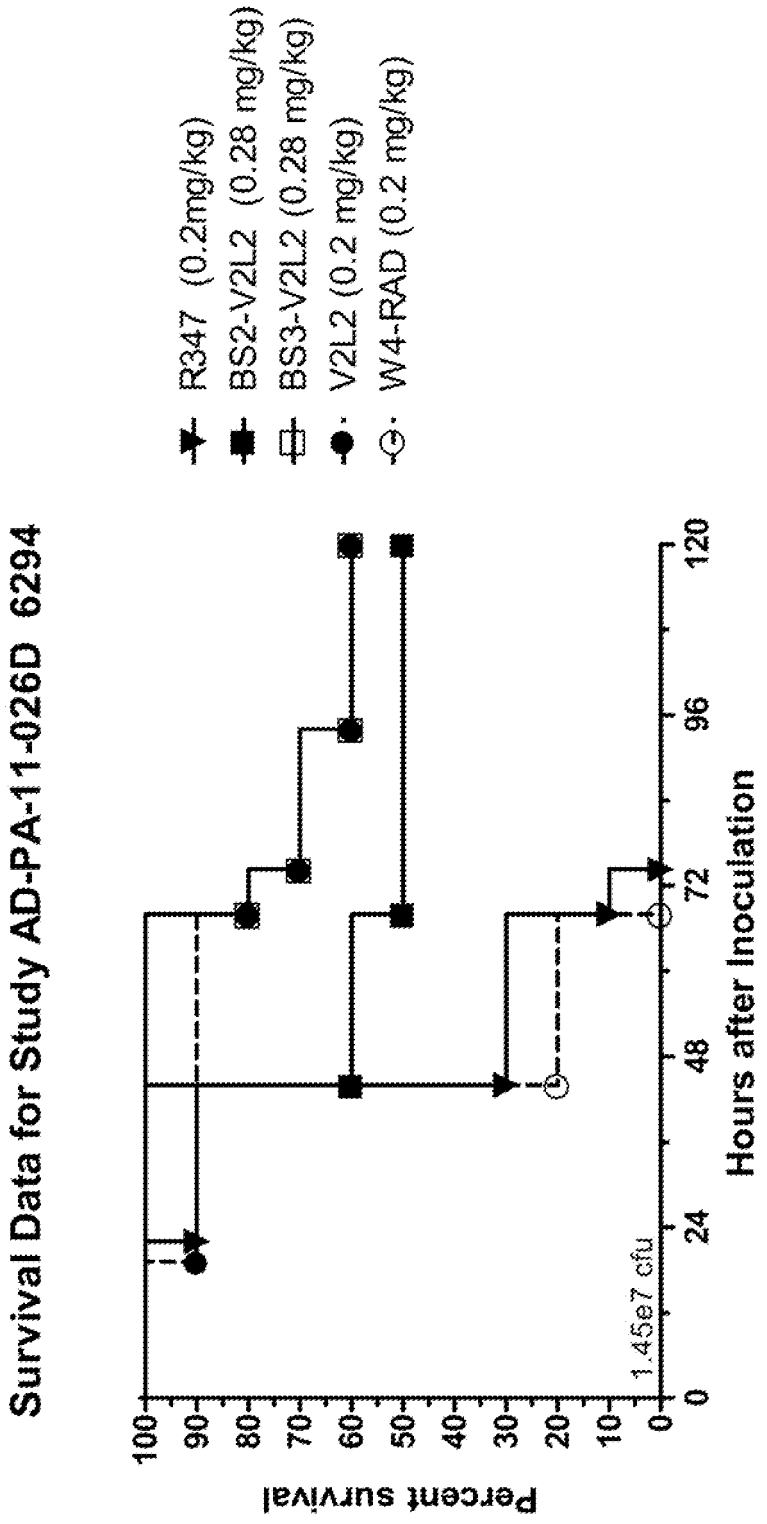
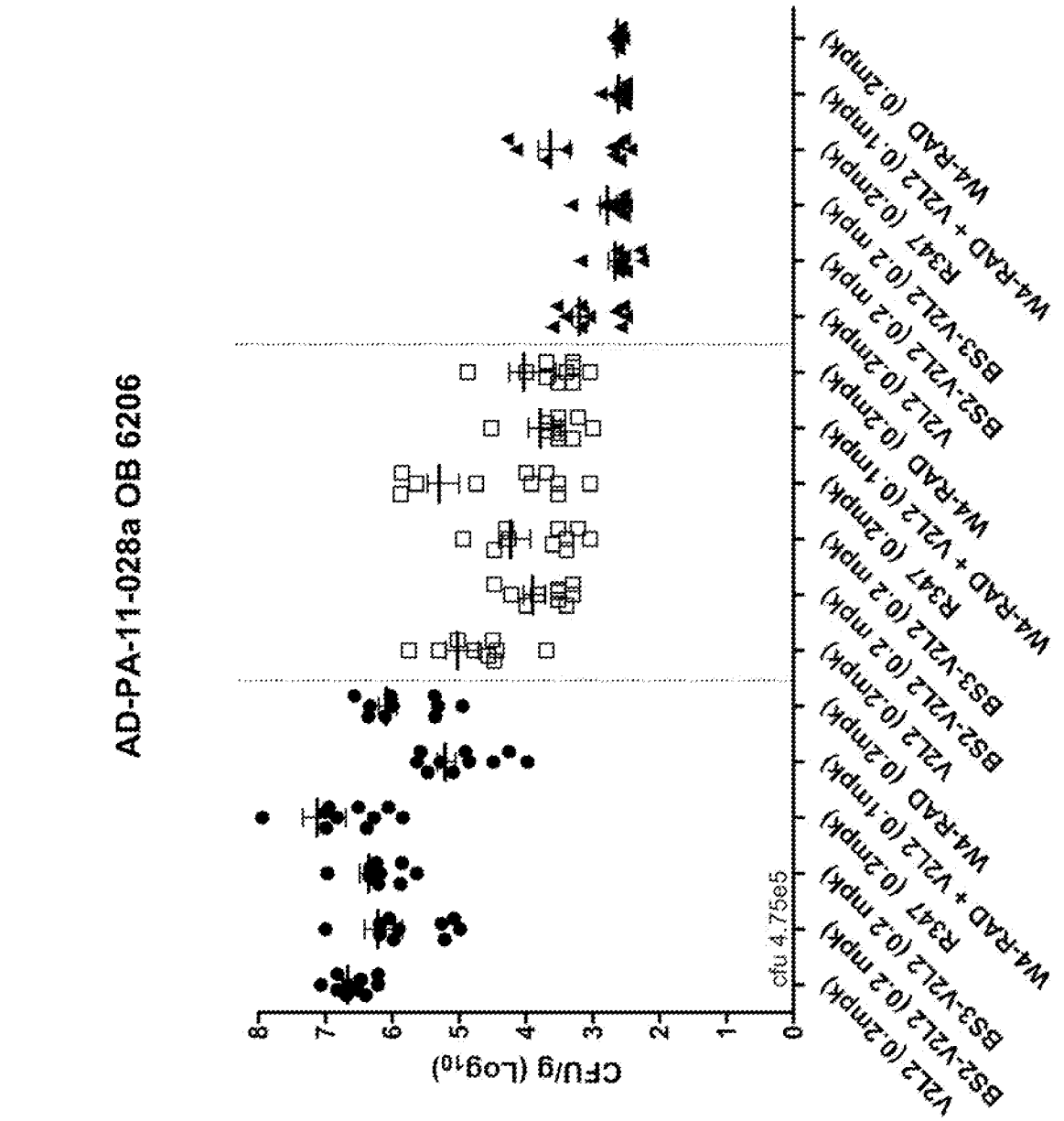

Survival Data for Study AD-PA-11-026D 6294
R347 (0.2mg/kg)
BS2-V2L2 (0.28 mg/kg)
BS3-V2L2 (0.28 mg/kg)
V2L2 (0.2 mg/kg)
W4-RAD (0.2 mg/kg)
Percent survival
Hours after Inoculation
1.45e7 cfu
0
10
20
30
40
50
60
70
80
90
100
0
24
48
72
96
120

FIG. 24


AD-PA-11-028a OB 6206
CFU/g (Log10)
8
7
6
5
4
3
2
1
0
cfu 4.75e5
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
W4-RAD + V2L2 (0.2mpk)
W4-RAD + V2L2 (0.1mpk)
W4-RAD (0.2mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
W4-RAD + V2L2 (0.2mpk)
W4-RAD + V2L2 (0.1mpk)
W4-RAD (0.2mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
W4-RAD + V2L2 (0.2mpk)
W4-RAD + V2L2 (0.1mpk)
W4-RAD (0.2mpk)

25A.

FIG. 25

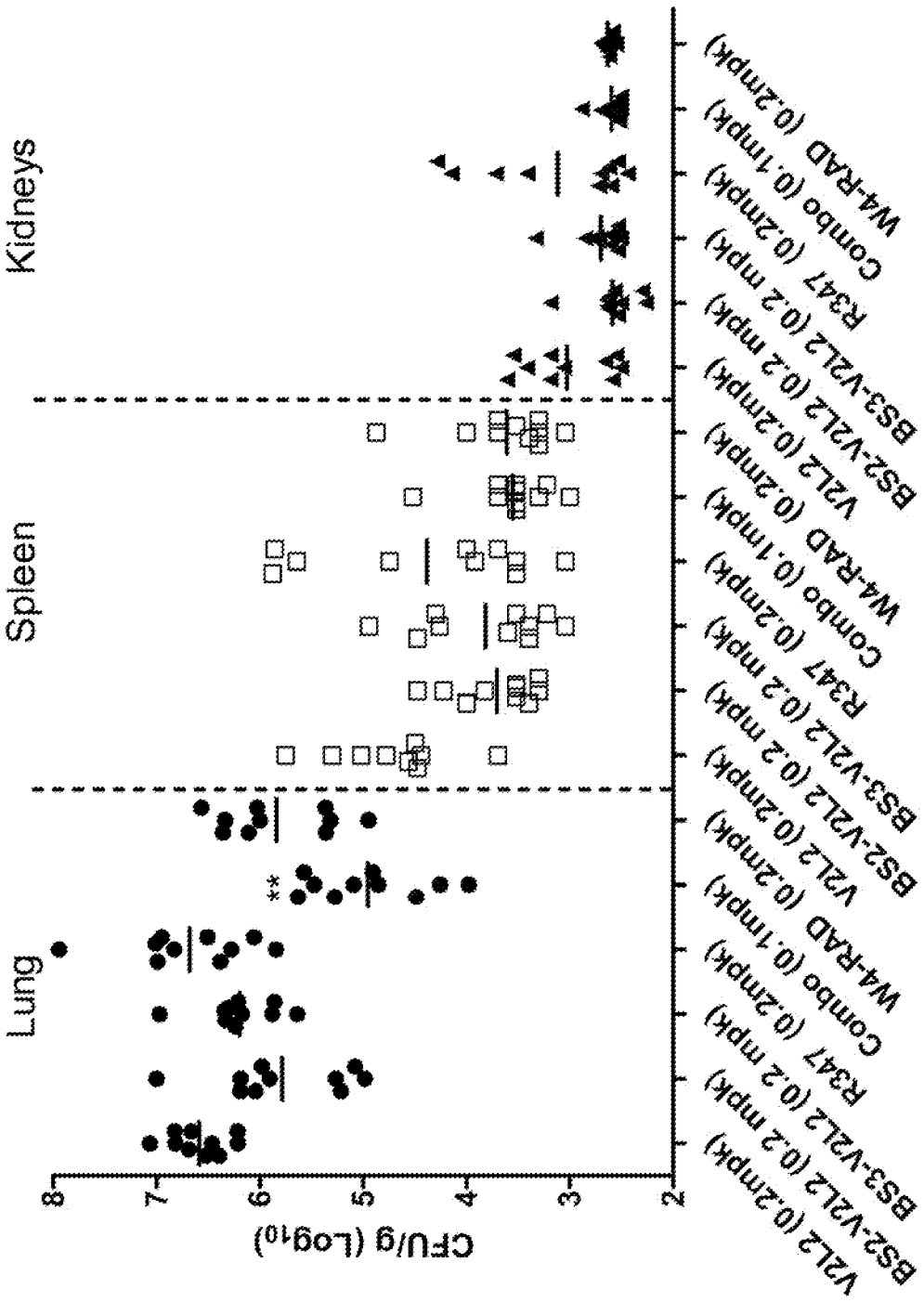
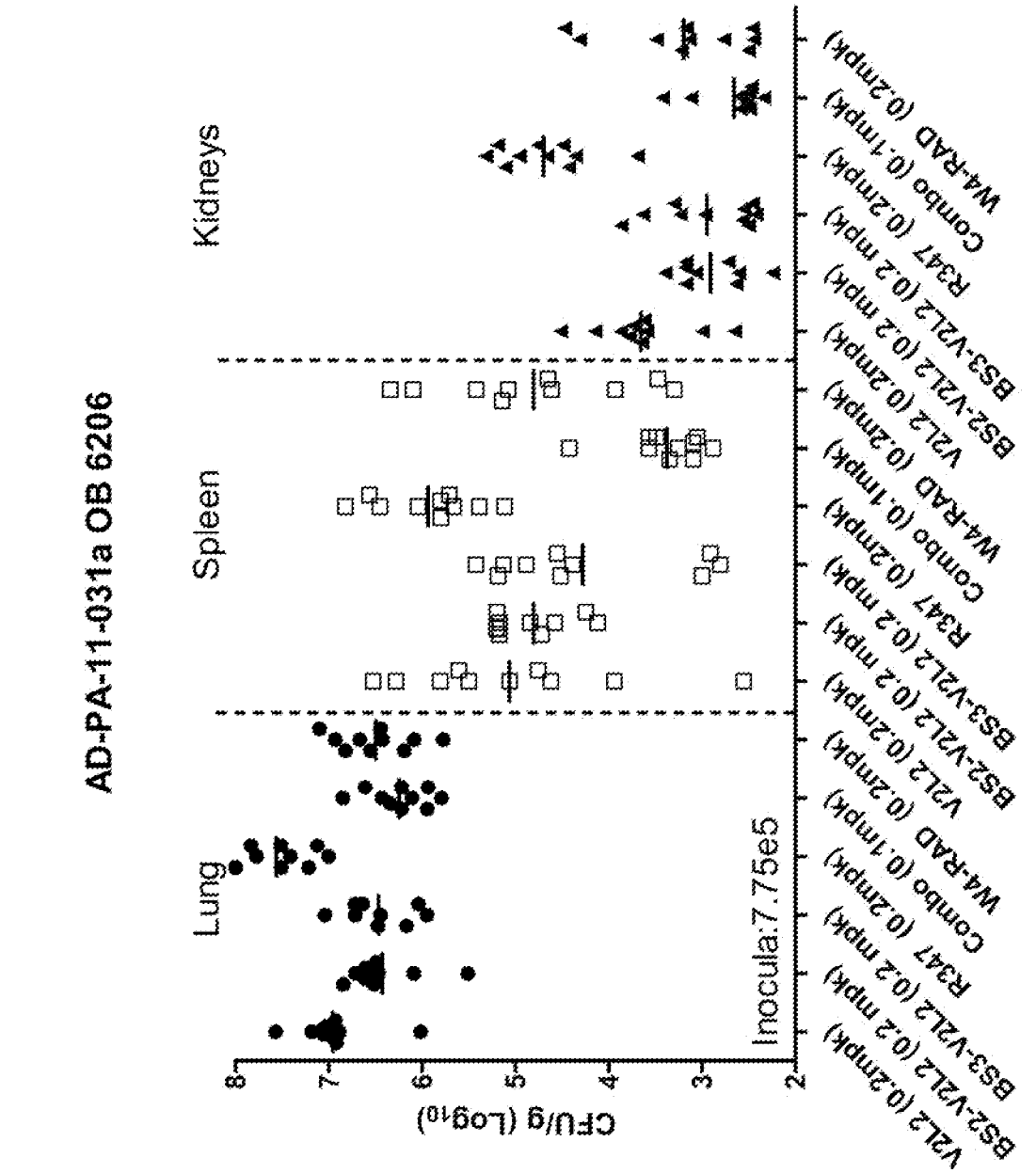

AD-PA-11-028a OB 6206
25B.
Lung
Spleen
Kidneys
CFU/g (Log10)
8
7
6
5
4
3
2
**
V2L2 (0.2mpk)
BS2-V2L2 (0.2mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
Combo (0.2mpk)
W4-RAD (0.1mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2 mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
Combo (0.2mpk)
W4-RAD (0.1mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2 mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
Combo (0.2mpk)
W4-RAD (0.1mpk)
V2L2 (0.2mpk)
BS2-V2L2 (0.2 mpk)
BS3-V2L2 (0.2 mpk)
R347 (0.2 mpk)
Combo (0.2mpk)
W4-RAD (0.1mpk)

FIG. 25


AD-PA-11-031a OB 6206
Lung
Spleen
Kidneys
CFU/g (Log10)
8
7
6
5
4
3
2
Inocula:7.75e5
V2L2 (0.2mpk)
B52-V2L2 (0.2 mpk)
B53-V2L2 (0.2 mpk)
R347 (0.2mpk)
Combo (0.1mpk)
W4-RAD (0.2mpk)
V2L2 (0.2mpk)
B52-V2L2 (0.2 mpk)
B53-V2L2 (0.2 mpk)
R347 (0.2mpk)
Combo (0.1mpk)
W4-RAD (0.2mpk)
V2L2 (0.2mpk)
B52-V2L2 (0.2 mpk)
B53-V2L2 (0.2 mpk)
R347 (0.2mpk)
Combo (0.1mpk)
W4-RAD (0.2mpk)

25C.

FIG. 25

25D.

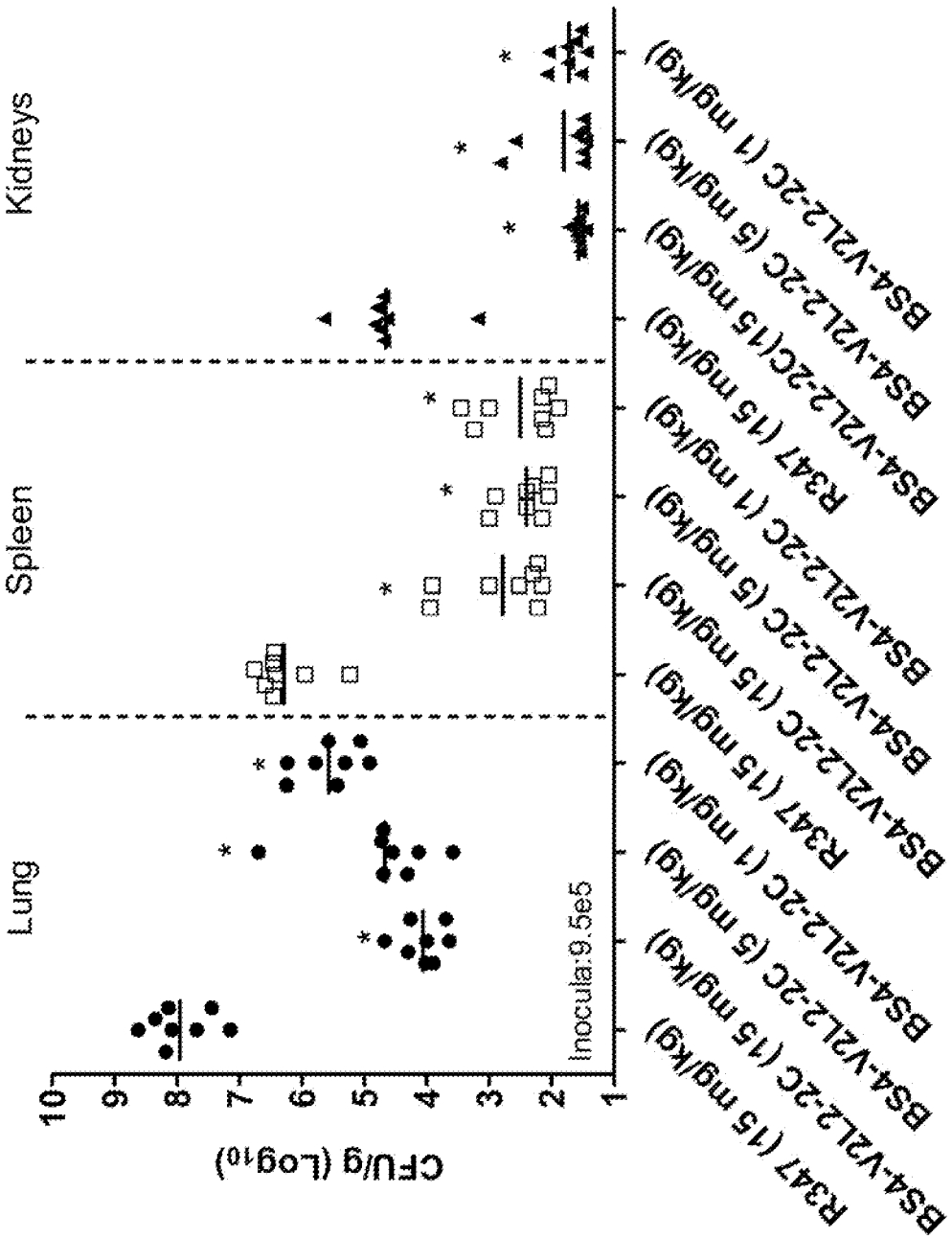

AD-PA-12-013D OB 6206 - 24hr
Lung
Spleen
Kidneys
CFU/g (Log10)
10
9
8
7
6
5
4
3
2
1
Inocula:9.5e5
R347 (15 mg/kg)
BS4-V2L2-2C (15 mg/kg)
BS4-V2L2-2C (5 mg/kg)
BS4-V2L2-2C (1 mg/kg)
R347 (15 mg/kg)
BS4-V2L2-2C (15 mg/kg)
BS4-V2L2-2C (5 mg/kg)
BS4-V2L2-2C (1 mg/kg)
R347 (15 mg/kg)
BS4-V2L2-2C (15 mg/kg)
BS4-V2L2-2C (5 mg/kg)
BS4-V2L2-2C (1 mg/kg)

FIG. 25

26A.

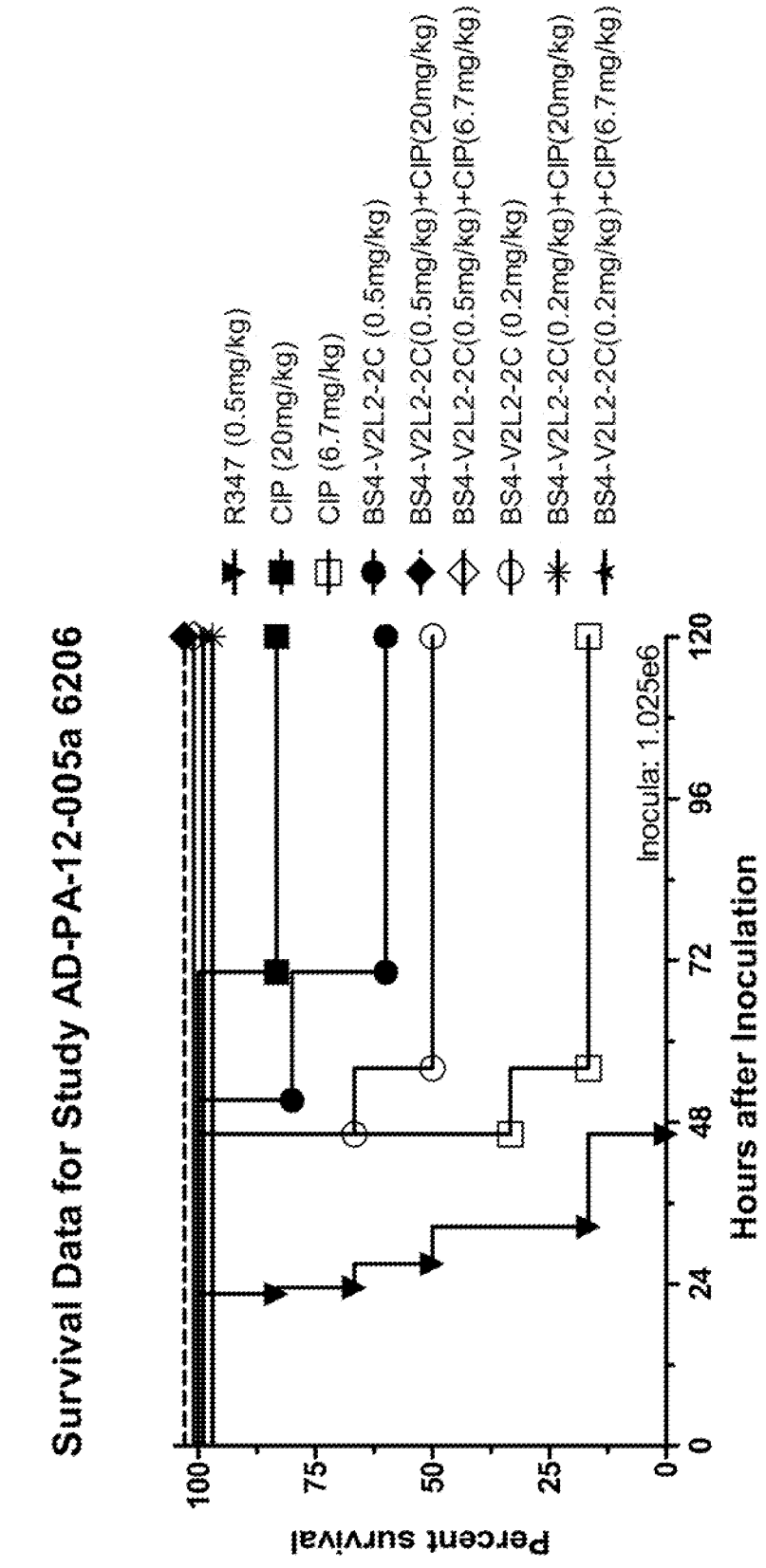

Survival Data for Study AD-PA-12-005a 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after Inoculation
Inocula: 1.025e6
R347 (0.5mg/kg)
CIP (20mg/kg)
CIP (6.7mg/kg)
BS4-V2L2-2C (0.5mg/kg)
BS4-V2L2-2C(0.5mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(0.5mg/kg)+CIP(6.7mg/kg)
BS4-V2L2-2C (0.2mg/kg)
BS4-V2L2-2C(0.2mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(0.2mg/kg)+CIP(6.7mg/kg)

FIG. 26

26B.

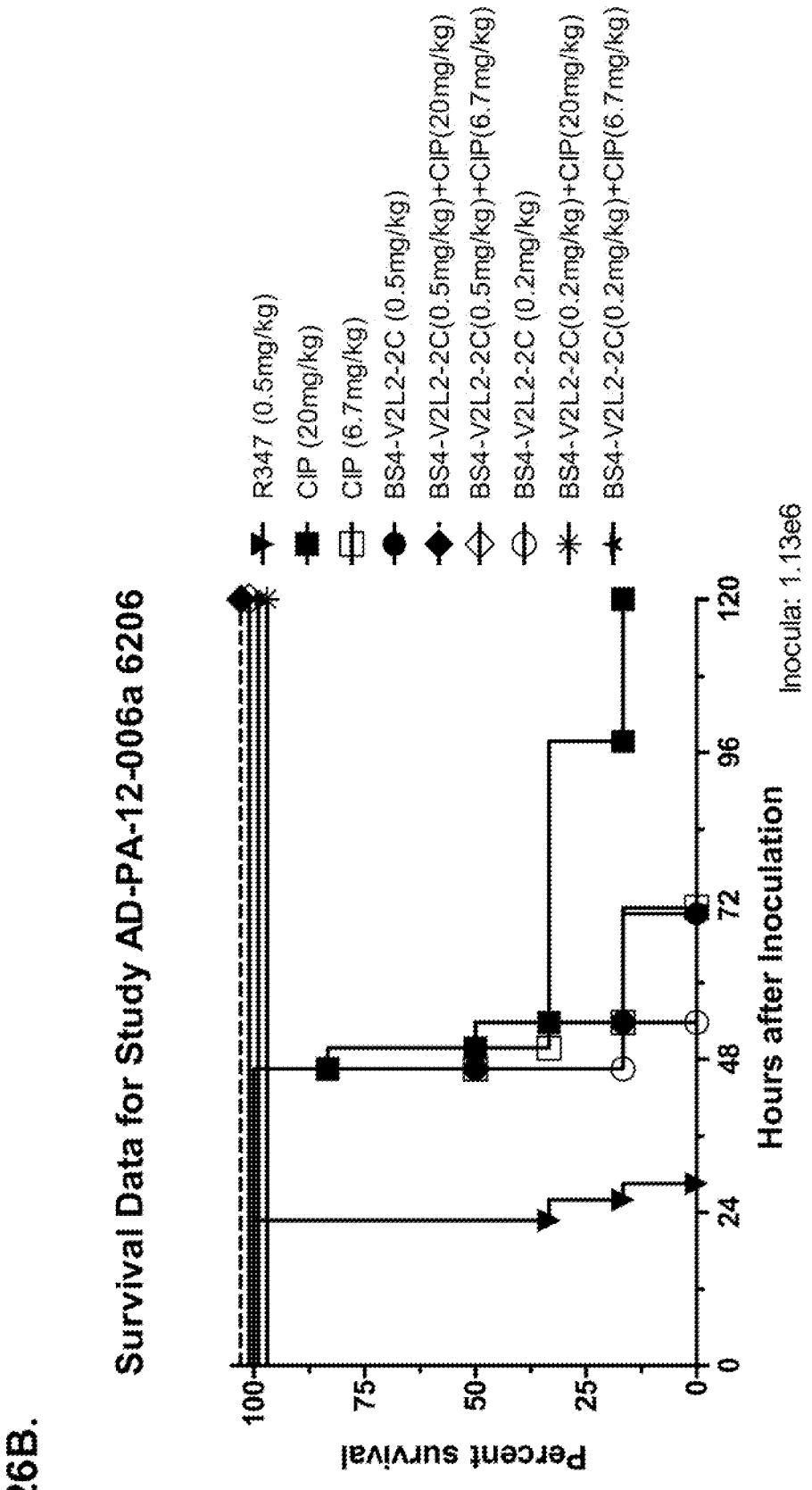
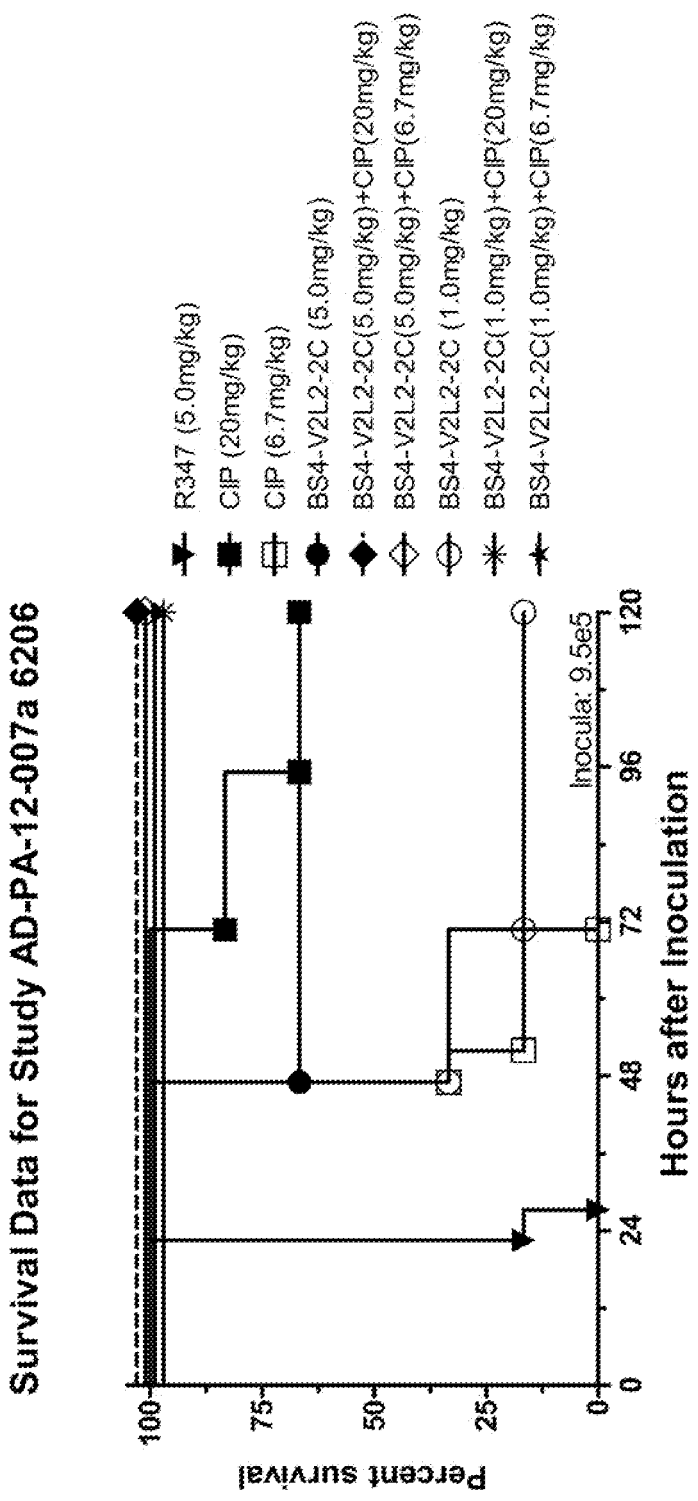

Survival Data for Study AD-PA-12-006a 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after inoculation
Inocula: 1.13e6
R347 (0.5mg/kg)
CIP (20mg/kg)
CIP (6.7mg/kg)
BS4-V2L2-2C (0.5mg/kg)
BS4-V2L2-2C(0.5mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(0.5mg/kg)+CIP(6.7mg/kg)
BS4-V2L2-2C (0.2mg/kg)
BS4-V2L2-2C(0.2mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(0.2mg/kg)+CIP(6.7mg/kg)

FIG. 26


Survival Data for Study AD-PA-12-007a 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after Inoculation
Inocula: 9.5e5
R347 (5.0mg/kg)
CIP (20mg/kg)
CIP (6.7mg/kg)
BS4-V2L2-2C (5.0mg/kg)
BS4-V2L2-2C(5.0mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(5.0mg/kg)+CIP(6.7mg/kg)
BS4-V2L2-2C (1.0mg/kg)
BS4-V2L2-2C(1.0mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(1.0mg/kg)+CIP(6.7mg/kg)

26C.

FIG. 26

26D.

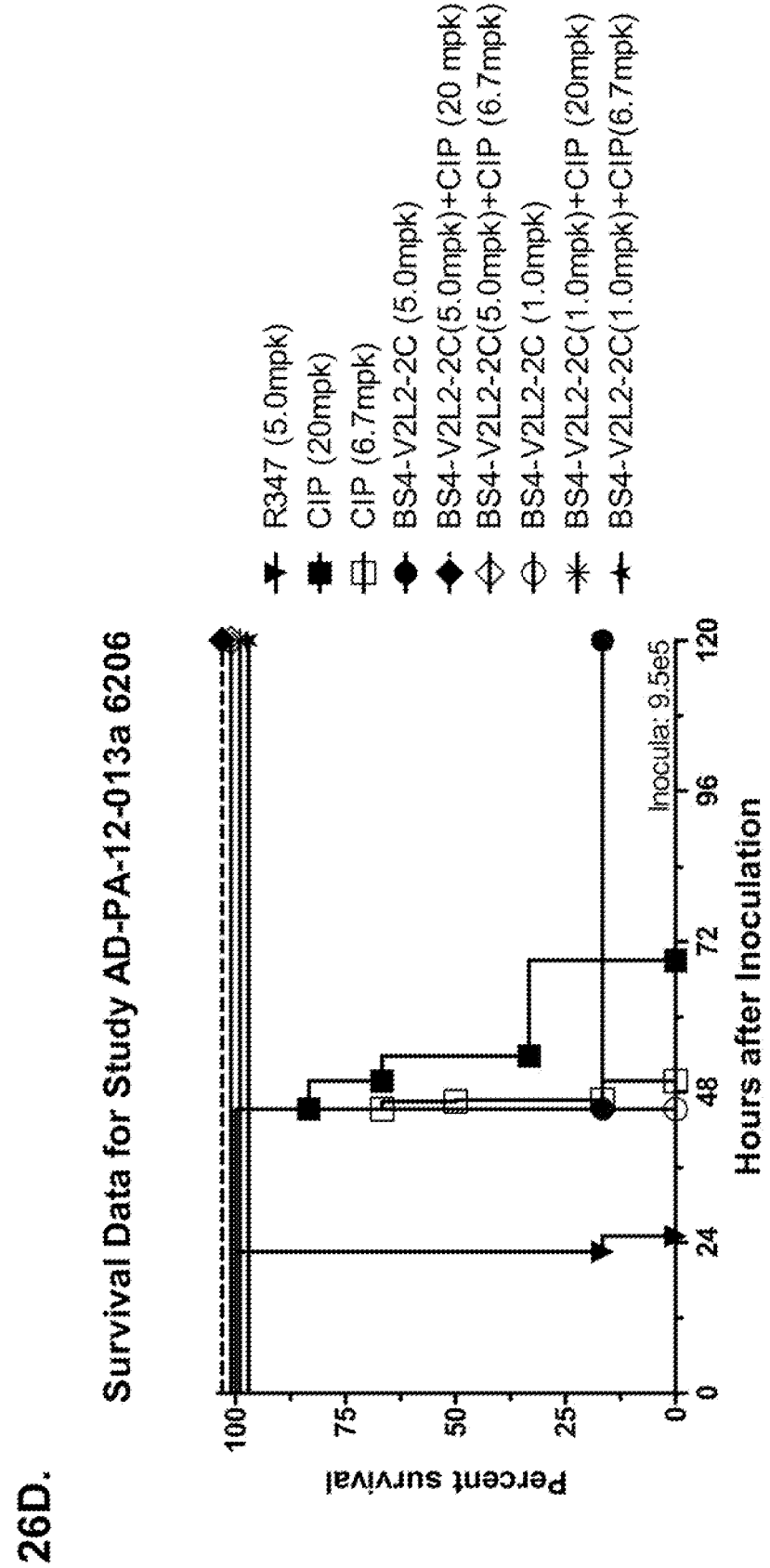

Survival Data for Study AD-PA-12-013a 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after Inoculation
Inoculla: 9.5e5
R347 (5.0mpk)
CIP (20mpk)
CIP (6.7mpk)
BS4-V2L2-2C (5.0mpk)
BS4-V2L2-2C(5.0mpk)+CIP (20 mpk)
BS4-V2L2-2C(5.0mpk)+CIP (6.7mpk)
BS4-V2L2-2C (1.0mpk)
BS4-V2L2-2C(1.0mpk)+CIP (20mpk)
BS4-V2L2-2C(1.0mpk)+CIP(6.7mpk)

FIG. 26

26E.

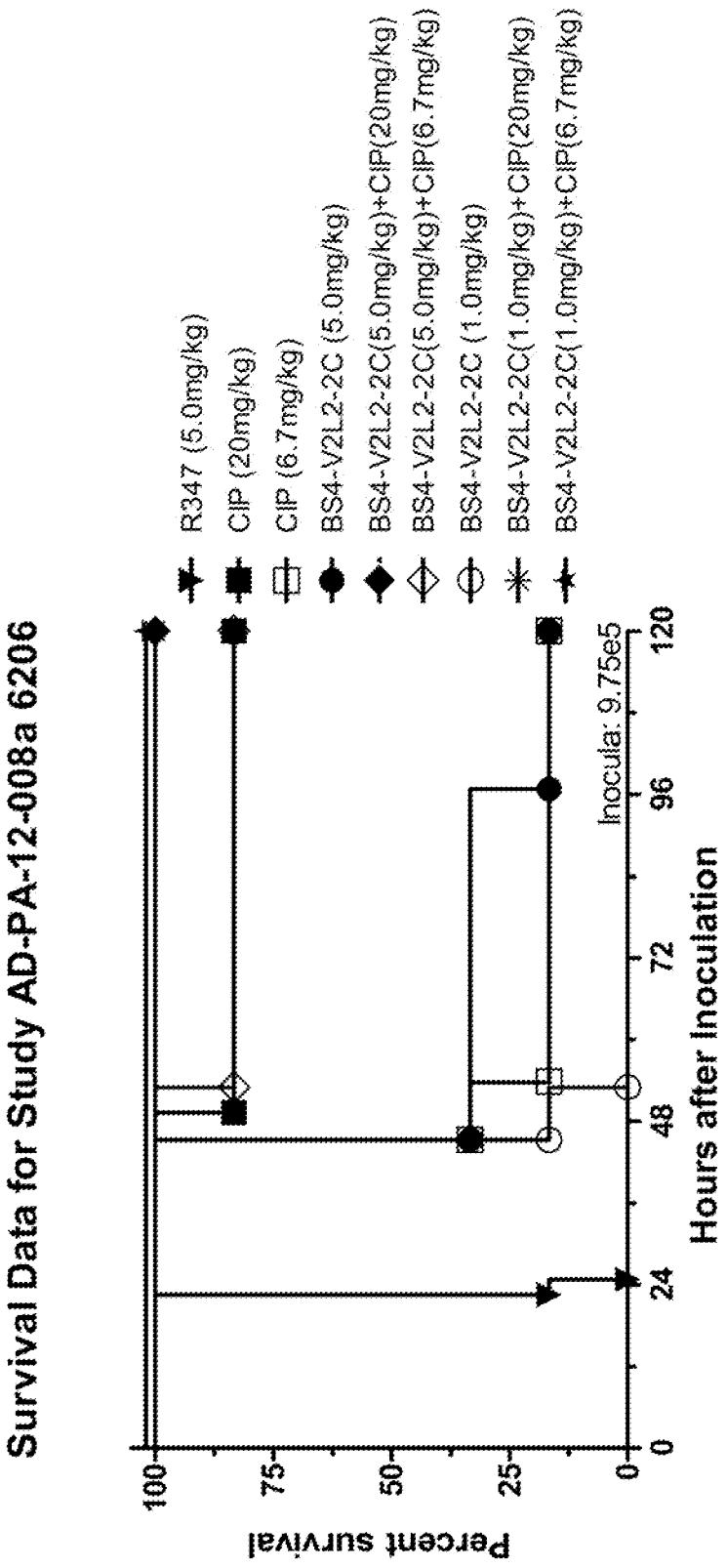
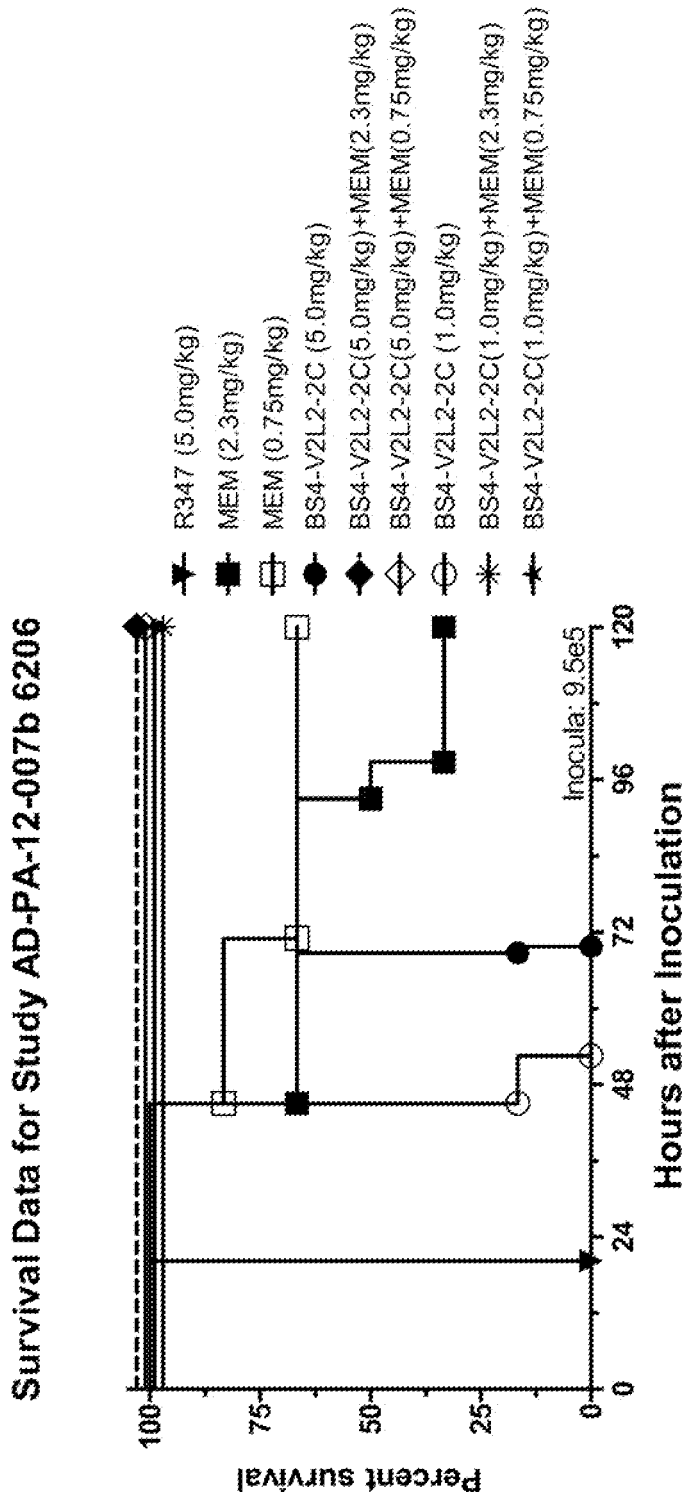
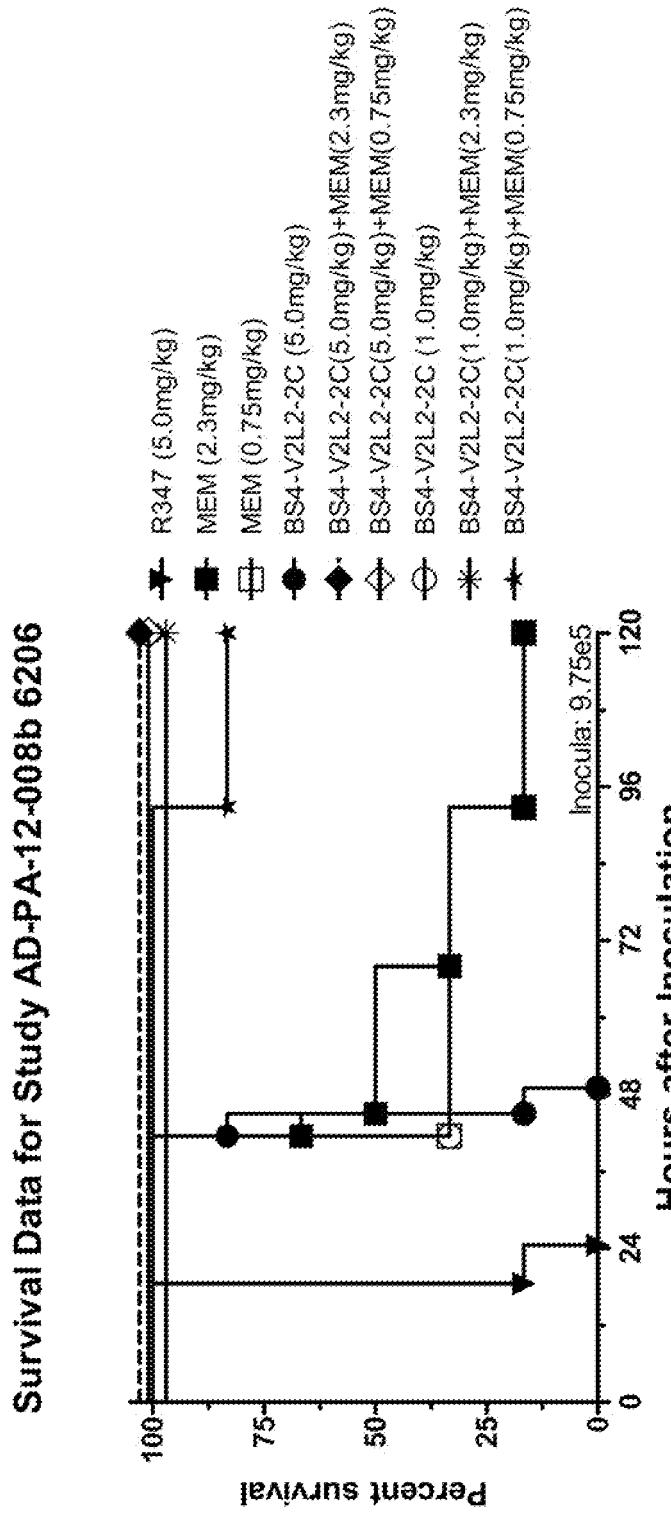

Survival Data for Study AD-PA-12-008a 6206
Percent survival
Hours after Inoculation
Inocula: 9.75e5
0
25
50
75
100
0
24
48
72
96
120
R347 (5.0mg/kg)
CIP (20mg/kg)
CIP (6.7mg/kg)
BS4-V2L2-2C (5.0mg/kg)
BS4-V2L2-2C(5.0mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(5.0mg/kg)+CIP(6.7mg/kg)
BS4-V2L2-2C (1.0mg/kg)
BS4-V2L2-2C(1.0mg/kg)+CIP(20mg/kg)
BS4-V2L2-2C(1.0mg/kg)+CIP(6.7mg/kg)

FIG. 26


Survival Data for Study AD-PA-12-007b 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after Inoculation
Inocula: 9.5e5
R347 (5.0mg/kg)
MEM (2.3mg/kg)
MEM (0.75mg/kg)
BS4-V2L2-2C (5.0mg/kg)
BS4-V2L2-2C(5.0mg/kg)+MEM(2.3mg/kg)
BS4-V2L2-2C(5.0mg/kg)+MEM(0.75mg/kg)
BS4-V2L2-2C (1.0mg/kg)
BS4-V2L2-2C(1.0mg/kg)+MEM(2.3mg/kg)
BS4-V2L2-2C(1.0mg/kg)+MEM(0.75mg/kg)

26F.

FIG. 26


Survival Data for Study AD-PA-12-008b 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after Inoculation
Inocula: 9.75e5
R347 (5.0mg/kg)
MEM (2.3mg/kg)
MEM (0.75mg/kg)
BS4-V2L2-2C (5.0mg/kg)
BS4-V2L2-2C(5.0mg/kg)+MEM(2.3mg/kg)
BS4-V2L2-2C(5.0mg/kg)+MEM(0.75mg/kg)
BS4-V2L2-2C (1.0mg/kg)
BS4-V2L2-2C(1.0mg/kg)+MEM(2.3mg/kg)
BS4-V2L2-2C(1.0mg/kg)+MEM(0.75mg/kg)

26G.

FIG. 26

26H.

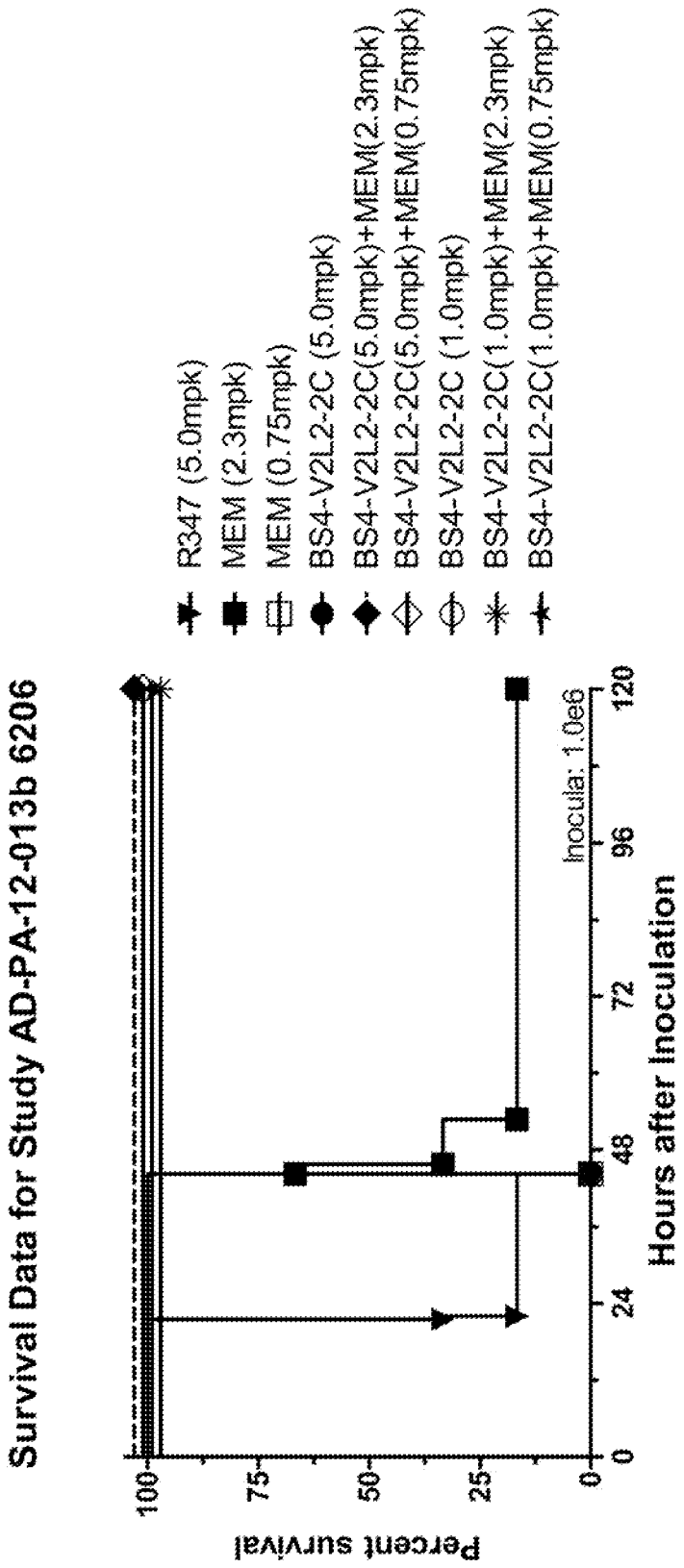
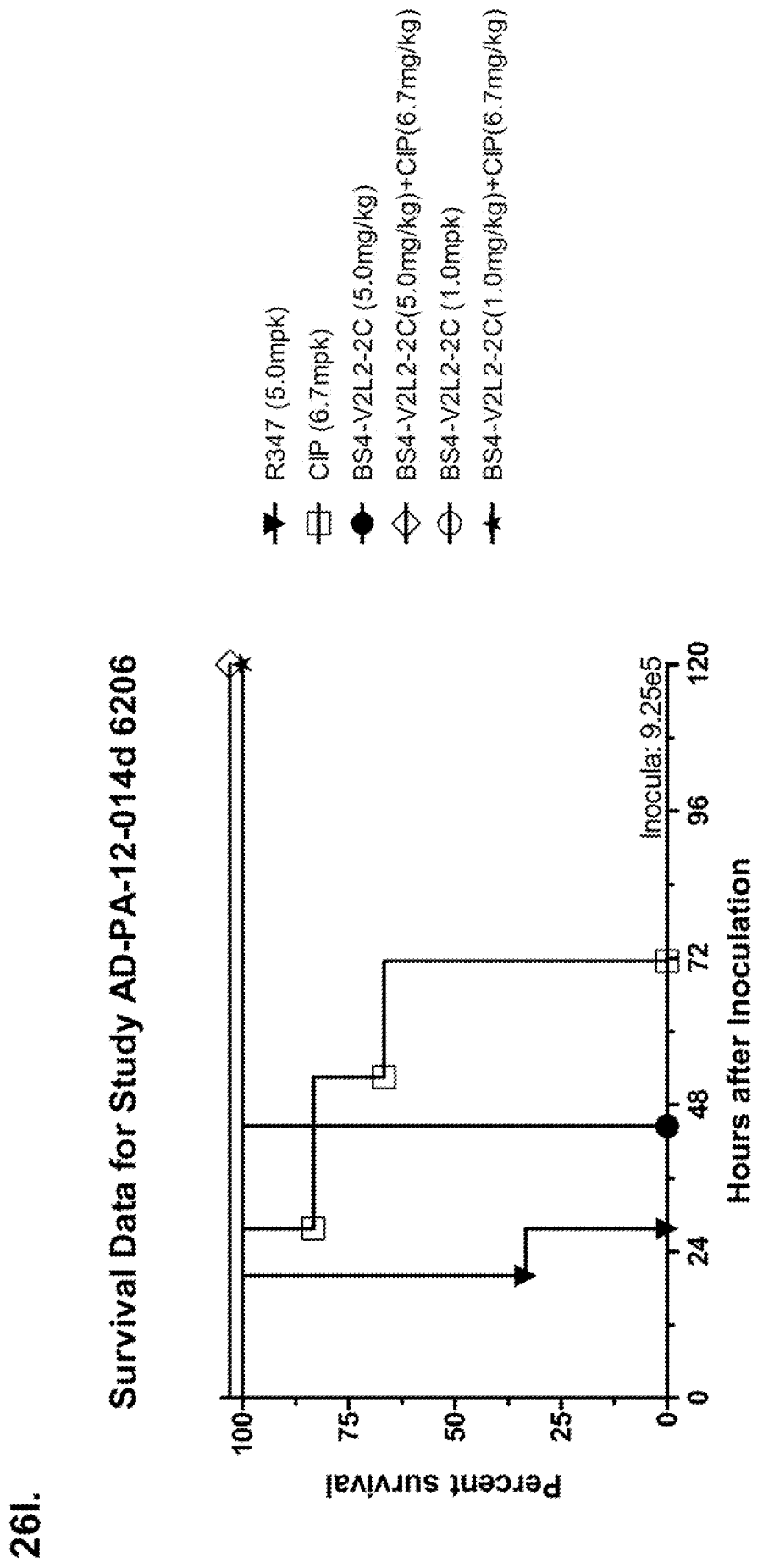
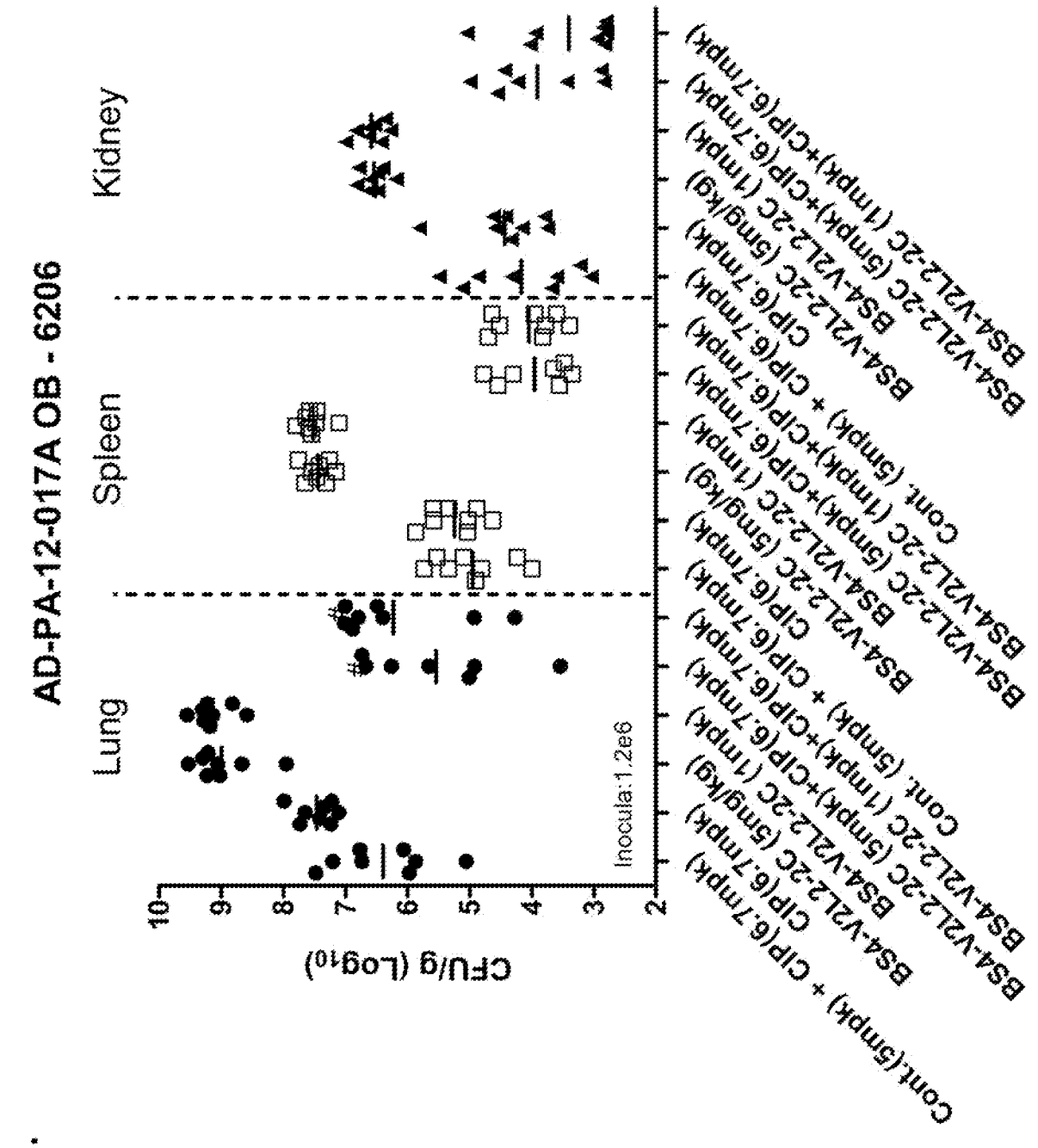

Survival Data for Study AD-PA-12-013b 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after inoculation
Inocula: 1.0e6
R347 (5.0mpk)
MEM (2.3mpk)
MEM (0.75mpk)
BS4-V2L2-2C (5.0mpk)
BS4-V2L2-2C(5.0mpk)+MEM(2.3mpk)
BS4-V2L2-2C(5.0mpk)+MEM(0.75mpk)
BS4-V2L2-2C (1.0mpk)
BS4-V2L2-2C(1.0mpk)+MEM(2.3mpk)
BS4-V2L2-2C(1.0mpk)+MEM(0.75mpk)

FIG. 26


Survival Data for Study AD-PA-12-014d 6206
Percent survival
100
75
50
25
0
0
24
48
72
96
120
Hours after Inoculation
Inocula: 9.25e5
R347 (5.0mpk)
CIP (6.7mpk)
BS4-V2L2-2C (5.0mg/kg)
BS4-V2L2-2C(5.0mg/kg)+CIP(6.7mg/kg)
BS4-V2L2-2C (1.0mpk)
BS4-V2L2-2C(1.0mg/kg)+CIP(6.7mg/kg)

26I.

FIG. 26


AD-PA-12-017A OB - 6206
Lung
Spleen
Kidney
CFU/g (Log10)
10
9
8
7
6
5
4
3
2
Inocula:1.2e6
Cont.(5mpk) + CIP(6.7mpk)
BS4-V2L2-2C (5mg/kg) + CIP(6.7mpk)
BS4-V2L2-2C (1mpk)+CIP(6.7mpk)
BS4-V2L2-2C (5mpk)+CIP(6.7mpk)
Cont. (1mpk) + CIP(6.7mpk)
BS4-V2L2-2C (5mg/kg) + CIP(6.7mpk)
BS4-V2L2-2C (1mpk)+CIP(6.7mpk)
BS4-V2L2-2C (5mpk)+CIP(6.7mpk)
Cont. (5mpk) + CIP(6.7mpk)
BS4-V2L2-2C (5mg/kg) + CIP(6.7mpk)
BS4-V2L2-2C (1mpk)+CIP(6.7mpk)
BS4-V2L2-2C (5mpk)+CIP(6.7mpk)

26J.

FIG. 26

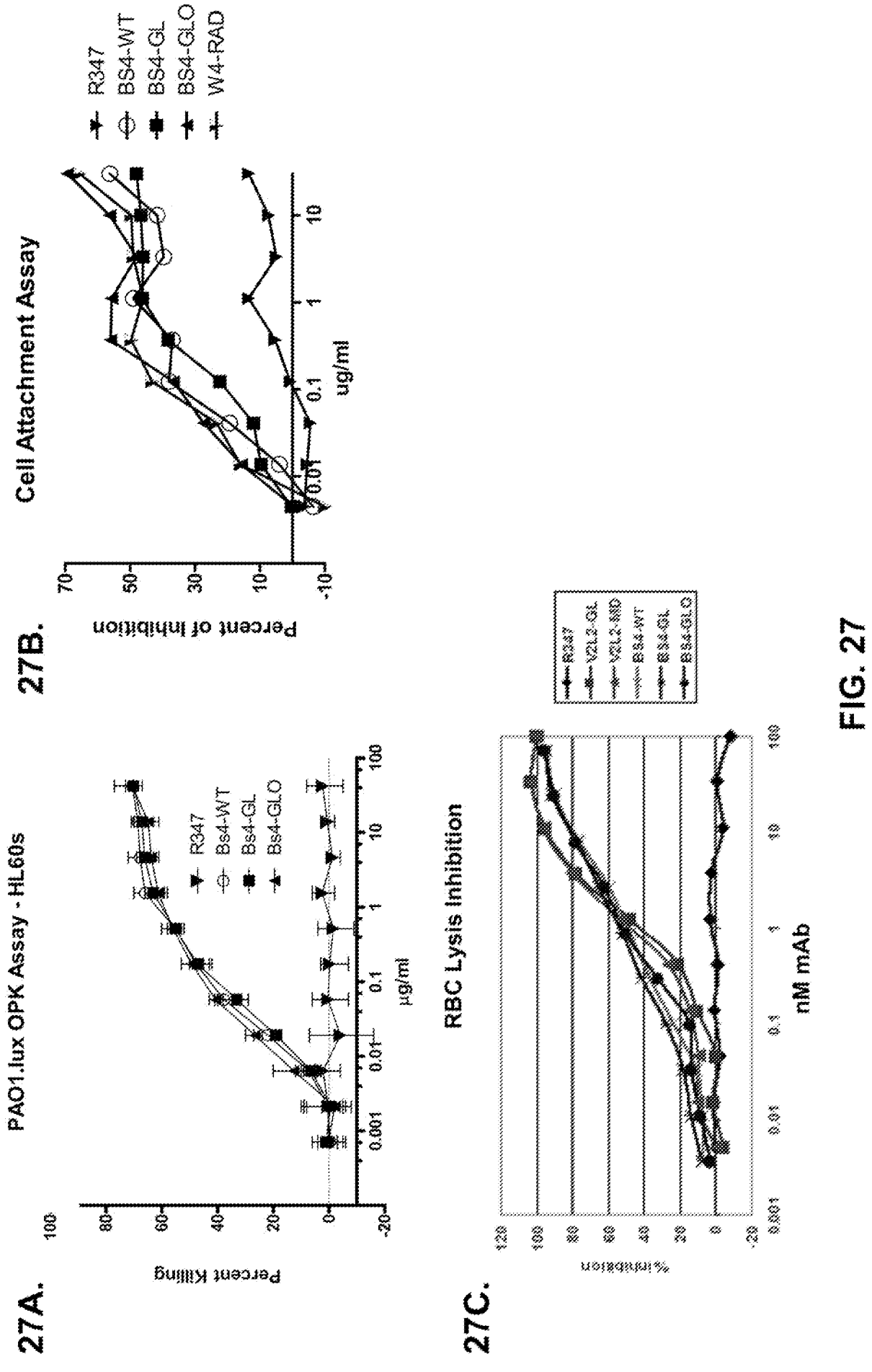

27A.
PAO1.lux OPK Assay - HL60s
Percent Killing
µg/ml
R347
Bs4-WT
Bs4-GL
Bs4-GLO
27B.
Cell Attachment Assay
Percent of Inhibition
ug/ml
R347
BS4-WT
BS4-GL
BS4-GLO
W4-RAD
27C.
RBC Lysis Inhibition
% Inhibition
nM mAb
R347
V2L2-GL
V2L2-MD
BS4-WT
BS4-GL
BS4-GLO

FIG. 27

28A. **Prophylaxis (T = -24h) – 120 hr post-infection**

BS4-GLO Dose (mg/kg)										
Strain/inoculum	15	10	5	3	1	0.5	0.2	0.07	0.02	0.007
6206 (1e6)	-	-	100 (60)	-	88 (60)	60 (60)	10 (60)	-	-	-
6077 (1e6)	-	-	-	-	100 (10)	100 (10)	95.8 (26)	91.6 (26)	50 (16)	12.5 (16)
6294 (2e7)	-	100 (5)	-	80 (5)	60 (5)	11.1 (18)	11.1 (18)	-	-	-
PA103 (1e6)	60 (5)	-	40 (5)	-	0 (5)	-	-	-	-	-

28B. **Therapy (T = 1h) – 120 hr post-infection**

BS4-GLO Dose (mg/kg)									
Strain/inoculum	45	15	10	5	2	1	0.5	0.3	0.03
6206 (1e6)	72.2 (18)	55.6 (18)	-	33.3 (18)	-	11.1 (18)	-	-	-
6077 (1e6)	-	-	-	-	-	92 (22)	83.3 (12)	80 (10)	30 (10)
6294 (2e7)	-	-	-	70 (10)	-	10 (10)	0 (10)	-	0 (10)
PA103 (1e6)	-	0 (5)	-	0 (5)	-	0 (5)	-	-	-

FIG. 28



Bacteremia model

FIG. 29

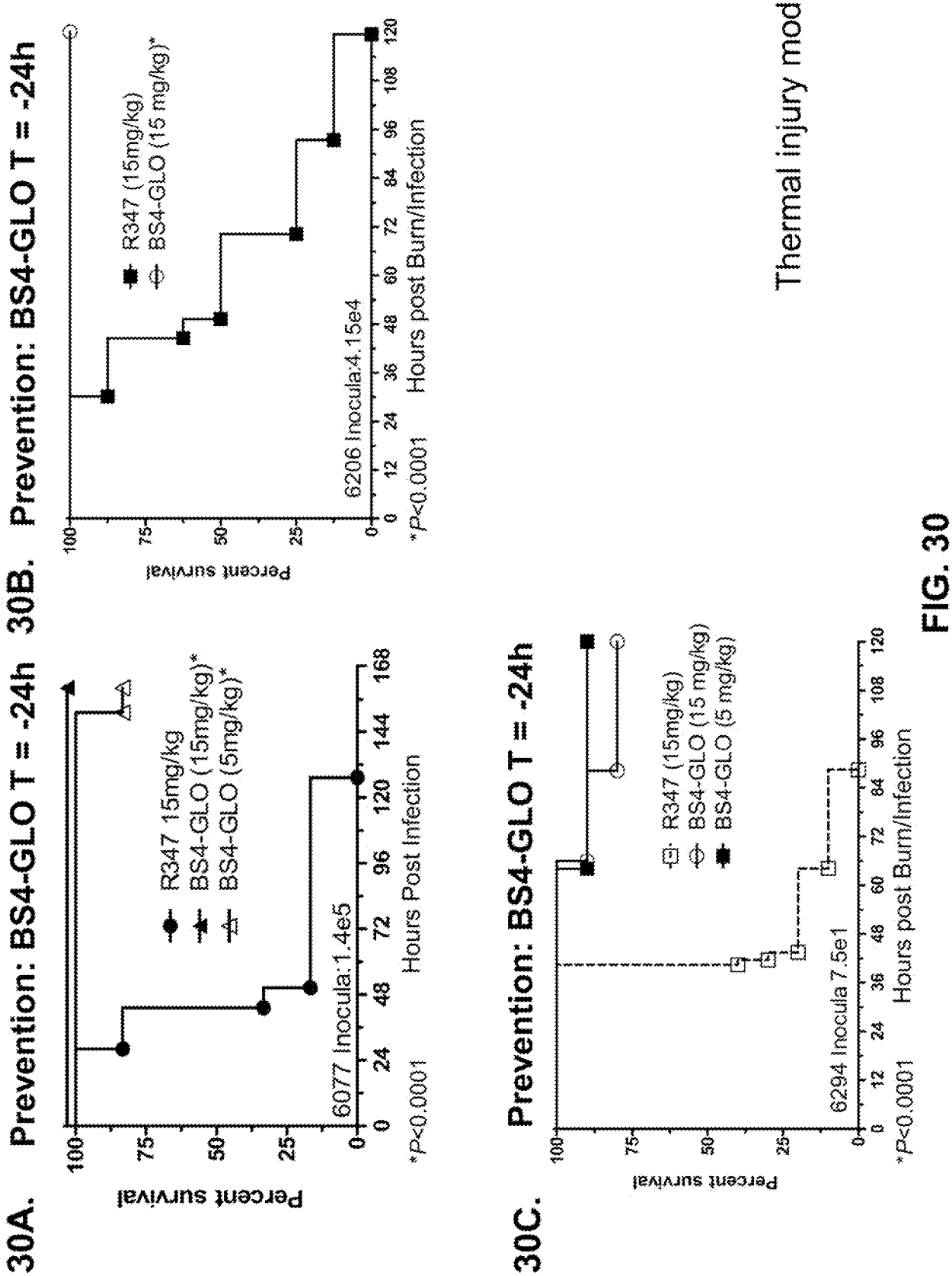
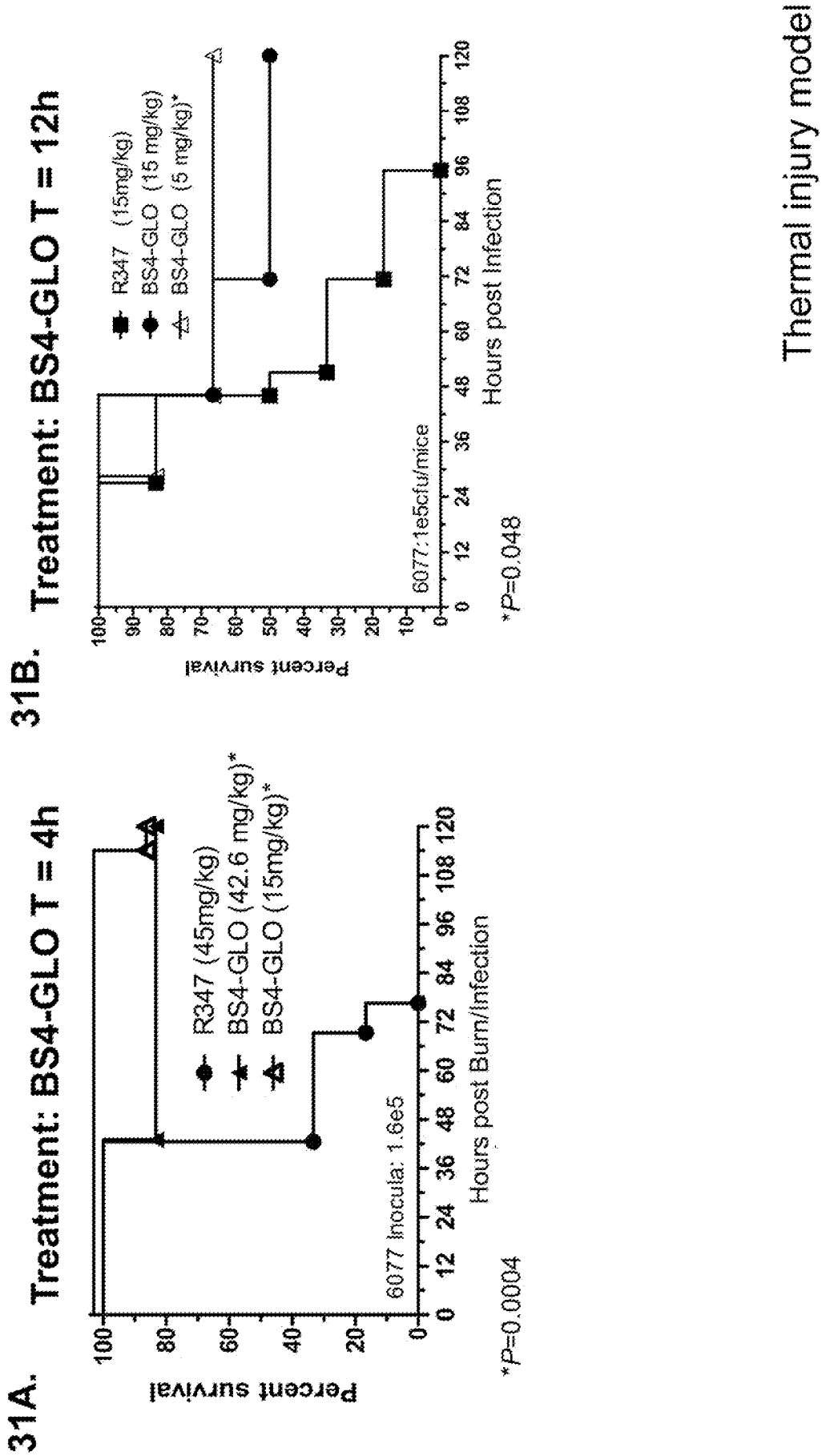

30A.
Prevention: BS4-GLO T = -24h
Percent survival
R347 15mg/kg
BS4-GLO (15mg/kg)*
BS4-GLO (5mg/kg)*
6077 Inocula:1.4e5
Hours Post Infection
*P<0.0001
30B.
Prevention: BS4-GLO T = -24h
Percent survival
R347 (15mg/kg)
BS4-GLO (15 mg/kg)*
6206 Inocula:4.15e4
Hours post Burn/Infection
*P<0.0001
30C.
Prevention: BS4-GLO T = -24h
Percent survival
R347 (15mg/kg)
BS4-GLO (15 mg/kg)
BS4-GLO (5 mg/kg)
6294 Inocula 7.5e1
Hours post Burn/Infection
*P<0.0001
Thermal injury model

FIG. 30



Thermal injury model

FIG. 31

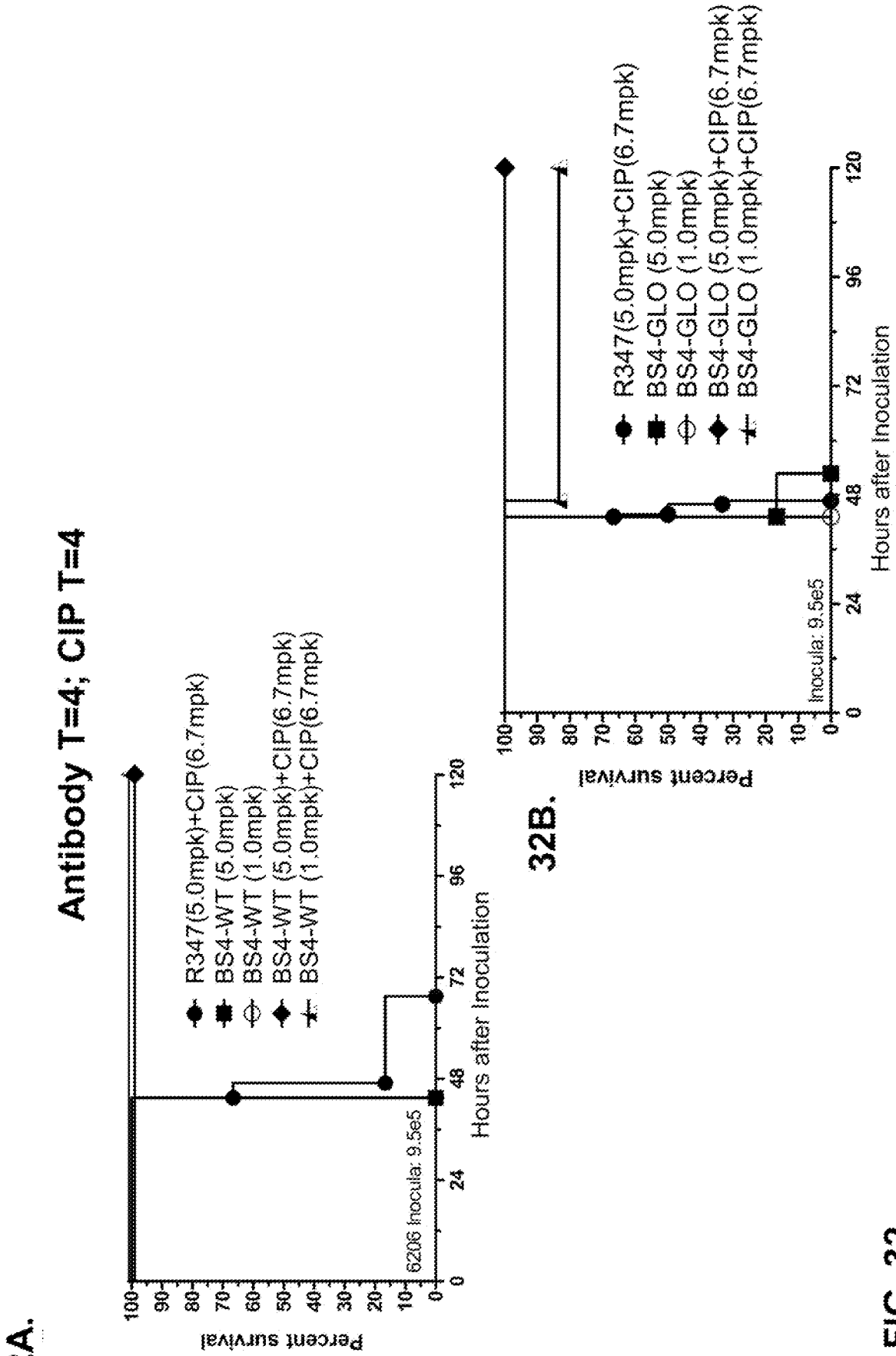

32A.
Antibody T=4; CIP T=4
R347(5.0mpk)+CIP(6.7mpk)
BS4-WT (5.0mpk)
BS4-WT (1.0mpk)
BS4-WT (5.0mpk)+CIP(6.7mpk)
BS4-WT (1.0mpk)+CIP(6.7mpk)
Percent survival
6206 inocula: 9.5e5
Hours after inoculation
32B.
R347(5.0mpk)+CIP(6.7mpk)
BS4-GLO (5.0mpk)
BS4-GLO (1.0mpk)
BS4-GLO (5.0mpk)+CIP(6.7mpk)
BS4-GLO (1.0mpk)+CIP(6.7mpk)
Percent survival
Inocula: 9.5e5
Hours after Inoculation

FIG. 32

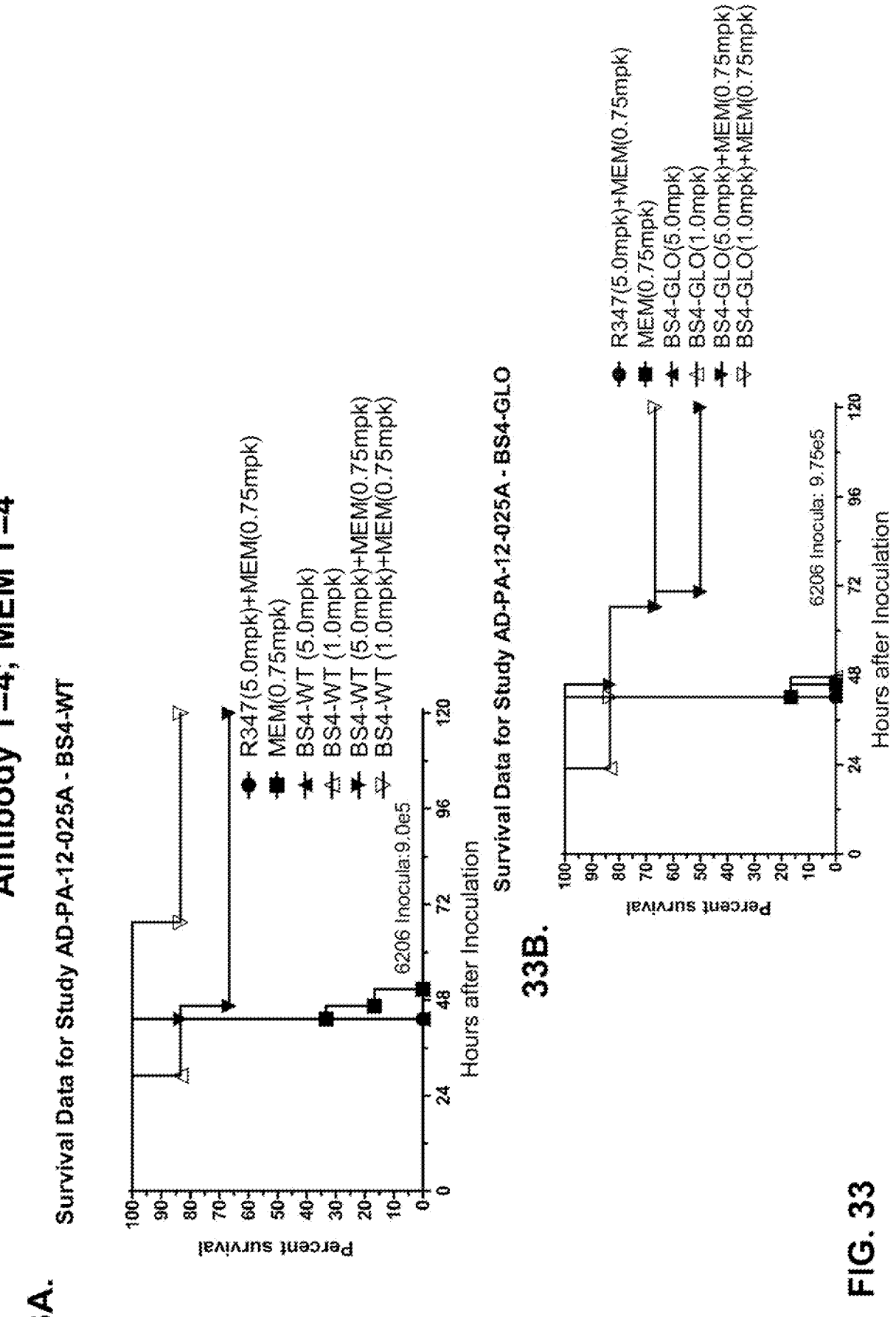

Antibody T=4; MEM T=4
33A.
Survival Data for Study AD-PA-12-025A - BS4-WT
R347(5.0mpk)+MEM(0.75mpk)
MEM(0.75mpk)
BS4-WT (5.0mpk)
BS4-WT (1.0mpk)
BS4-WT (5.0mpk)+MEM(0.75mpk)
BS4-WT (1.0mpk)+MEM(0.75mpk)
6206 Inocula:9.0e5
Percent survival
Hours after Inoculation
33B.
Survival Data for Study AD-PA-12-025A - BS4-GLO
R347(5.0mpk)+MEM(0.75mpk)
MEM(0.75mpk)
BS4-GLO(5.0mpk)
BS4-GLO(1.0mpk)
BS4-GLO(5.0mpk)+MEM(0.75mpk)
BS4-GLO(1.0mpk)+MEM(0.75mpk)
6206 Inocula: 9.75e5
Percent survival
Hours after Inoculation

FIG. 33

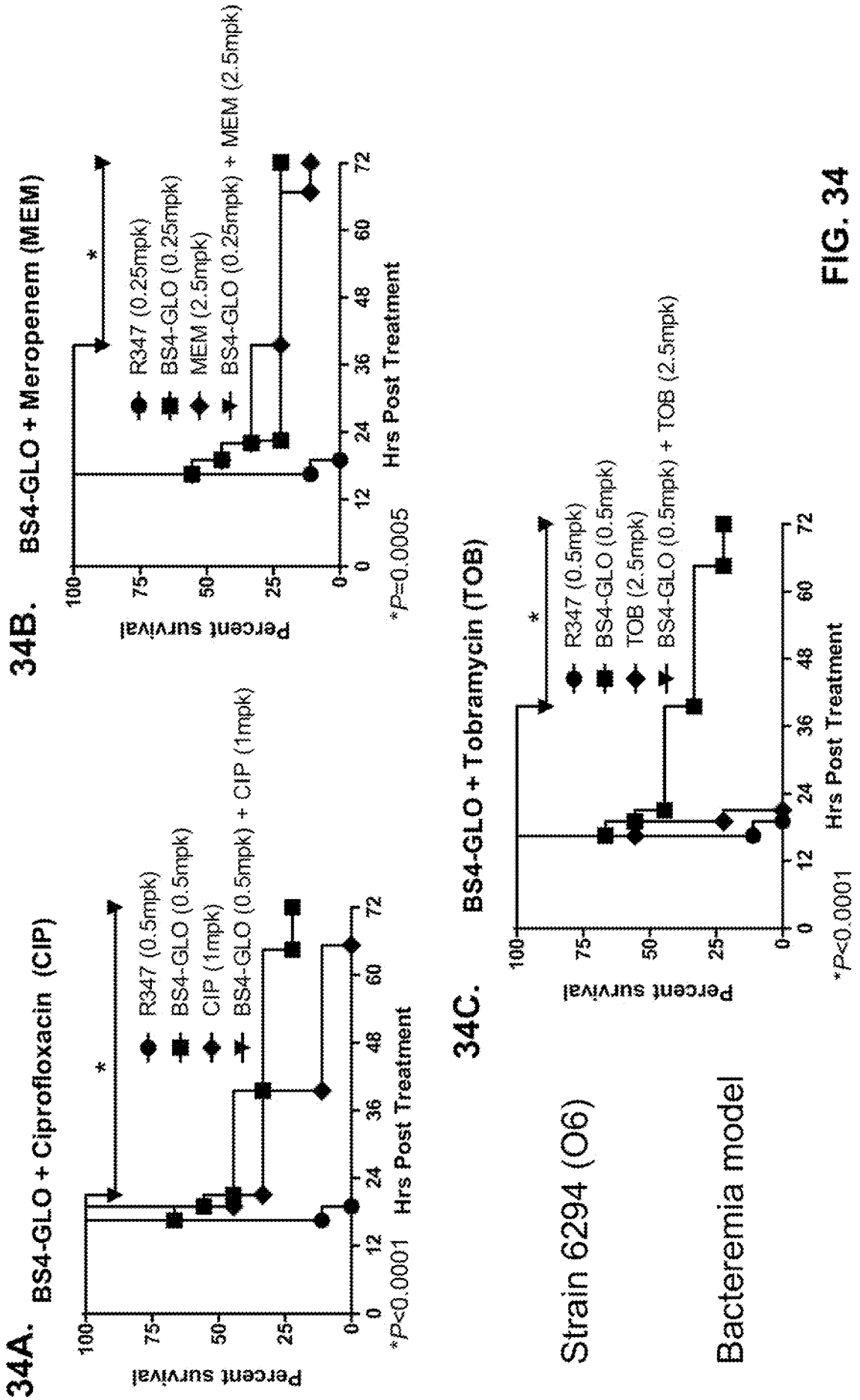

Bs4 T=-24h; Abx T=1h
34A.
BS4-GLO + Ciprofloxacin (CIP)
R347 (0.5mpk)
BS4-GLO (0.5mpk)
CIP (1mpk)
BS4-GLO (0.5mpk) + CIP (1mpk)
Percent survival
Hrs Post Treatment
*P<0.0001
34B.
BS4-GLO + Meropenem (MEM)
R347 (0.25mpk)
BS4-GLO (0.25mpk)
MEM (2.5mpk)
BS4-GLO (0.25mpk) + MEM (2.5mpk)
Percent survival
Hrs Post Treatment
*P=0.0005
34C.
BS4-GLO + Tobramycin (TOB)
R347 (0.5mpk)
BS4-GLO (0.5mpk)
TOB (2.5mpk)
BS4-GLO (0.5mpk) + TOB (2.5mpk)
Percent survival
Hrs Post Treatment
*P<0.0001
Strain 6294 (O6)
Bacteremia model

FIG. 34

35A.

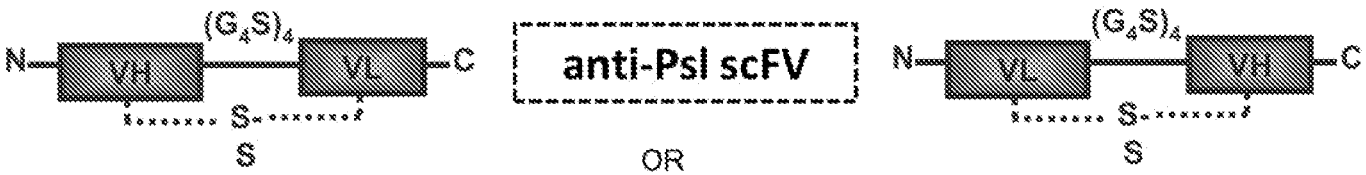
Bs4 Version I

Light Chain

Anti – PcrV light chain variable region –
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
WKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(Kappa light chain constant region represented here – could be a lambda region

Heavy Chain

Anti – PcrV heavy chain variable region –
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV
SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV***EPKSC***GGGGS
G GGGS – anti-Psl scFV –
*GGGGSGGGGS****DKTHTCPPCP***APELLGGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK



hinge regions are ***underlined in bolded italics***
G4S linkers *underlined in italics*

FIG. 35

35B. Bs4 Version II

Light Chain

Anti–Psl light chain variable region–RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
WKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
C (Kappa light chain constant region represented here – could be a lambda region)

Heavy Chain

Anti – Psl heavy chain variable region –ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTV
SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRV***EPKSC***GGGGS
G GGGS – anti-PcrV scFV –
GGGGSGGGGS***DKTHTCPPCP***APELLGGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

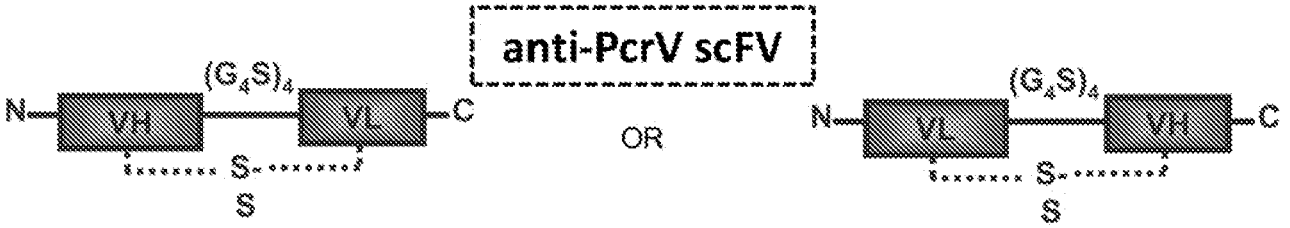


FIG. 35

hinge regions are ***underlined in bolded italics***
G4S linkers *underlined in italics*