
TN-20LEU-19
SP
Leu16(VL-VH)
linker
FMC63(VH-VL)
hinge
CD28 TM
4-1BB
CD3z
TN-20OF-19 (C-CAR039)
SP
OF (VL-VH)
linker
FMC63(VH-VL)
hinge
CD28 TM
4-1BB
CD3z

FIG. 1

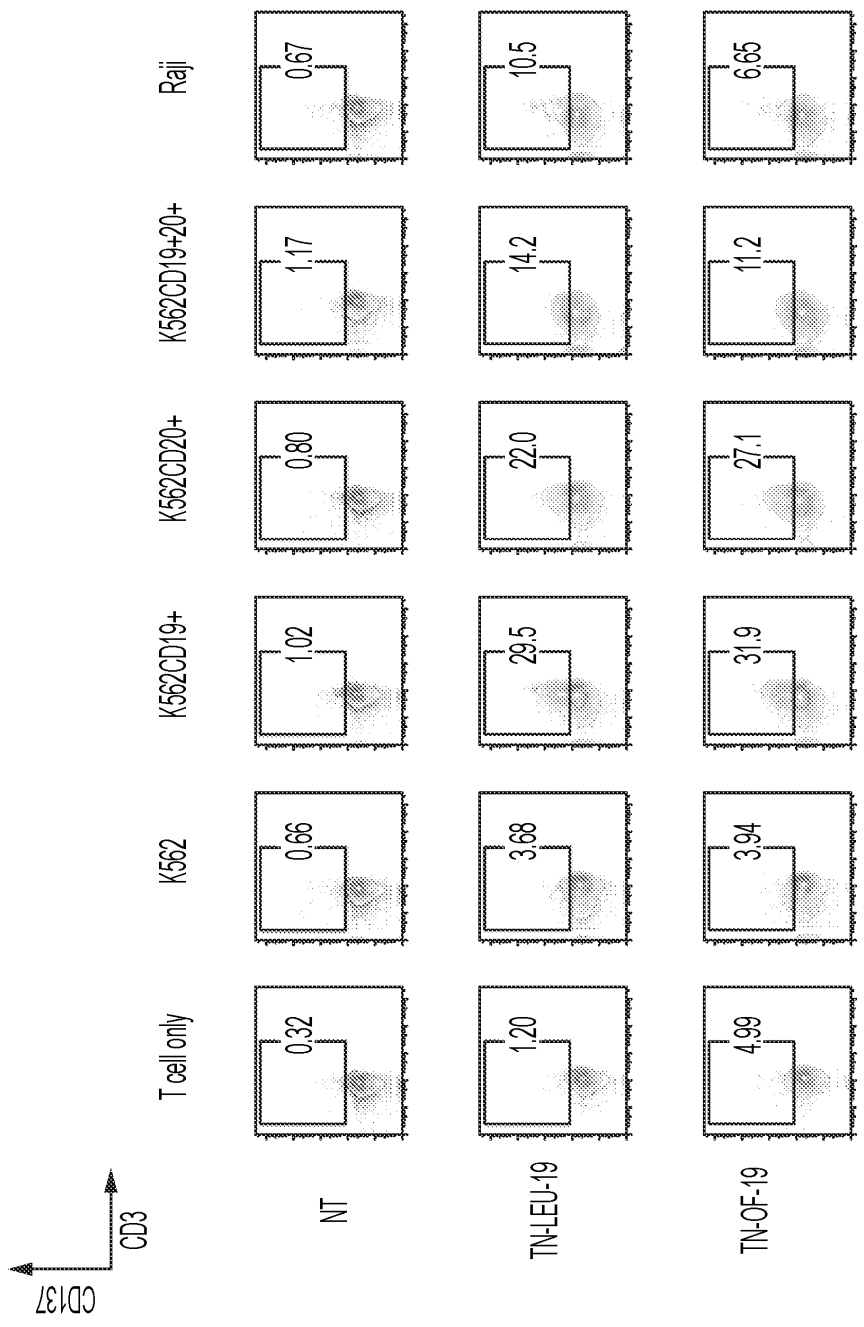

T cell only
K562
K562CD19+
K562CD20+
K562CD19+20+
Raji
0.32
0.66
1.02
0.80
1.17
0.67
1.20
3.68
29.5
22.0
14.2
10.5
4.99
3.94
31.9
27.1
11.2
6.65
NT
TN-LEU-19
TN-OF-19
CD3
CD137

FIG. 2A

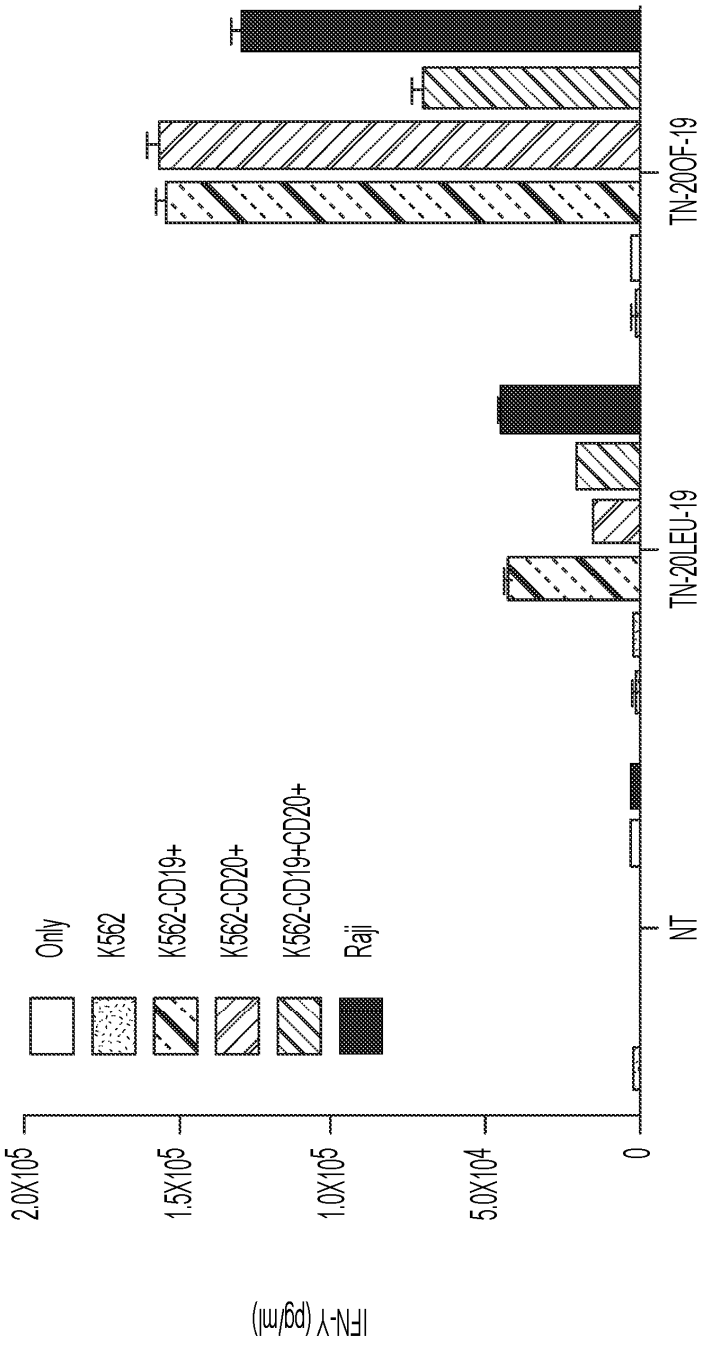

IFN-γ (pg/ml)
2.0X10^5
1.5X10^5
1.0X10^5
5.0X10^4
0
Only
K562
K562-CD19+
K562-CD20+
K562-CD19+CD20+
Raji
NT
TN-20LEU-19
TN-20OF-19

FIG. 2B

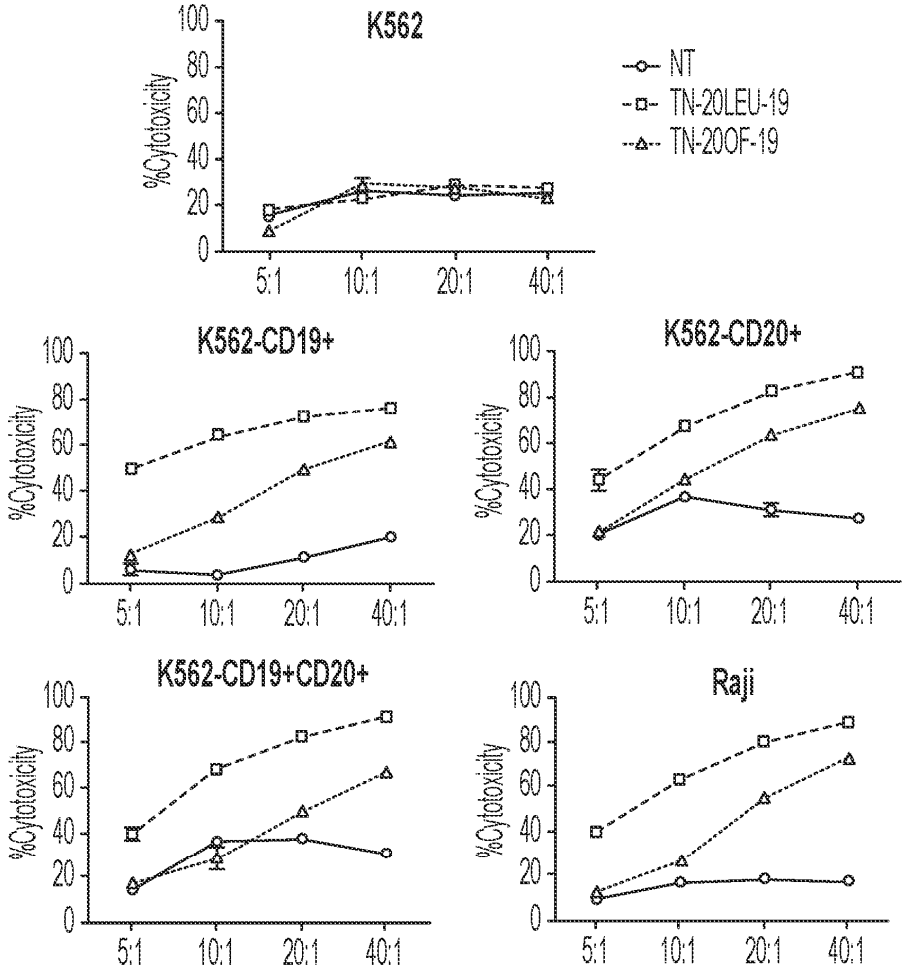

K562
%Cytotoxicity
100
80
60
40
20
0
5:1
10:1
20:1
40:1
NT
TN-20LEU-19
TN-20OF-19
K562-CD19+
K562-CD20+
K562-CD19+CD20+
Raji

FIG. 3A

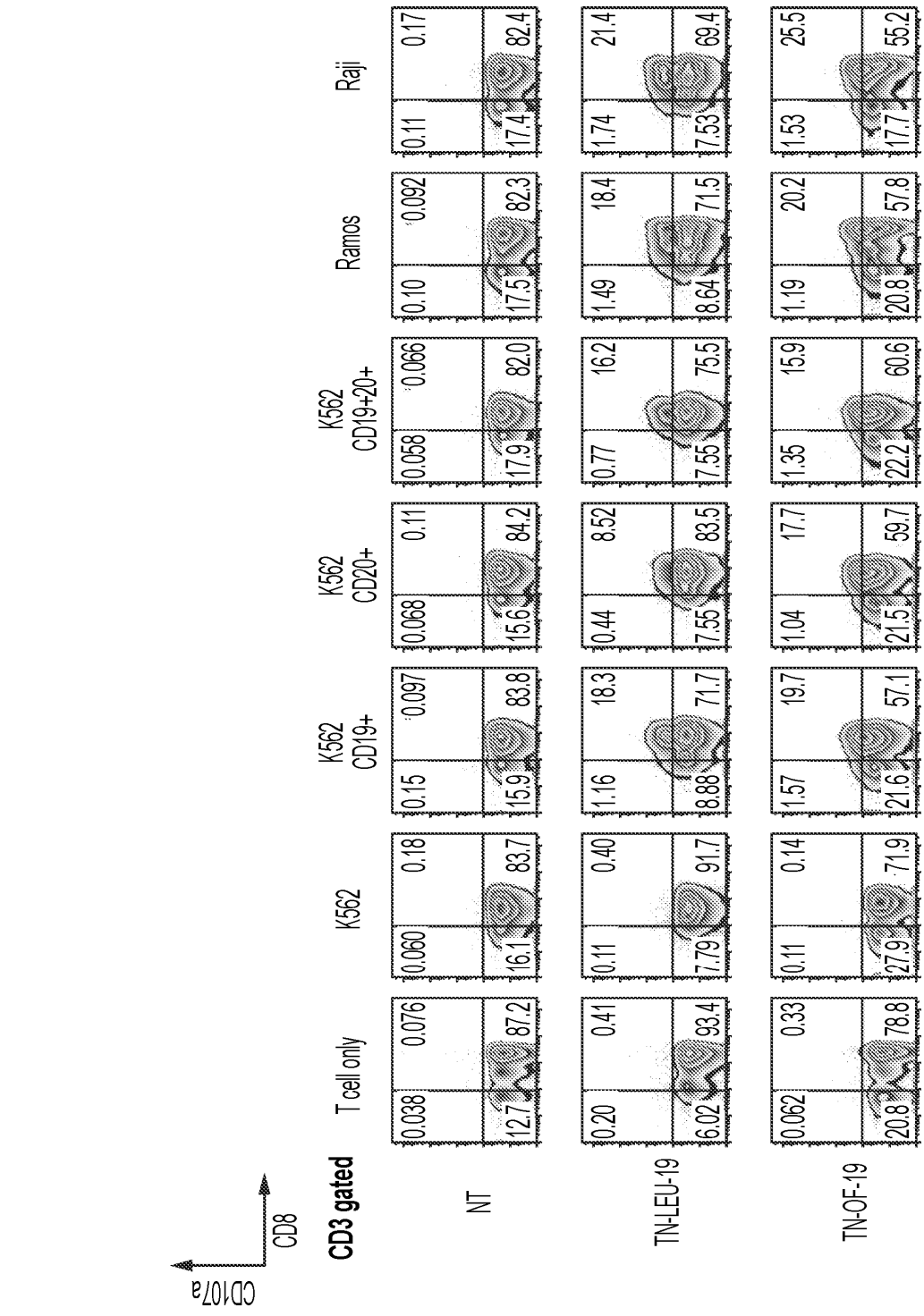

CD107a
CD8
CD3 gated
T cell only
K562
K562 CD19+
K562 CD20+
K562 CD19+20+
Ramos
Raji
NT
TN-LEU-19
TN-OF-19
0.038
0.076
0.060
0.18
0.15
0.097
0.068
0.11
0.058
0.066
0.10
0.092
0.11
0.17
12.7
87.2
16.1
83.7
15.9
83.8
15.6
84.2
17.9
82.0
17.5
82.3
17.4
82.4
0.20
0.41
0.11
0.40
1.16
18.3
0.44
8.52
0.77
16.2
1.49
18.4
1.74
21.4
6.02
93.4
7.79
91.7
8.88
71.7
7.55
83.5
7.55
75.5
8.64
71.5
7.53
69.4
0.062
0.33
0.11
0.14
1.57
19.7
1.04
17.7
1.35
15.9
1.19
20.2
1.53
25.5
20.8
78.8
27.9
71.9
21.6
57.1
21.5
59.7
22.2
60.6
20.8
57.8
17.7
55.2

FIG. 3B

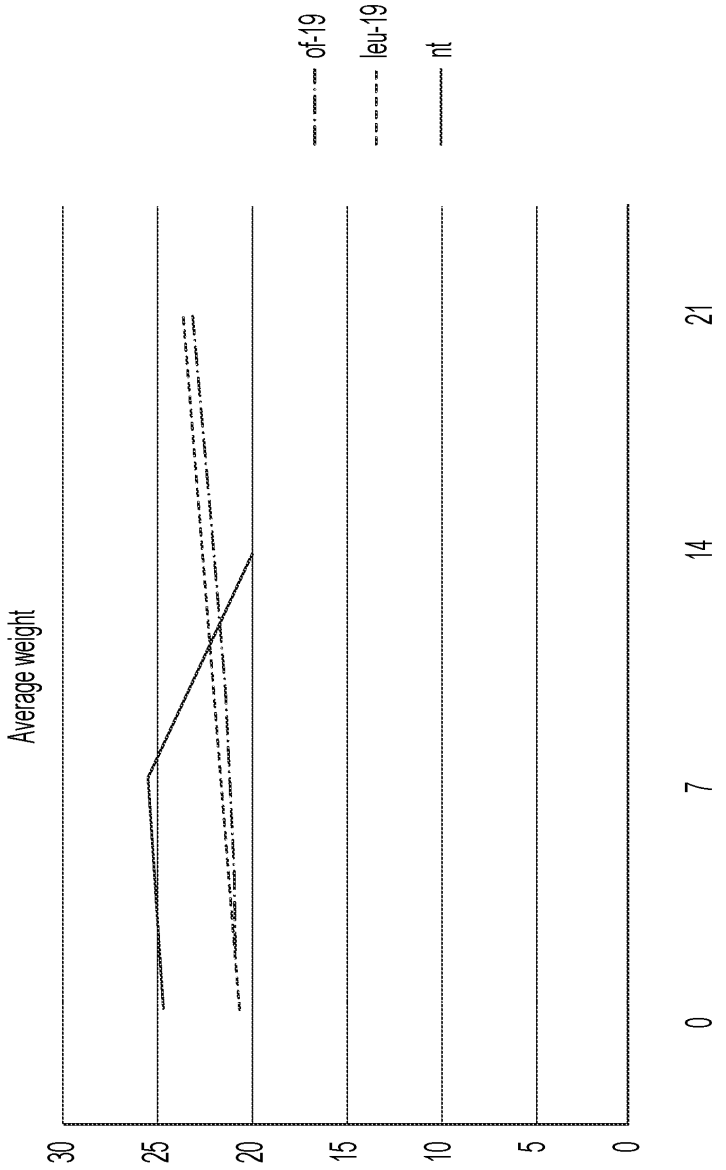


FIG. 4A

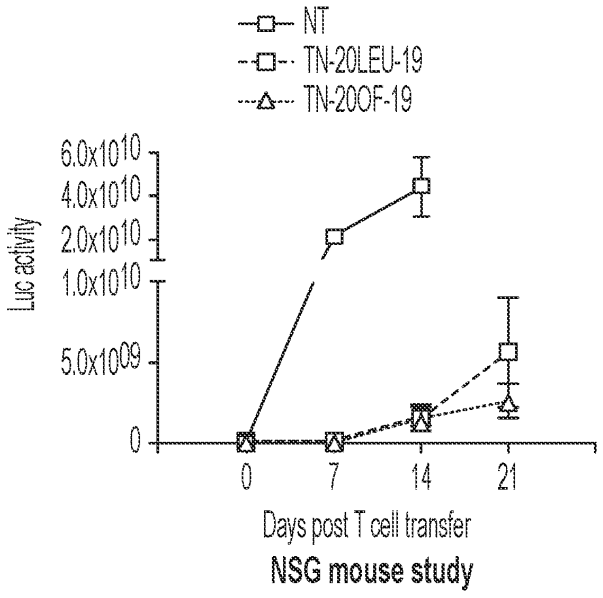

NT
TN-20LEU-19
TN-20OF-19
6.0x10^10
4.0x10^10
2.0x10^10
1.0x10^10
5.0x10^09
0
Luc activity
0
7
14
21
Days post T cell transfer
NSG mouse study

FIG. 4B

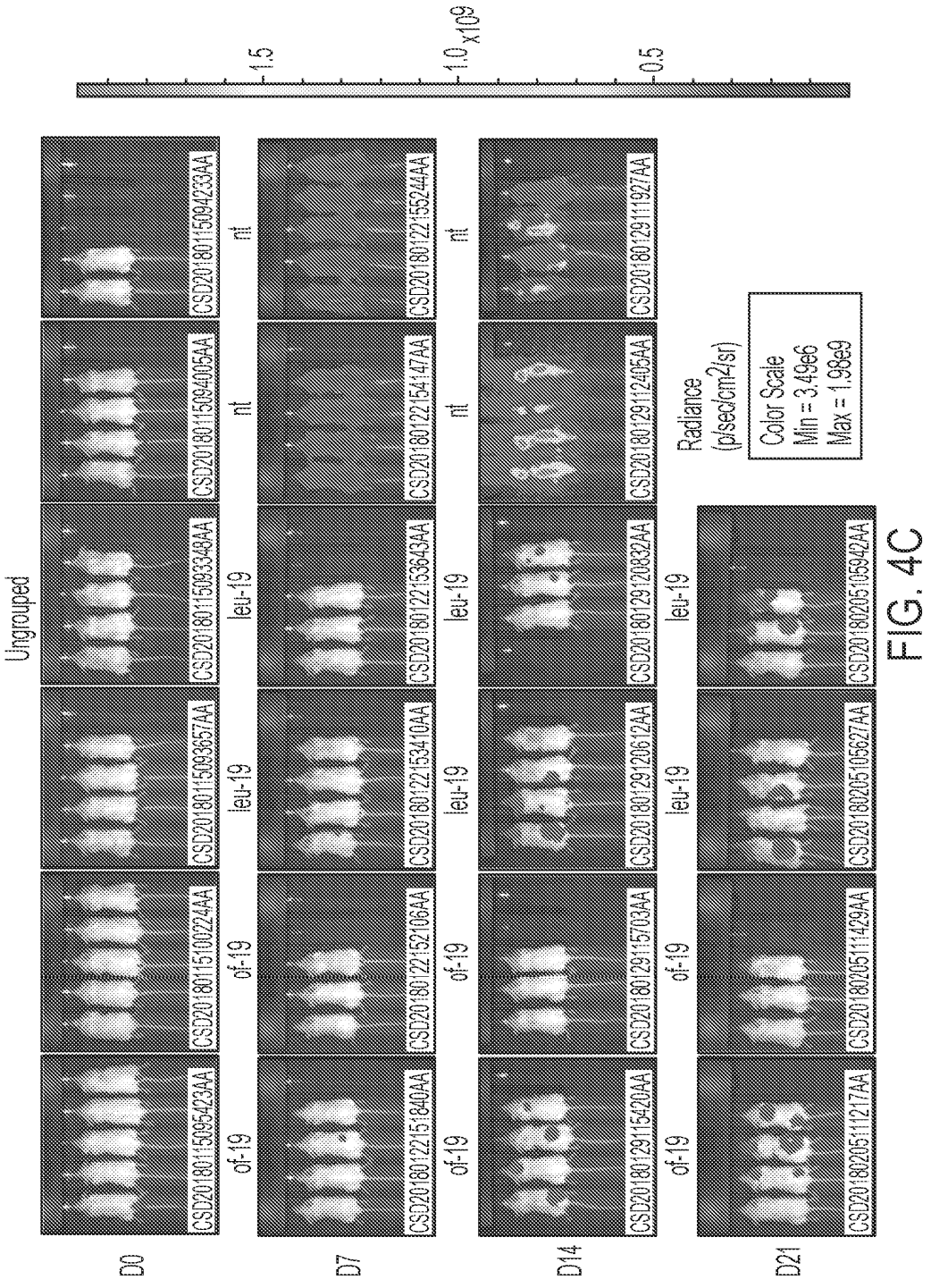

1.5
1.0 x10^9
0.5
Ungrouped
D0
D7
D14
D21
of-19
leu-19
nt
Radiance (p/sec/cm2/sr)
Color Scale
Min = 3.49e6
Max = 1.98e9

FIG. 4C

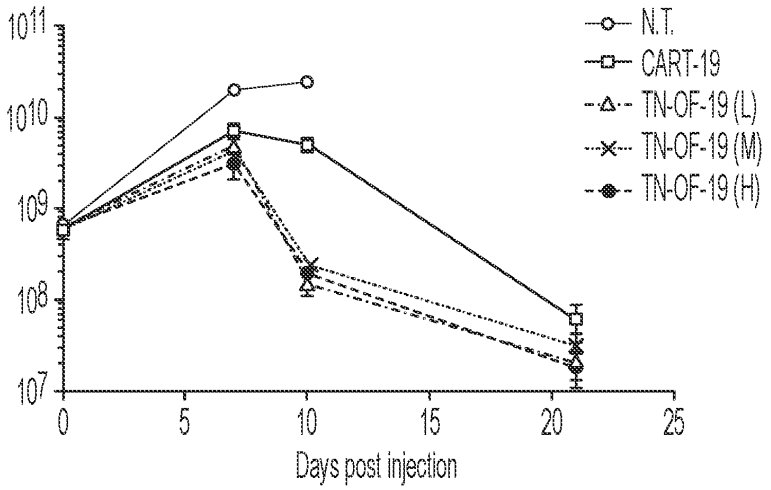

10^{11}
10^{10}
10^{9}
10^{8}
10^{7}
0
5
10
15
20
25
Days post injection
N.T.
CART-19
TN-OF-19 (L)
TN-OF-19 (M)
TN-OF-19 (H)

FIG. 5A

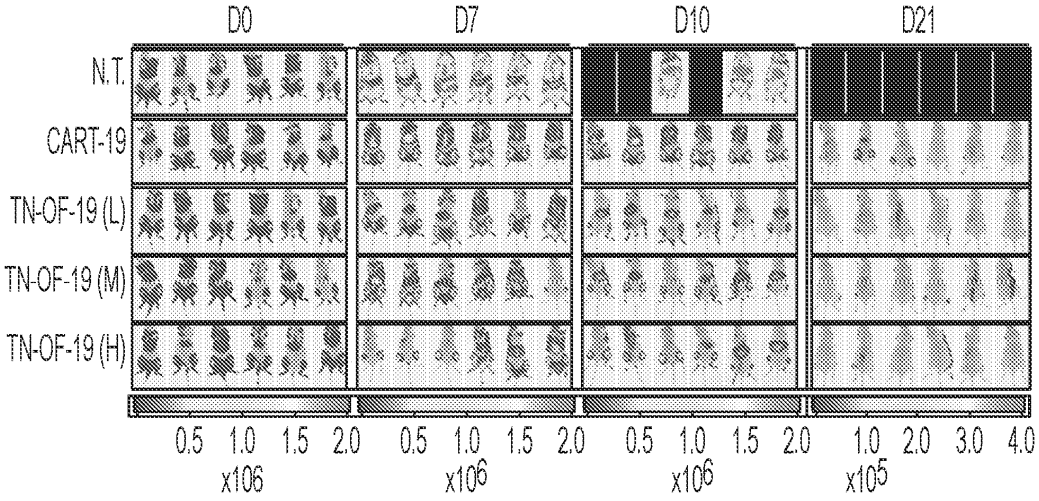

D0
D7
D10
D21
N.T.
CART-19
TN-OF-19 (L)
TN-OF-19 (M)
TN-OF-19 (H)
0.5 1.0 1.5 2.0
x106
0.5 1.0 1.5 2.0
x10^6
0.5 1.0 1.5 2.0
x10^6
1.0 2.0 3.0 4.0
x10^5

FIG. 5B

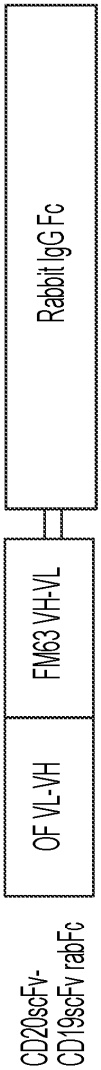


FIG. 6A

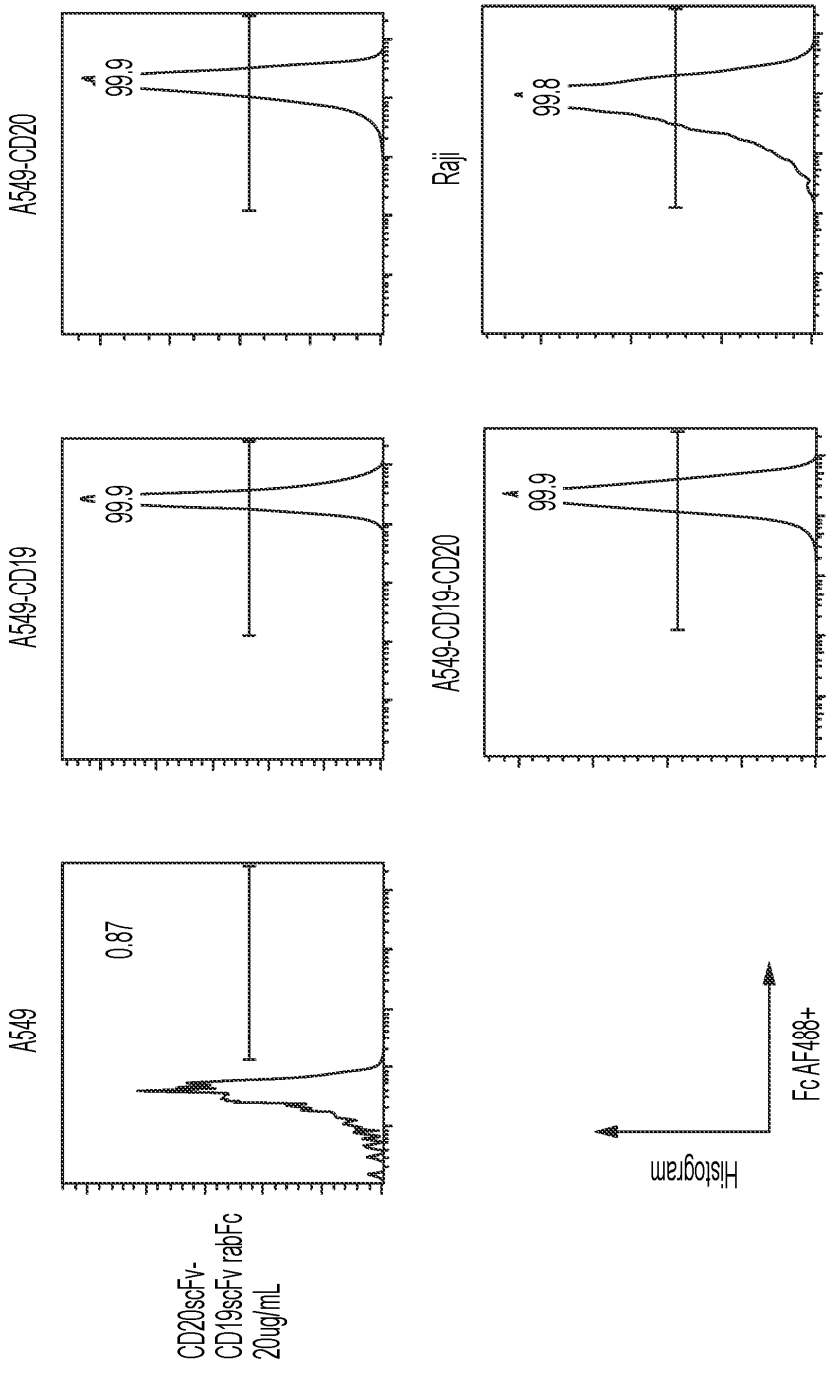

A549
0.87
A549-CD19
99.9
A549-CD20
99.9
Raji
99.8
A549-CD19-CD20
99.9
CD20scFv-CD19scFv rabFc 20ug/mL
Histogram
Fc AF488+

FIG. 6B

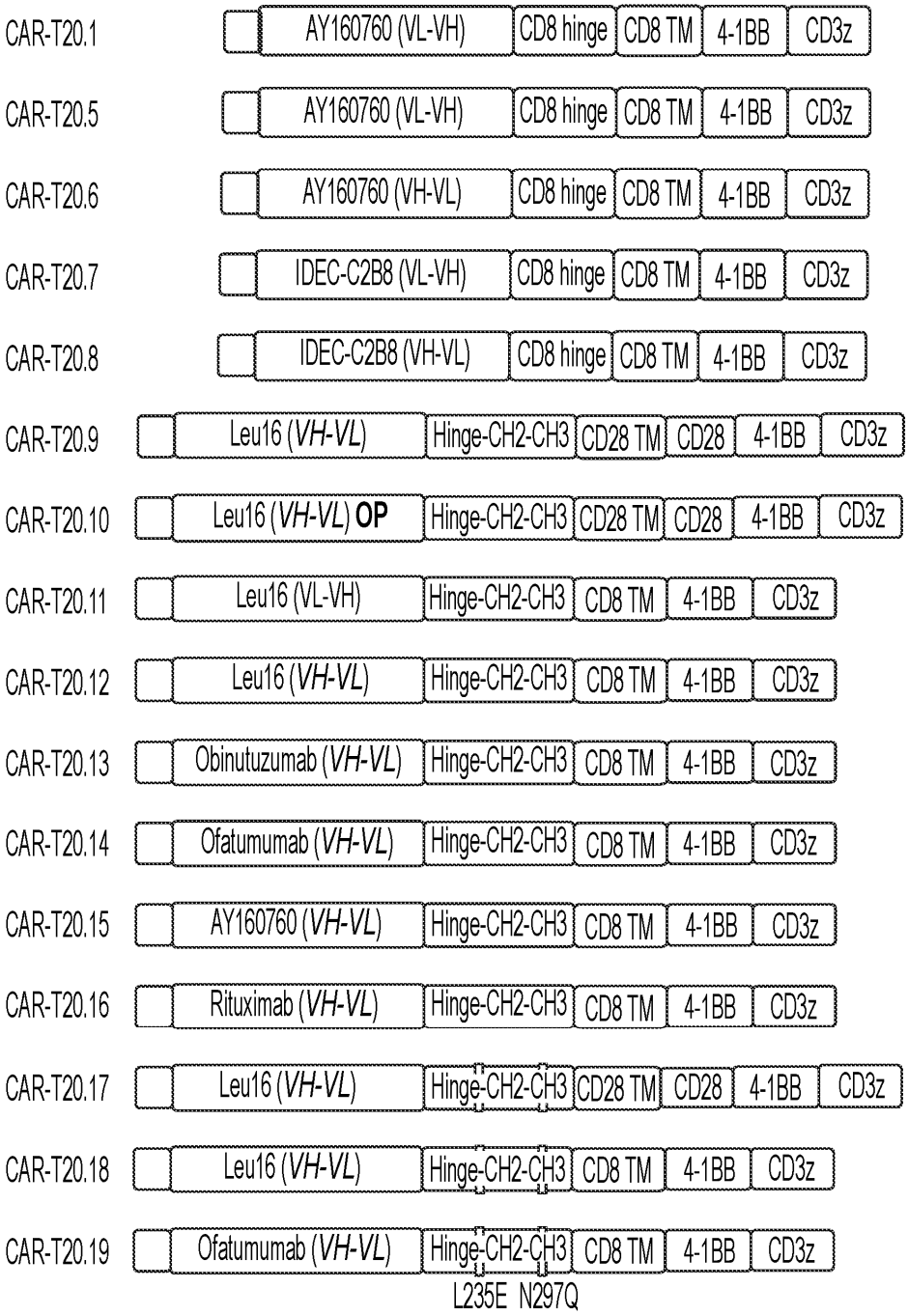

CAR-T20.1
AY160760 (VL-VH)
CD8 hinge
CD8 TM
4-1BB
CD3z
CAR-T20.5
AY160760 (VL-VH)
CD8 hinge
CD8 TM
4-1BB
CD3z
CAR-T20.6
AY160760 (VH-VL)
CD8 hinge
CD8 TM
4-1BB
CD3z
CAR-T20.7
IDEC-C2B8 (VL-VH)
CD8 hinge
CD8 TM
4-1BB
CD3z
CAR-T20.8
IDEC-C2B8 (VH-VL)
CD8 hinge
CD8 TM
4-1BB
CD3z
CAR-T20.9
Leu16 (VH-VL)
Hinge-CH2-CH3
CD28 TM
CD28
4-1BB
CD3z
CAR-T20.10
Leu16 (VH-VL) OP
Hinge-CH2-CH3
CD28 TM
CD28
4-1BB
CD3z
CAR-T20.11
Leu16 (VL-VH)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.12
Leu16 (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.13
Obinutuzumab (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.14
Ofatumumab (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.15
AY160760 (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.16
Rituximab (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.17
Leu16 (VH-VL)
Hinge-CH2-CH3
CD28 TM
CD28
4-1BB
CD3z
CAR-T20.18
Leu16 (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
CAR-T20.19
Ofatumumab (VH-VL)
Hinge-CH2-CH3
CD8 TM
4-1BB
CD3z
L235E N297Q

FIG. 7

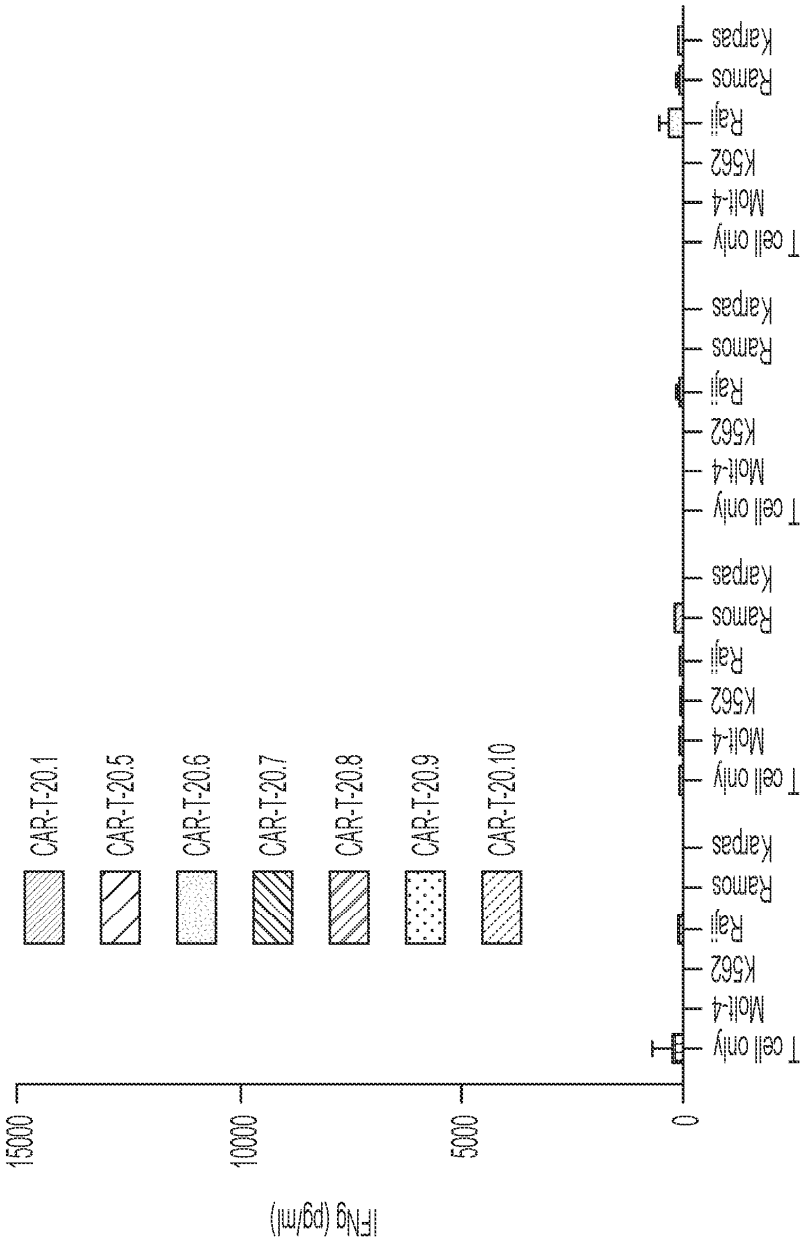

IFNg (pg/ml)
15000
10000
5000
0
NT
CAR-T-20.1
CAR-T-20.5
CAR-T-20.6
CAR-T-20.7
CAR-T-20.8
CAR-T-20.9
CAR-T-20.10
T cell only
Molt-4
K562
Raji
Ramos
Karpas
T cell only
Molt-4
K562
Raji
Ramos
Karpas
T cell only
Molt-4
K562
Raji
Ramos
Karpas
T cell only
Molt-4
K562
Raji
Ramos
Karpas

FIG. 8A

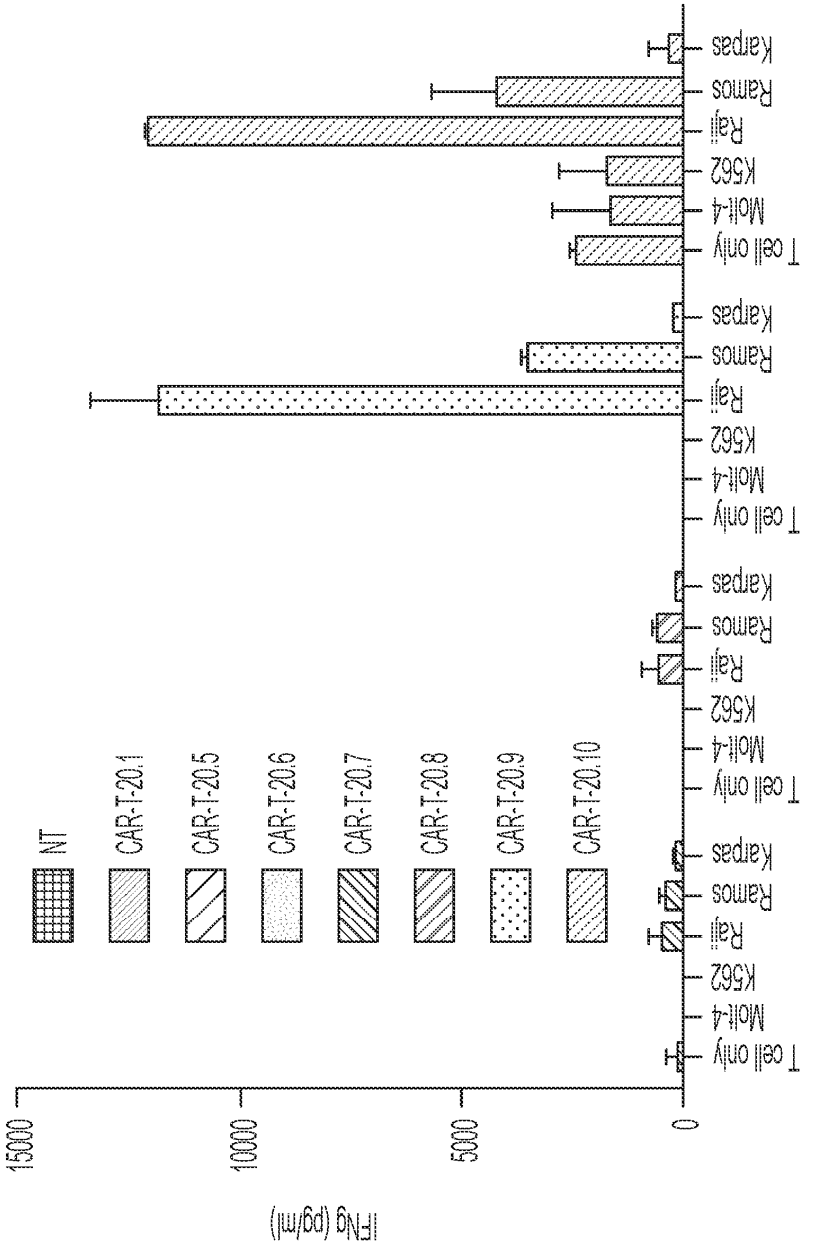


FIG. 8A CONTINUED

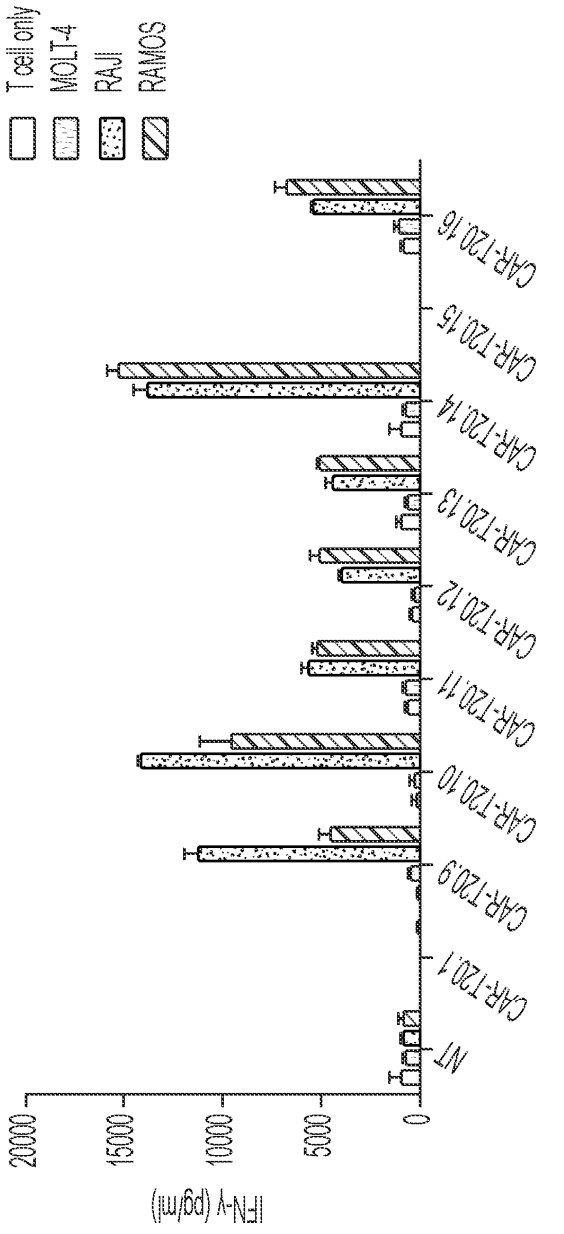

T cell only
MOLT-4
RAJI
RAMOS
IFN-γ (pg/ml)
20000
15000
10000
5000
0
NT
CAR-T20.1
CAR-T20.9
CAR-T20.10
CAR-T20.11
CAR-T20.12
CAR-T20.13
CAR-T20.14
CAR-T20.15
CAR-T20.16

FIG. 8B

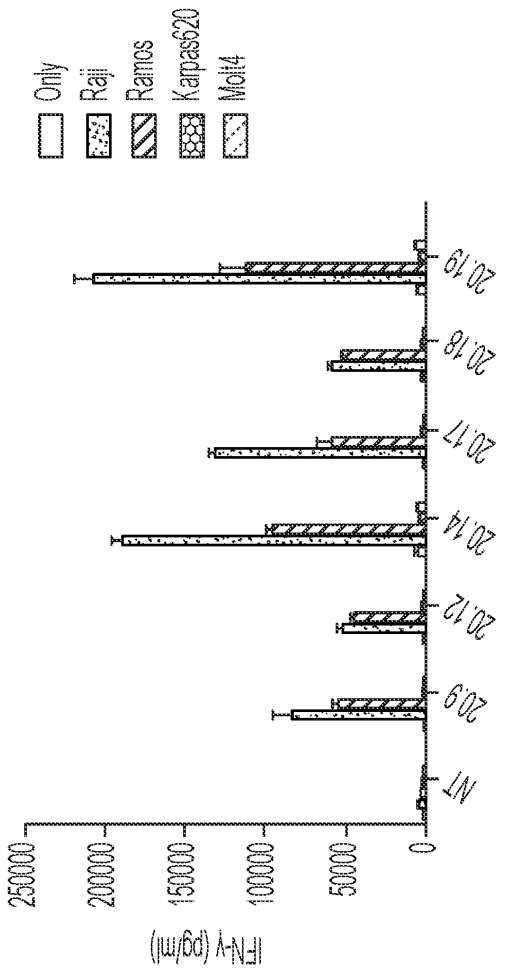

Only
Raji
Ramos
Karpas620
Molt4
IFN-γ (pg/ml)
250000
200000
150000
100000
50000
0
NT
20.9
20.12
20.14
20.17
20.18
20.19

FIG. 8C

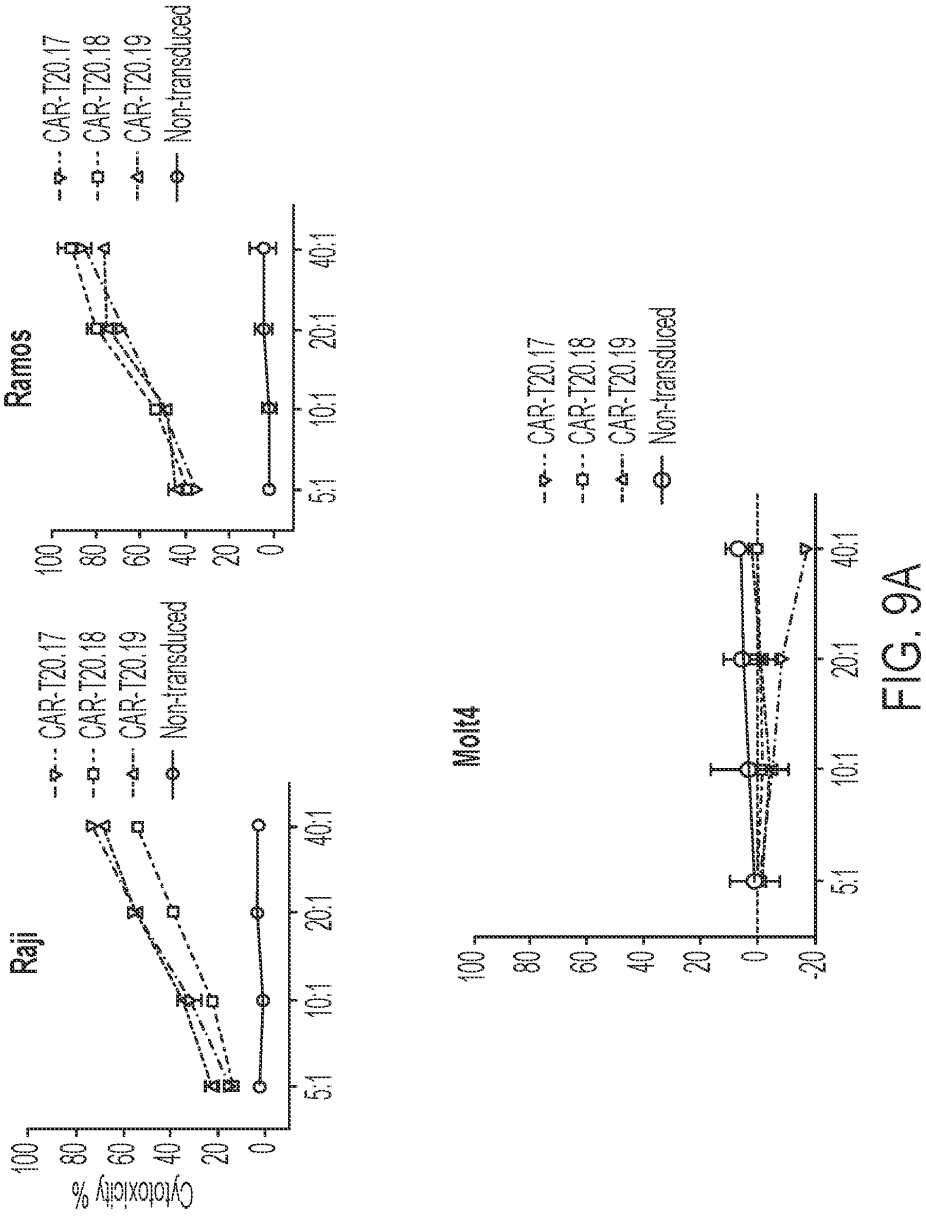

Raji
Ramos
Molt4
Cytotoxicity %
CAR-T20.17
CAR-T20.18
CAR-T20.19
Non-transduced
100
80
60
40
20
0
-20
5:1
10:1
20:1
40:1

FIG. 9A

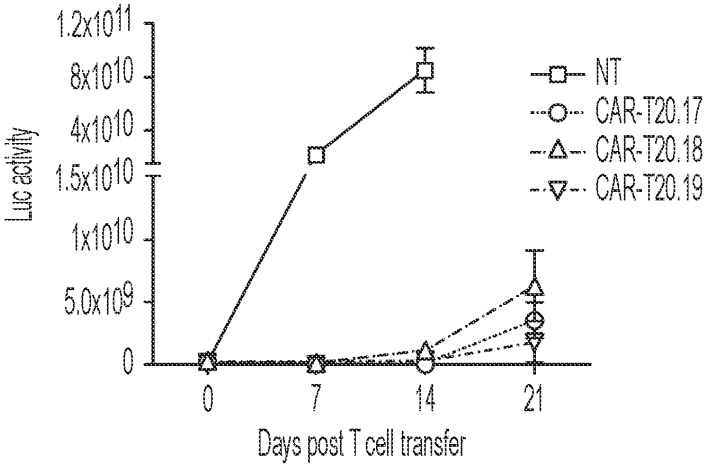

1.2x10^11
8x10^10
4x10^10
1.5x10^10
1x10^10
5.0x10^9
0
Luc activity
0
7
14
21
Days post T cell transfer
NT
CAR-T20.17
CAR-T20.18
CAR-T20.19

FIG. 9B

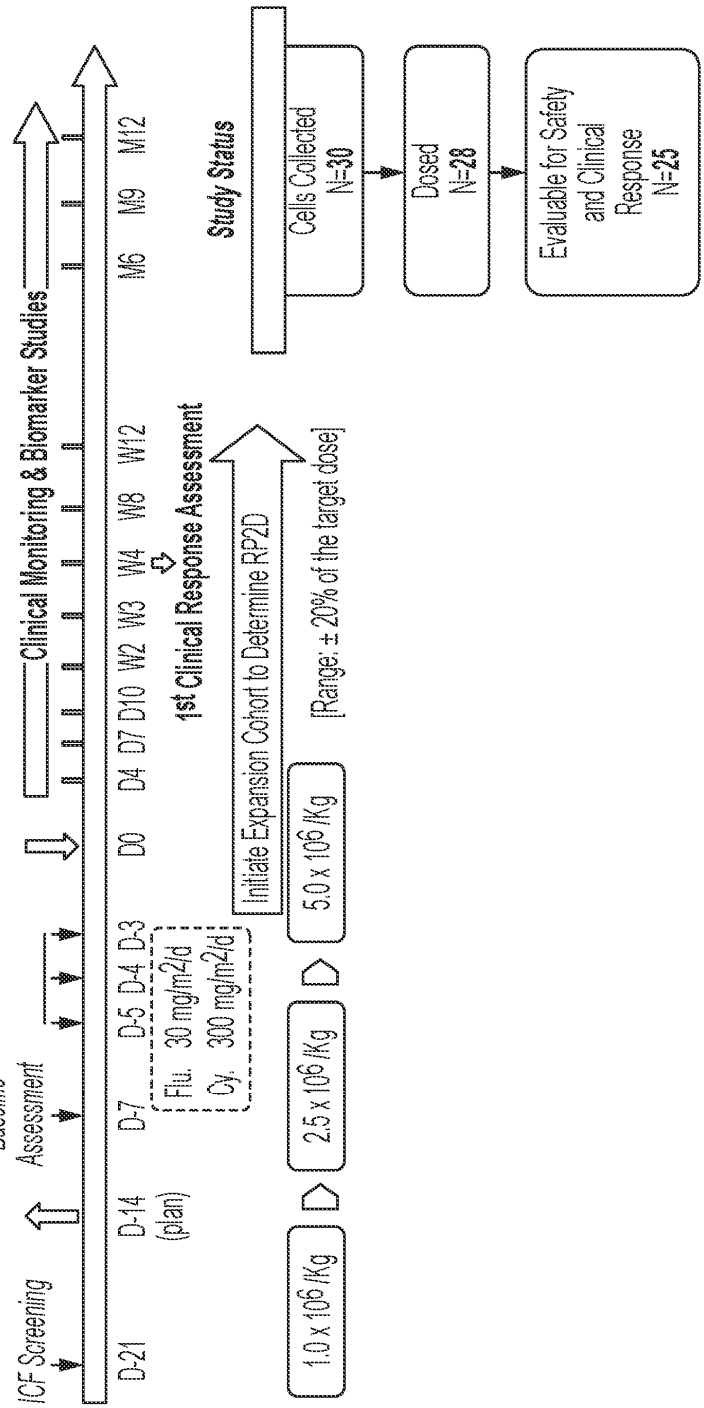

C-CAR039
Apheresis
Manufacturing & QC
Infusion
Open-Label Study
Baseline Assessment
ICF Screening
Clinical Monitoring & Biomarker Studies
D-21
D-14 (plan)
D-7
D-5 D-4 D-3
Flu. 30 mg/m2/d
Cy. 300 mg/m2/d
D0
D4 D7 D10 W2 W3 W4 W8 W12
M6 M9 M12
1st Clinical Response Assessment
Initiate Expansion Cohort to Determine RP2D
1.0 x 10^6 /Kg
2.5 x 10^6 /Kg
5.0 x 10^6 /Kg
[Range: ± 20% of the target dose]
Study Status
Cells Collected N=30
Dosed N=28
Evaluable for Safety and Clinical Response N=25

FIG. 10

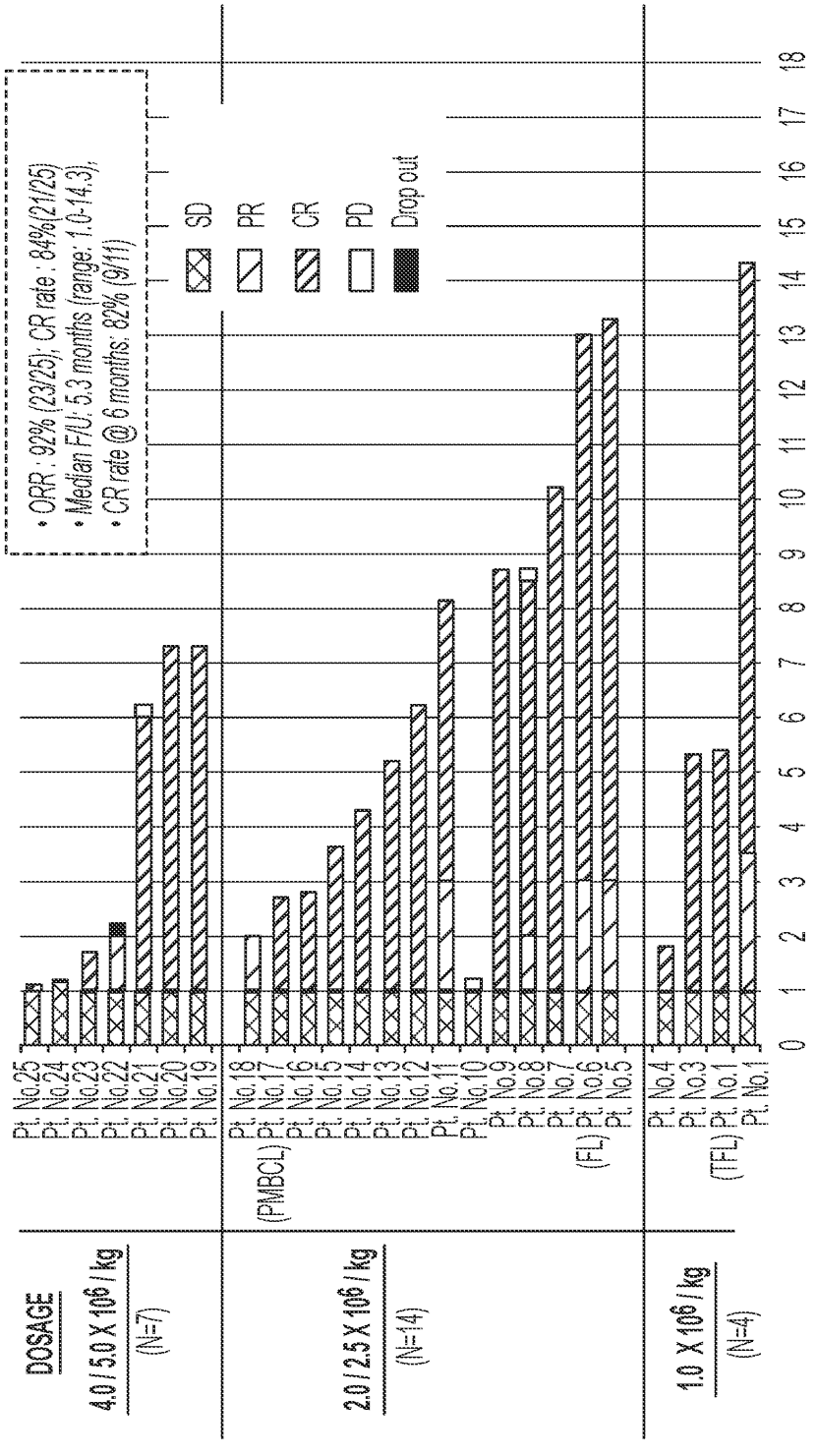

DOSAGE
4.0 / 5.0 X 10⁶ / kg
(N=7)
2.0 / 2.5 X 10⁶ / kg
(N=14)
1.0 X 10⁶ / kg
(N=4)
Pt. No.25
Pt. No.24
Pt. No.23
Pt. No.22
Pt. No.21
Pt. No.20
Pt. No.19
Pt. No.18
(PMBCL) Pt. No.17
Pt. No.16
Pt. No.15
Pt. No.14
Pt. No.13
Pt. No.12
Pt. No.11
Pt. No.10
Pt. No.9
Pt. No.8
Pt. No.7
(FL) Pt. No.6
Pt. No.5
Pt. No.4
Pt. No.3
(TFL) Pt. No.1
Pt. No.1
• ORR : 92% (23/25); CR rate : 84%(21/25)
• Median F/U: 5.3 months (range: 1.0-14.3),
• CR rate @ 6 months: 82% (9/11)
SD
PR
CR
PD
Drop out
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Months after C-CAR039 infusion
Data cut-off date: Jan 31, 2021. 20 patients are evaluable for efficacy., Pt. No.22 dropped out at month 2 for SPM (AML)

FIG. 11

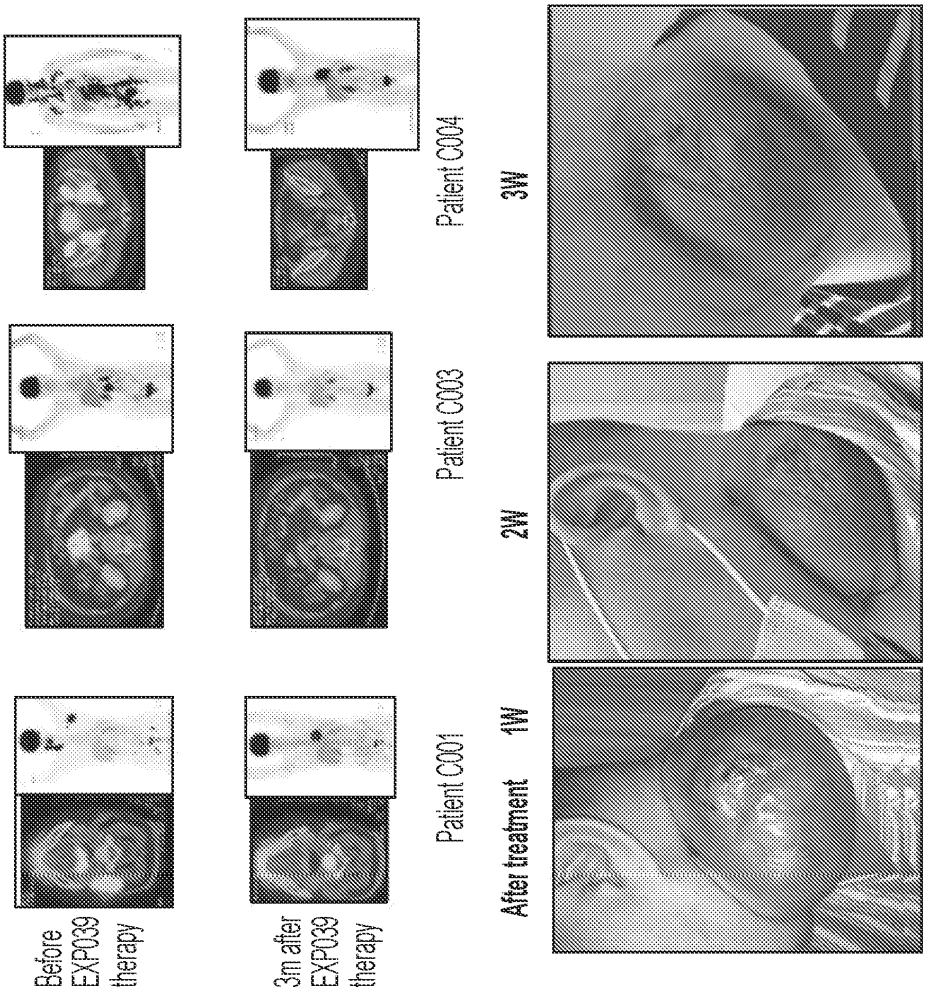

Before EXP039 therapy
3m after EXP039 therapy
Patient 0001
Patient 0003
Patient 0004
After treatment 1W
2W
3W

FIG. 12

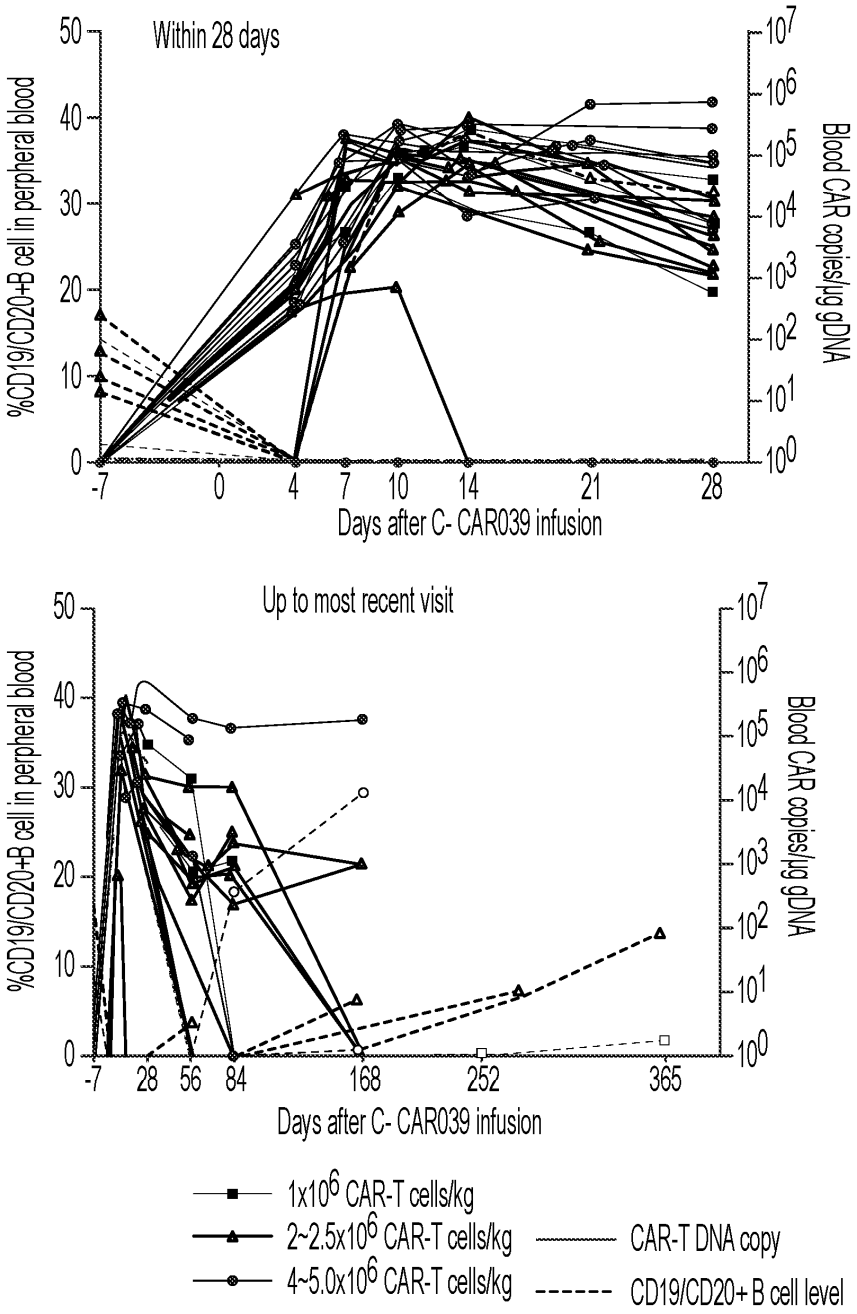

Within 28 days
%CD19/CD20+B cell in perpheral blood
Blood CAR copies/μg gDNA
Days after C- CAR039 infusion
Up to most recent visit
%CD19/CD20+B cell in perpheral blood
Blood CAR copies/μg gDNA
Days after C- CAR039 infusion
1x10^6 CAR-T cells/kg
2~2.5x10^6 CAR-T cells/kg
4~5.0x10^6 CAR-T cells/kg
CAR-T DNA copy
CD19/CD20+ B cell level

FIG. 13

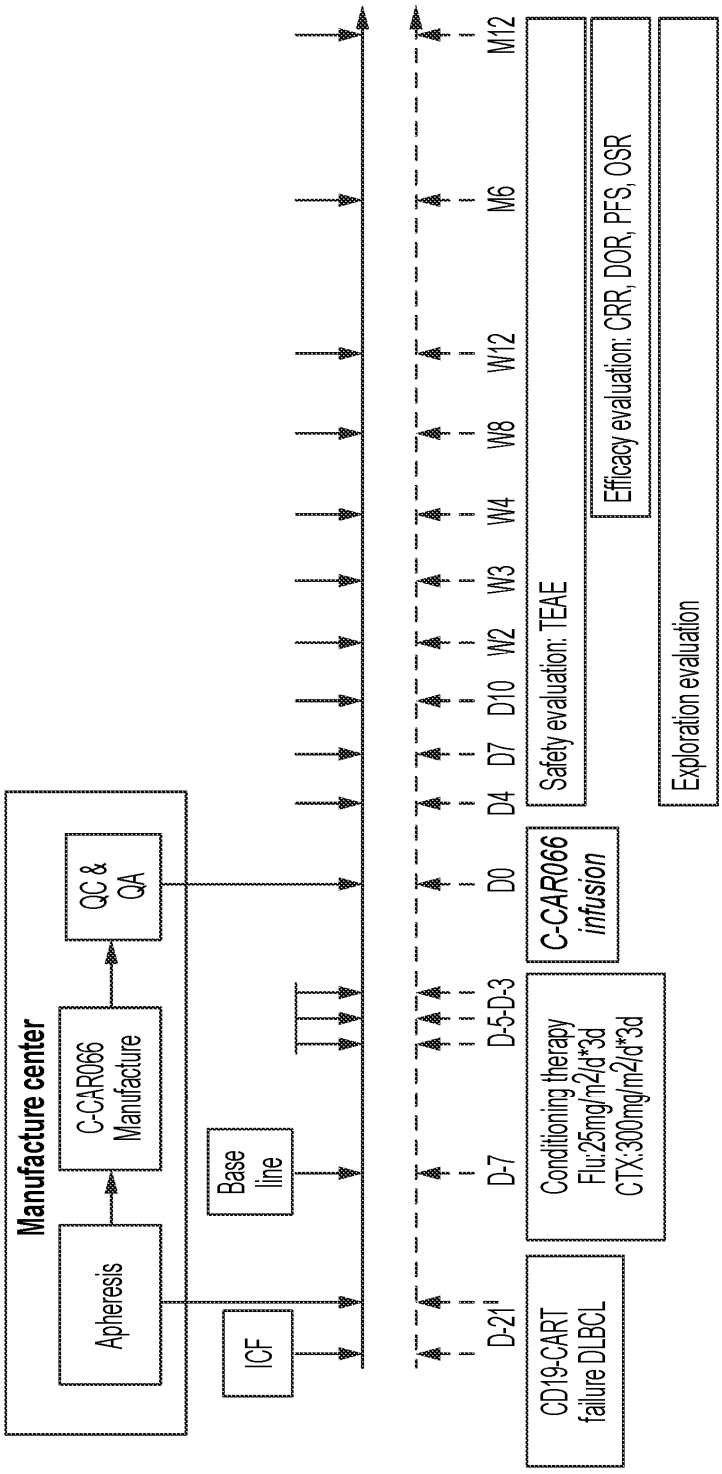

Manufacture center
Apheresis
C-CAR066 Manufacture
QC & QA
ICF
Base line
CD19-CART failure DLBCL
Conditioning therapy Flu:25mg/m2/d*3d CTX:300mg/m2/d*3d
C-CAR066 infusion
Safety evaluation: TEAE
Efficacy evaluation: CRR, DOR, PFS, OSR
Exploration evaluation
D-21[1]
D-7
D-5-D-3
D0
D4
D7
D10
W2
W3
W4
W8
W12
M6
M12

FIG. 14

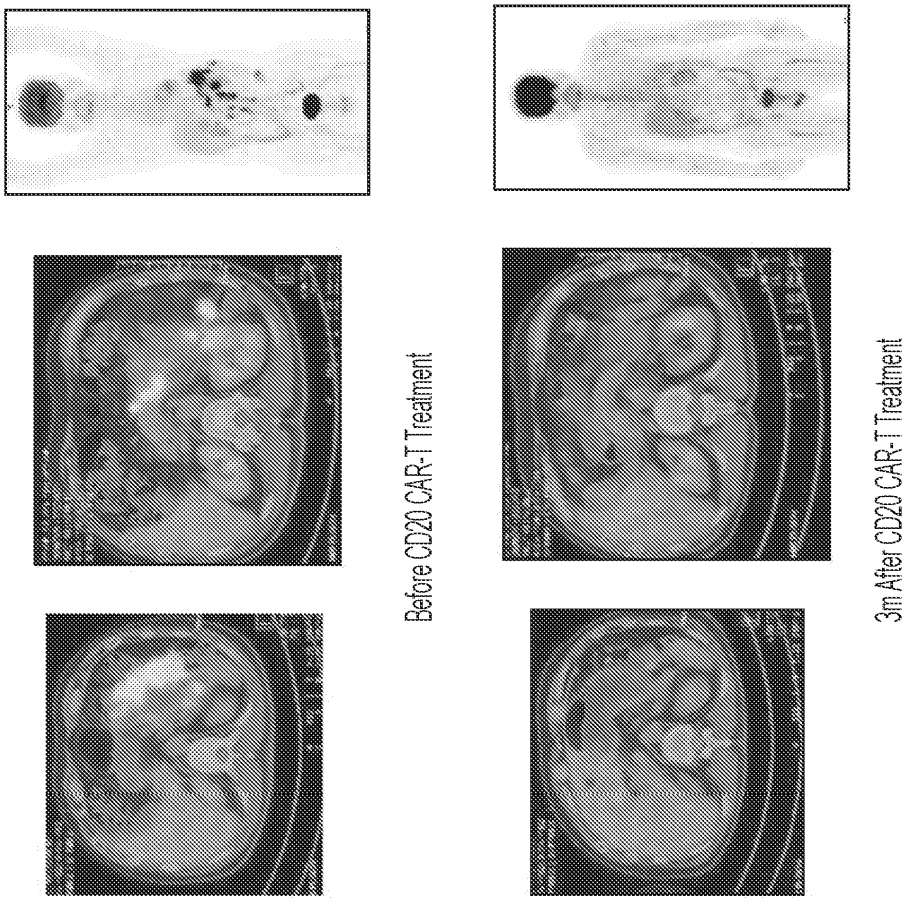


FIG. 15

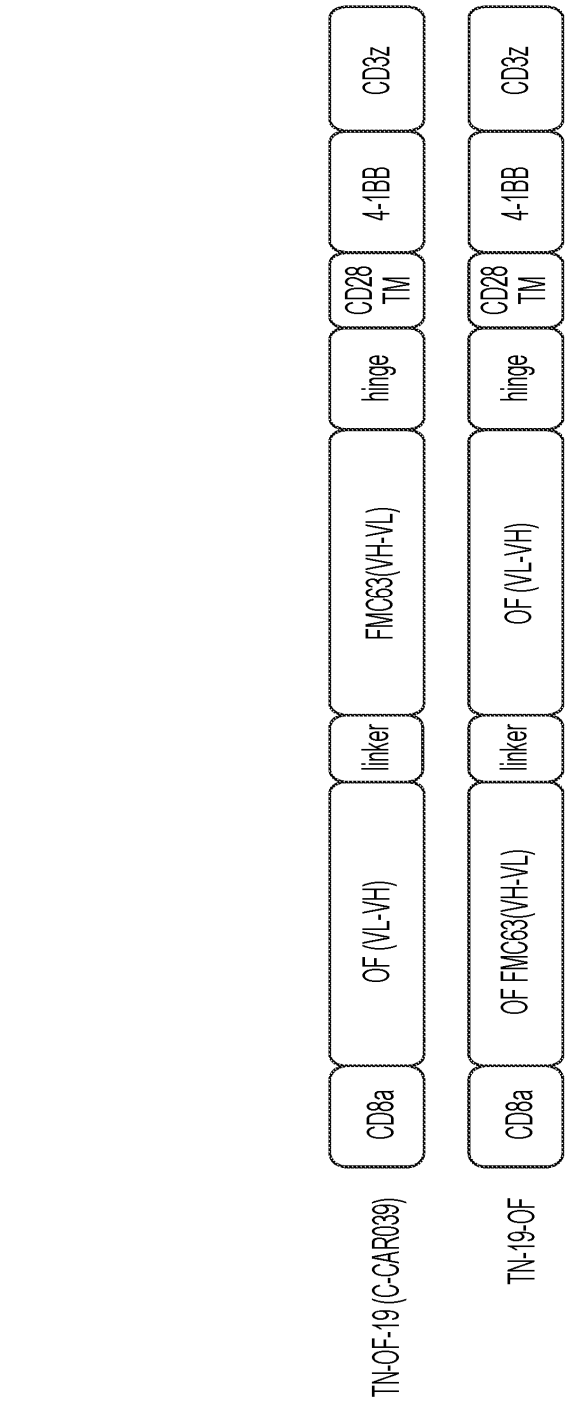

TN-OF-19 (C-CAR039)
CD8a
OF (VL-VH)
linker
FMC63(VH-VL)
hinge
CD28 TM
4-1BB
CD3z
TN-19-OF
CD8a
OF FMC63(VH-VL)
linker
OF (VL-VH)
hinge
CD28 TM
4-1BB
CD3z

FIG. 16A

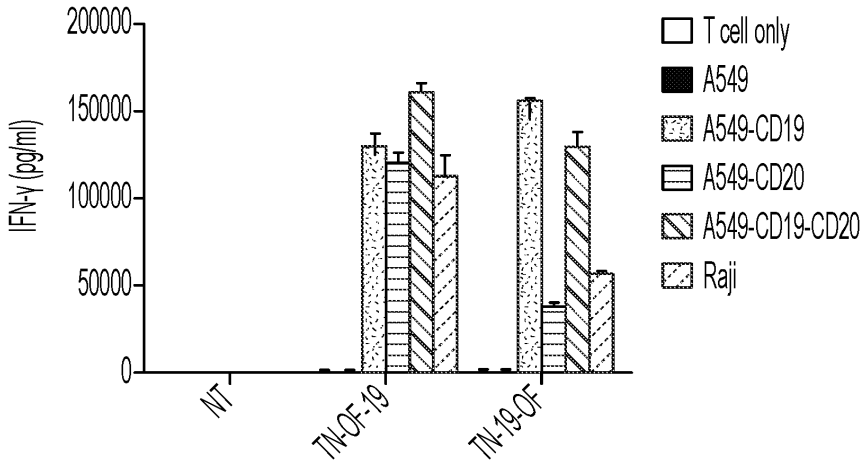

200000
150000
100000
50000
0
IFN-γ (pg/ml)
NT
TN-OF-19
TN-19-OF
T cell only
A549
A549-CD19
A549-CD20
A549-CD19-CD20
Raji

FIG. 16B

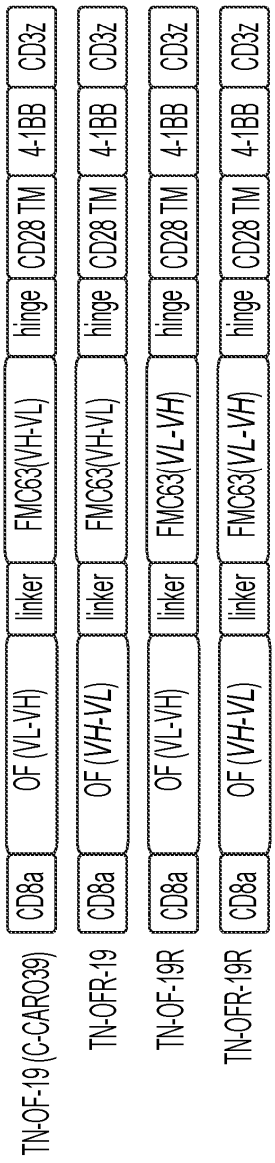

TN-OF-19 (C-CARO39)
CD8a
OF (VL-VH)
linker
FMC63(VH-VL)
hinge
CD28 TM
4-1BB
CD3z
TN-OFR-19
CD8a
OF (VH-VL)
linker
FMC63(VH-VL)
hinge
CD28 TM
4-1BB
CD3z
TN-OF-19R
CD8a
OF (VL-VH)
linker
FMC63(VL-VH)
hinge
CD28 TM
4-1BB
CD3z
TN-OFR-19R
CD8a
OF (VH-VL)
linker
FMC63(VL-VH)
hinge
CD28 TM
4-1BB
CD3z

FIG. 16C

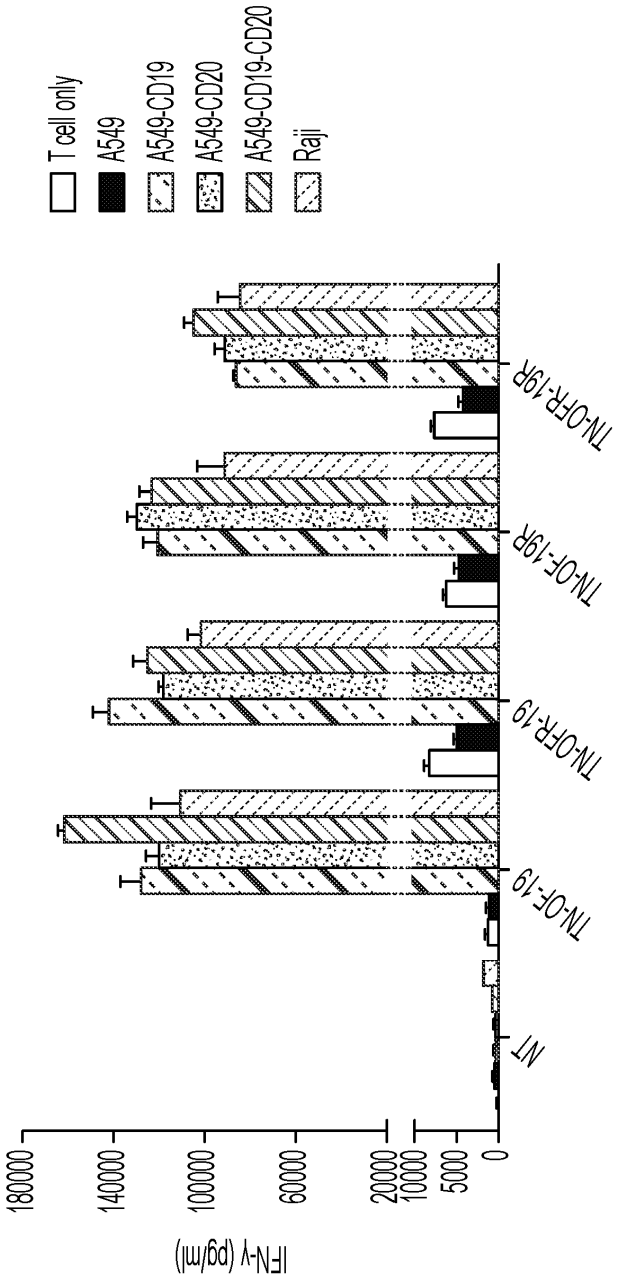

T cell only
A549
A549-CD19
A549-CD20
A549-CD19-CD20
Raji
IFN-γ (pg/ml)
180000
140000
100000
60000
20000
10000
5000
0
NT
TN-OF-19
TN-OFR-19
TN-OF-19R
TN-OFR-19R

FIG. 16D

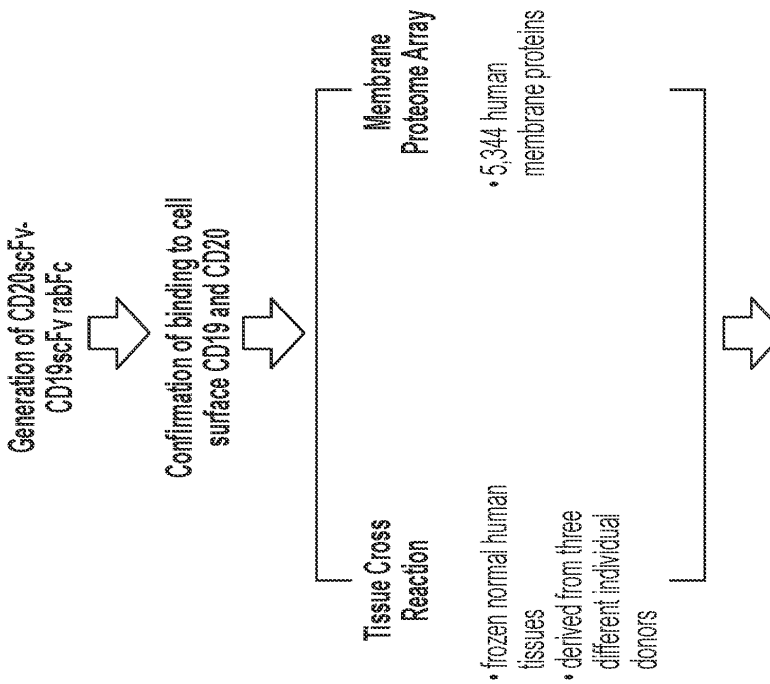

Generation of CD20scFv-CD19scFv rabFc
Confirmation of binding to cell surface CD19 and CD20
Tissue Cross Reaction
• frozen normal human tissues
• derived from three different individual donors
Membrane Proteome Array
• 5,344 human membrane proteins
Validation by co-culture primary cells or antigen over-expressing cells with CAR-T cells

FIG. 17A

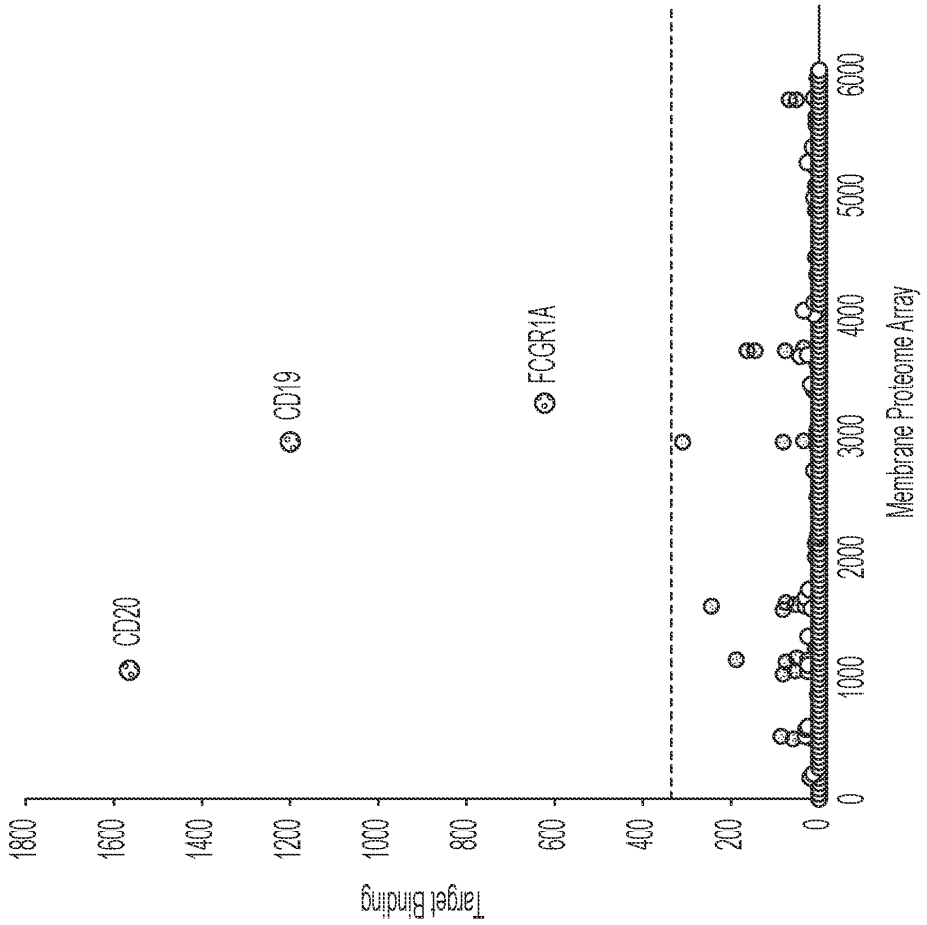
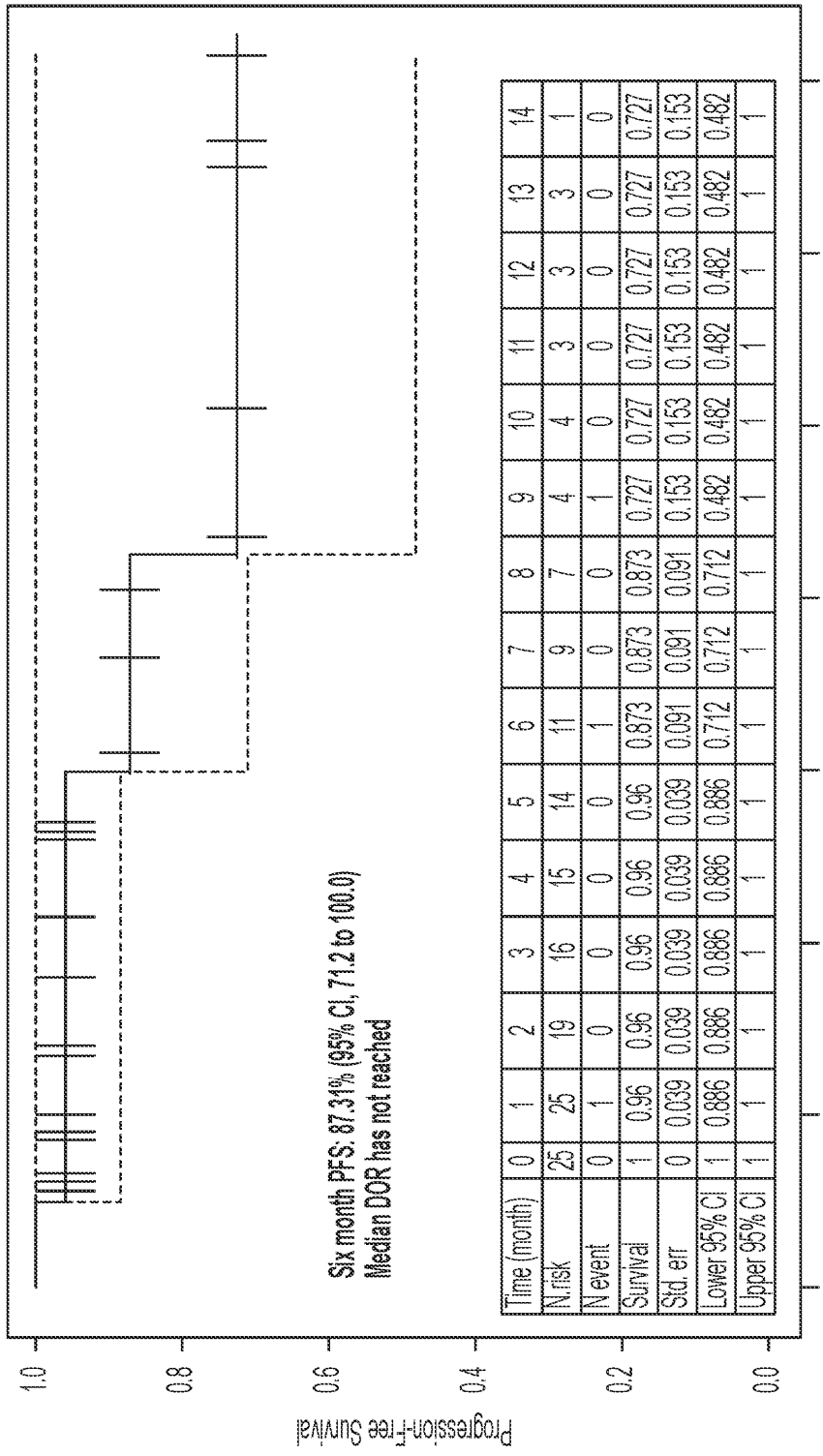

CD20
CD19
FCGR1A
Target Binding
Membrane Proteome Array
0
200
400
600
800
1000
1200
1400
1600
1800
0
1000
2000
3000
4000
5000
6000

FIG. 17B



Time (month)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
N.risk	25	25	19	16	15	14	11	9	7	4	4	3	3	3	1
N event	0	1	0	0	0	0	1	0	0	1	0	0	0	0	0
Survival	1	0.96	0.96	0.96	0.96	0.96	0.873	0.873	0.873	0.727	0.727	0.727	0.727	0.727	0.727
Std. err	0	0.039	0.039	0.039	0.039	0.039	0.091	0.091	0.091	0.153	0.153	0.153	0.153	0.153	0.153
Lower 95% CI	1	0.886	0.886	0.886	0.886	0.886	0.712	0.712	0.712	0.482	0.482	0.482	0.482	0.482	0.482
Upper 95% CI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

FIG. 18

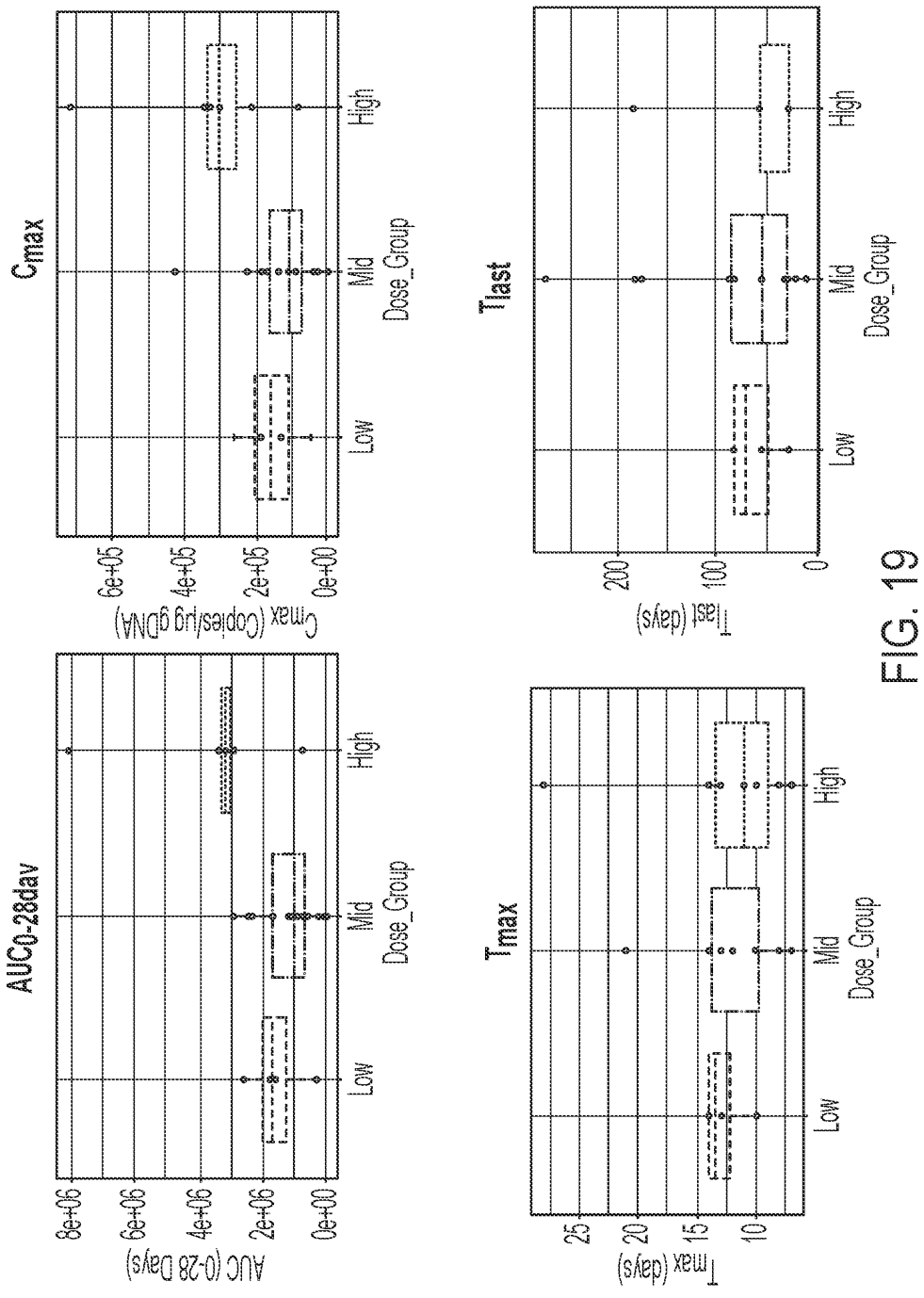

Cmax
Cmax (Copies/µg gDNA)
0e+00
2e+05
4e+05
6e+05
Low
Mid
High
Dose_Group
Tlast
Tlast (days)
0
100
200
Low
Mid
High
Dose_Group
AUC0-28day
AUC (0-28 Days)
0e+00
2e+06
4e+06
6e+06
8e+06
Low
Mid
High
Dose_Group
Tmax
Tmax (days)
10
15
20
25
Low
Mid
High
Dose_Group

FIG. 19

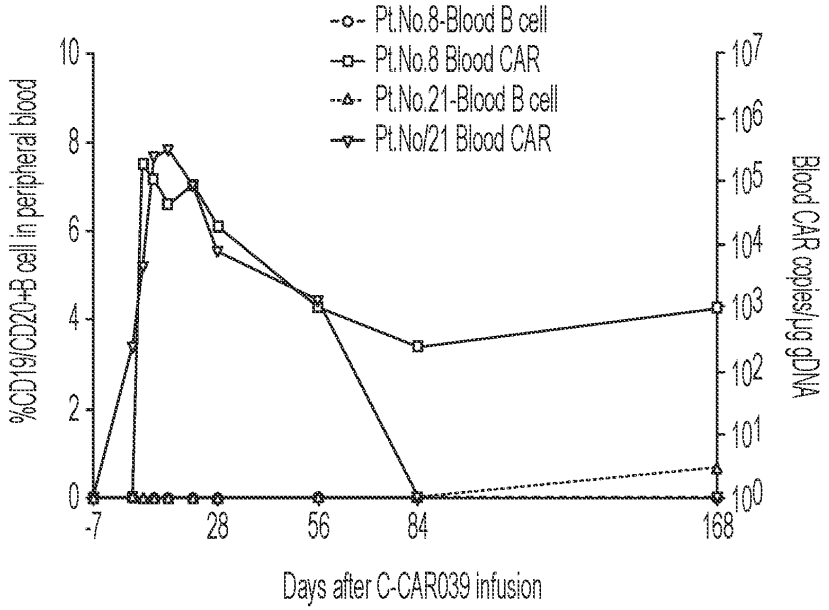

Pt.No.8-Blood B cell
Pt.No.8 Blood CAR
Pt.No.21-Blood B cell
Pt.No/21 Blood CAR
%CD19/CD20+B cell in peripheral blood
Blood CAR copies/ug gDNA
Days after C-CAR039 infusion
0
2
4
6
8
10
-7
28
56
84
168
10^0
10^1
10^2
10^3
10^4
10^5
10^6
10^7

FIG. 20