

WT 3E10 antibody sequences

>3E10-HC

EVQLVESGGGLVKPGGSRKLSCAASGFTTFSDYGMHWVRQAPEKGLEWVAYIISGSSSTIYYADTVKGRFTISRDNAK
NTLFLQMTSLRSEDAMYYCARRGLLLDYWGQGTTTLTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC
PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:1)

>3E10-VH

EVQLVESGGGLVKPGGSRKLSCAASGFTTFSDYGMHWVRQAPEKGLEWVAYIISGSSSTIYYADTVKGRFTISRDNAK
NTLFLQMTSLRSEDAMYYCARRGLLLDYWGQGTTTLTVSS (SEQ ID NO:2)

>3E10-VH-CDR1

DYGMH (SEQ ID NO:3)

>3E10-VH-CDR2

YISGSSSTIYYADTVKG (SEQ ID NO:4)

>3E10-VH-CDR3

RGLLLDY (SEQ ID NO:5)

>3E10-HC-SP

MGWSCIILFLVATATGVHS (SEQ ID NO:6)

>3E10-LC

DIVLTQSPASLAVSLGQRATISCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLES¹GPV²PARFSGSGSGTDFT
LN³HPVEEEDAATYYCQHSREFPWT⁴FGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASV⁵VCLLN⁶FYPREAKVQW
KVDNALQSGNSQESVTEQDSKDS⁷TYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID
NO:7)

>3E10-VL

DIVLTQSPASLAVSLGQRATISCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLES¹GPV²PARFSGSGSGTDFT
LN³HPVEEEDAATYYCQHSREFPWT⁴FGGGTKLEIK (SEQ ID NO:8)

>3E10-VL-CDR1

RASKSVSTSSYSYMH (SEQ ID NO:9)

>3E10-VL-CDR2

YASYLES (SEQ ID NO:10)

>3E10-VL-CDR3

QHSREFPWT (SEQ ID NO:11)

>3E10-LC-SP

MGWSCIILFLVATATGVHS (SEQ ID NO:12)

FIG. 1

D31N 3E10 antibody sequences**>3E10-HC_D31N**

EVQLVESGGGLV^KPGGSRKLS^{CAASGFTFS}NYGMHWVRQAP^EKGLEWVAYISSGSSTIYYADTVKGRFTISRDN^AKNTLF
LQMTSLRSED^TAMYYCARR^GLLLDYWGQGT^TLTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSG
ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVF
LFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNAKALPAPIEK^TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK^TTPPVLDSD
GSFFLYSKLTVDKSRWQQGNV^FSCSV^MHEALHNHYTQKSLSLSPGK (SEQ ID NO:13)

>3E10-VH_D31N

EVQLVESGGGLV^KPGGSRKLS^{CAASGFTFS}NYGMHWVRQAP^EKGLEWVAYISSGSSTIYYADTVKGRFTISRDN^AKNTLF
LQMTSLRSED^TAMYYCARR^GLLLDYWGQGT^TLTVSS (SEQ ID NO:14)

>3E10-VH-CDR1_D31N

NYGMH (SEQ ID NO:15)

>3E10-VH-CDR1a

XYGMH, where X is D or N (SEQ ID NO:16)

>3E10-VH-CDR2_D31N

YISSGSSTIYYADTVKG (SEQ ID NO:17)

>3E10-VH-CDR3_D31N

RGLLLDY (SEQ ID NO:18)

>3E10-HC-SP_D31N

MGWSCIIILFLVATATGVHS (SEQ ID NO:19)

>3E10-VL_D31N

DIVLTQSPASLAVSLGQRATISCRASKSVSTSSYSY^MHWYQQKPGQP^PKLLIKYASYLESGV^PARFSGSGSGTDFTLN^IH
PVEEEDAATYYCQHSREFPWT^FGGG^TKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:20)

>3E10-VL-VR_D31N

DIVLTQSPASLAVSLGQRATISCRASKSVSTSSYSY^MHWYQQKPGQP^PKLLIKYASYLESGV^PARFSGSGSGTDFTLN^IH
PVEEEDAATYYCQHSREFPWT^FGGG^TKLEIK (SEQ ID NO:21)

>3E10-VL-CDR1_D31N

RASKSVSTSSYSY^MH (SEQ ID NO:22)

>3E10-VL-CDR2_D31N

YASYLE^S (SEQ ID NO:23)

>3E10-VL-CDR3_D31N

QHSREFPWT (SEQ ID NO:24)

>3E10-LC-SP_D31N

MGWSCIIILFLVATATGVHS (SEQ ID NO:25)

FIG. 2A

Other known 3E10 CDR variants

3E10-VH-CDR2 Variants3E10-VH-CDR2.1 YISSGSSTIYYADSVKG (SEQ ID NO:26)3E10-VH-CDR2.2 YISSSSSTIYYADSVKG (SEQ ID NO:27)3E10-VL-CDR1 Variants3E10-VL-CDR1.1 RASKSVSTSSYSYLA (SEQ ID NO:28)3E10-VL-CDR1.2 RASKTVSTSSYSYMH (SEQ ID NO:29)3E10-VL-CDR2 Variants3E10-VL-CDR2.1 YASYLQS (SEQ ID NO:30)

FIG. 2B

Additionally contemplated 3E10 CDR variants

3E10-VH-CDR2 Variants3E10-VH-CDR2.3 YISSX₁SSTIYYADX₂VKG, where:X₁ and X₁ are separately any amino acid (SEQ ID NO:31)3E10-VL-CDR1 Variants3E10-VL-CDR1.3 RASKX₁VSTSSYSYX₂X₃, where:X₁, X₁, and X₁ and are separately any amino acid (SEQ ID NO:32)3E10-VL-CDR2 Variants3E10-VL-CDR2.2 YASYLX₁S, where:X₁ is any amino acid (SEQ ID NO:33)

FIG. 2C

Charge-conserved Variant 3E10 CDRs**VH CDR1 Variants**

3E10-VH-CDR1.c1 QYGMH (SEQ ID NO:34)
 3E10-VH-CDR1.c2 EYGMH (SEQ ID NO:35)
 3E10-VH-CDR1.c3 X₁YGMX₂, where:
 X₁ is D or N, and X₂ is K or R (SEQ ID NO:36)
 3E10-VH-CDR1.c4 QYGMX₁, where X₁ is K or R (SEQ ID NO:37)
 3E10-VH-CDR1.c5 EYGMX₁, where X₁ is K or R (SEQ ID NO:38)

VH CDR2 Variants

3E10-VH-CDR2.c1 YISSGSSTIYYAETVKG (SEQ ID NO:39)
 3E10-VH-CDR2.c2 YISSGSSTIYYADTVX₁G, where X₁ is R or H (SEQ ID NO:40)
 3E10-VH-CDR2.c3 YISSGSSTIYYAETVX₁G, where X₁ is R or H (SEQ ID NO:41)

VH CDR3 Variants

3E10-VH-CDR3.c1 X₁GLLLDY, where X₁ is K or H (SEQ ID NO:42)
 3E10-VH-CDR3.c2 RGLLLEY (SEQ ID NO:43)
 3E10-VH-CDR3.c3 X₁GLLLEY, where X₁ is K or H (SEQ ID NO:44)

VL CDR1 Variants

3E10-VL-CDR1.c1 X₁ASKSVSTSSYSYMH, where X₁ is K or H (SEQ ID NO:45)
 3E10-VL-CDR1.c2 RASX₁SVSTSSYSYMH, where X₁ is R or H (SEQ ID NO:46)
 3E10-VL-CDR1.c3 RASKSVSTSSYSYMX₁, where X₁ is K or R (SEQ ID NO:47)
 3E10-VL-CDR1.c4 X₁ASX₂SVSTSSYSYMH, where:
 X₁ is K or H, and X₂ is R or H (SEQ ID NO:48)
 3E10-VL-CDR1.c5 X₁ASKSVSTSSYSYMX₂, where:
 X₁ is K or H, and X₂ is K or R (SEQ ID NO:49)
 3E10-VL-CDR1.c6 RASX₁SVSTSSYSYMX₂, where:
 X₁ is R or H, and X₂ is K or R (SEQ ID NO:50)

VL CDR2 Variants

3E10-VL-CDR2.c1 YASYLDS (SEQ ID NO:51)

VL CDR3 Variants

3E10-VL-CDR3.c1 QX₁SREFPWT, where X₁ is K or R (SEQ ID NO:52)
 3E10-VL-CDR3.c2 QHSX₁EFPWT, where X₁ is K or H (SEQ ID NO:53)
 3E10-VL-CDR3.c3 QHSRDFPWT (SEQ ID NO:54)
 3E10-VL-CDR3.c4 QX₁SX₂EFPWT, where:
 X₁ is K or R, and X₂ is K or H (SEQ ID NO:55)
 3E10-VL-CDR3.c5 QX₁SRDFPWT, where X₁ is K or R (SEQ ID NO:56)
 3E10-VL-CDR3.c6 QHSX₁DFPWT, where X₁ is K or H (SEQ ID NO:57)

FIG. 3

Compound Variant 3E10 CDRs

VH CDR1 Variants

3E10-VH-CDR1m X_1YGMX_2 , where:

X_1 is D, E, N, Q, R, or K and

X_2 is K, R, or H (SEQ ID NO:58)

VH CDR2 Variants

3E10-VH-CDR2m $YISSX_1SSTIYYAX_2X_3VX_4G$, where:

X_1 is G or S,

X_2 is D or E,

X_3 is T or S, and

X_4 is K, R, or H (SEQ ID NO:59)

VH CDR3 Variants

3E10-VH-CDR3m X_1GLLLX_2Y , where:

X_1 is K, R, or H, and

X_2 is D or E (SEQ ID NO:60)

VL CDR1 Variants

3E10-VL-CDR1m $X_1ASX_2X_3VSTSSYSYX_4X_5$, where:

X_1 is K, R, or H,

X_2 is K, R, or H,

X_3 is T or S,

X_4 is M or L, and

X_5 is K, R, H, or A (SEQ ID NO:61)

VL CDR2 Variants

3E10-VL-CDR2m $YASYLX_1S$, where:

X_1 is D, E, N, or Q (SEQ ID NO:62)

VL CDR3 Variants

3E10-VL-CDR3m $QX_1SX_2X_3FPWT$, where:

X_1 is K, R, or H,

X_2 is K, R, or H, and

X_3 is D or E (SEQ ID NO:63)

FIG. 4

Humanized 3E10 Heavy Chain Variable Regions**>3E10-VH-h1**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVSYISSGSSTIYYADTVKGRFTI
SRDNAKNSLYLQMNSLRAEDTAVYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:64)

>3E10-VH-h2

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTI
SRDNAKNSLYLQMNSLRAEDTAMYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:65)

>3E10-VH-h3

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTI
SRDNAKNSLYLQMTSLRAEDTAMYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:66)

>3E10-VH-h4

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPEKGLEWVAYISSGSSTIYYADTVKGRFTI
SRDNAKNSLYLQMTSLRAEDTAMYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:67)

>3E10-VH-h5

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTI
SRDNAKNTLFLQMNSLRAEDTAVYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:68)

>3E10-VH-h6

EVQLVESGGGLVQPGGSRKLSAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTI
SRDNAKNTLFLQMNSLRAEDTAVYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:69)

>3E10-VH-h7

EVQLVESGGGLVQPGGSRKLSAASGFTFSNYGMHWVRQAPEKGLEWVAYISSGSSTIYYADTVKGRFTI
SRDNAKNTLFLQMTSLRAEDTAVYYCARRGLLLDYWGQGTLLVTVSS (SEQ ID NO:70)

FIG. 5

Humanized 3E10 Heavy Chain (without signal peptide)**>3E10-HC-h1m**

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVSYISSGSSTIYYADTVKGRFTISRDNAKNSLYLQMN
SLRAEDTAVYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:71)

>3E10-HC-h2m

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTISRDNAKNSLYLQMN
SLRAEDTAMYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:72)

>3E10-HC-h3m

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTISRDNAKNSLYLQMT
SLRAEDTAMYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:73)

>3E10-HC-h4m

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTISRDNAKNSLYLQMT
SLRAEDTAMYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:74)

>3E10-HC-h5m

EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTISRDNAKNTLFLQMN
SLRAEDTAVYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:75)

>3E10-HC-h6m

EVQLVESGGGLVQPGGSRKLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTISRDNAKNTLFLQMN
SLRAEDTAVYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:76)

>3E10-HC-h7m

EVQLVESGGGLVQPGGSRKLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVKGRFTISRDNAKNTLFLQMT
SLRAEDTAVYYCARRGLLLDYWGQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT
FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI
SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGN
VFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO:77)

FIG. 6

Humanized 3E10 Heavy Chain (with signal peptide)**>3E10-HC-h1**

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVS YISSGSSTIYYADTVK
GRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:78)

>3E10-HC-h2

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVK
GRFTISRDNAKNSLYLQMNSLRAEDTAMYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:79)

>3E10-HC-h3

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVK
GRFTISRDNAKNSLYLQMTSLRAEDTAMYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:80)

>3E10-HC-h4

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPEKGLEWVAYISSGSSTIYYADTVK
GRFTISRDNAKNSLYLQMTSLRAEDTAMYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:81)

>3E10-HC-h5

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSLRLSCAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVK
GRFTISRDNAKNTLFLQMNSLRAEDTAVYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:82)

>3E10-HC-h6

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSRKLSAASGFTFSNYGMHWVRQAPGKGLEWVAYISSGSSTIYYADTVK
GRFTISRDNAKNTLFLQMNSLRAEDTAVYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:83)

>3E10-HC-h7

MGWSCIILFLVATATGVHSEVQLVESGGGLVQPGGSRKLSAASGFTFSNYGMHWVRQAPEKGLEWVAYISSGSSTIYYADTVK
GRFTISRDNAKNTLFLQMTSLRAEDTAVYYCARRGLLLDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:84)

FIG. 7

Humanized 3E10 Light Chain Variable Regions**>3E10-VL-h1**

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIYYASYLESGVPARFSGSG
SGTDFTLTINPVEANDTANYYCQHSREFPWTFGGGTKVEIK (SEQ ID NO:85)

>3E10-VL-h2

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESGVPARFSGSG
SGTDFTLTINPVEAEDTATYYCQHSREFPWTFGGGTKVEIK (SEQ ID NO:86)

>3E10-VL-h3

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESGVPARFSGSG
SGTDFTLTINPVEAEDTANYYCQHSREFPWTFGGGTKVEIK (SEQ ID NO:87)

>3E10-VL-h4

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESGVPARFSGSG
SGTDFTLTINPVEAEDAATYYCQHSREFPWTFGGGTKVEIK (SEQ ID NO:88)

>3E10-VL-h5

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESGVPARFSGSG
SGTDFTLNIHPVEAEDTANYYCQHSREFPWTFGGGTKVEIK (SEQ ID NO:89)

>3E10-VL-h6

DIVLTQSPASLAVSPGQRATISCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESGVPARFSGSG
SGTDFTLNIHPVEEEDTANYYCQHSREFPWTFGGGTKVEIK (SEQ ID NO:90)

FIG. 8

Humanized 3E10 Light Chain (without signal peptide)**>3E10-LC-h1m**

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIYYASYLESQVPAFSGSG
SGTDFTLTINPVEANDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO:91)

>3E10-LC-h2m

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESQVPAFSGSG
SGTDFTLTINPVEAEDTATYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO:92)

>3E10-LC-h3m

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESQVPAFSGSG
SGTDFTLTINPVEAEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO:93)

>3E10-LC-h4m

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESQVPAFSGSG
SGTDFTLTINPVEAEDAATYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO:94)

>3E10-LC-h5m

DIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESQVPAFSGSG
SGTDFTLNIHPVEAEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO:95)

>3E10-LC-h6m

DIVLTQSPASLAVSPGQRATISCRASKSVSTSSYSYMHWYQQKPGQPPKLLIKYASYLESQVPAFSGSG
SGTDFTLNIHPVEEEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL
NNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO:96)

FIG. 9

Humanized 3E10 Light Chain (with signal peptide)**>3E10-LC-h1**

MGWSCIIILFLVATATGVHSDIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLL
IYYASYLESQVGFARFSGSGSGTDFTLTINPVEANDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:97)

>3E10-LC-h2

MGWSCIIILFLVATATGVHSDIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLL
IKYASYLESQVGFARFSGSGSGTDFTLTINPVEAEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:98)

>3E10-LC-h3

MGWSCIIILFLVATATGVHSDIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLL
IKYASYLESQVGFARFSGSGSGTDFTLTINPVEAEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:99)

>3E10-LC-h4

MGWSCIIILFLVATATGVHSDIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLL
IKYASYLESQVGFARFSGSGSGTDFTLTINPVEAEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:100)

>3E10-LC-h5

MGWSCIIILFLVATATGVHSDIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLL
IKYASYLESQVGFARFSGSGSGTDFTLNHPVEAEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:101)

>3E10-LC-h6

MGWSCIIILFLVATATGVHSDIVLTQSPASLAVSPGQRATITCRASKSVSTSSYSYMHWYQQKPGQPPKLL
IKYASYLESQVGFARFSGSGSGTDFTLNHPVEEEDTANYYCQHSREFPWTFGGGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYE
KHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:102)

FIG. 10

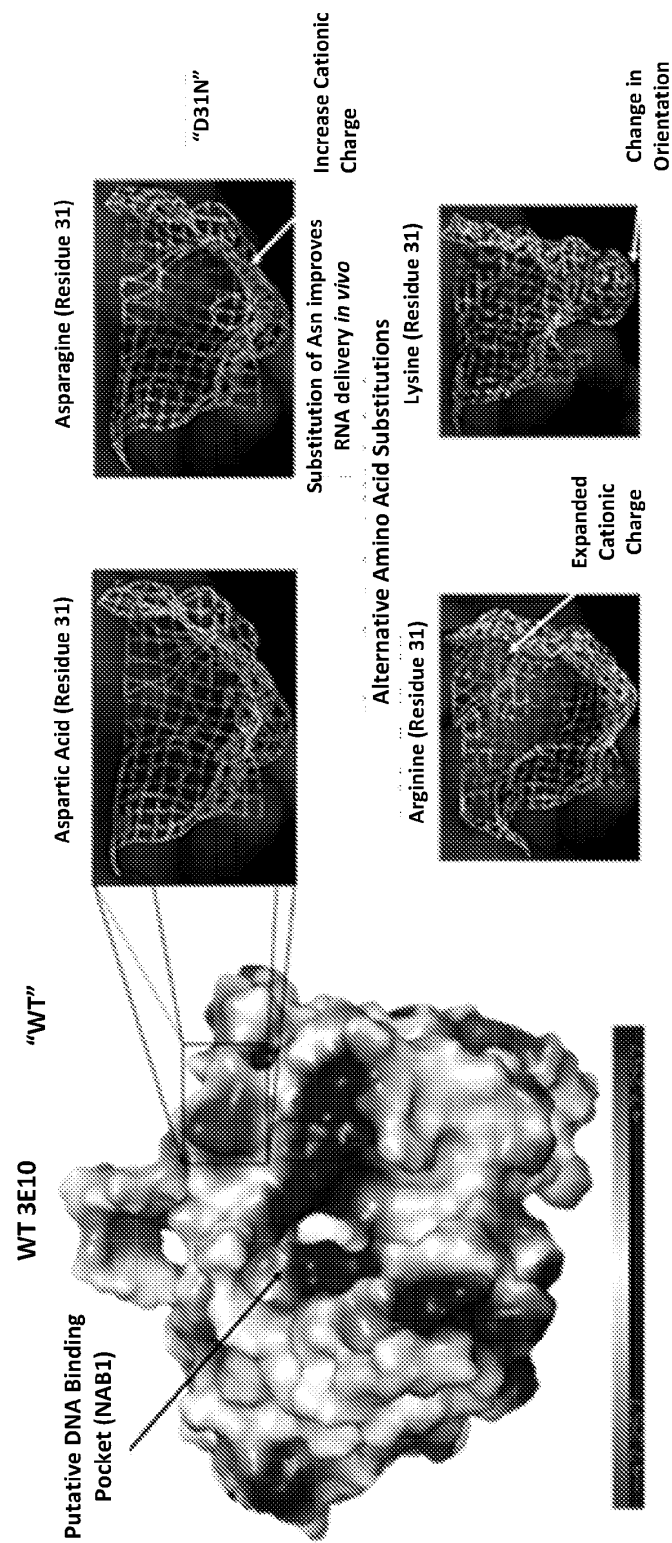


FIG. 11A

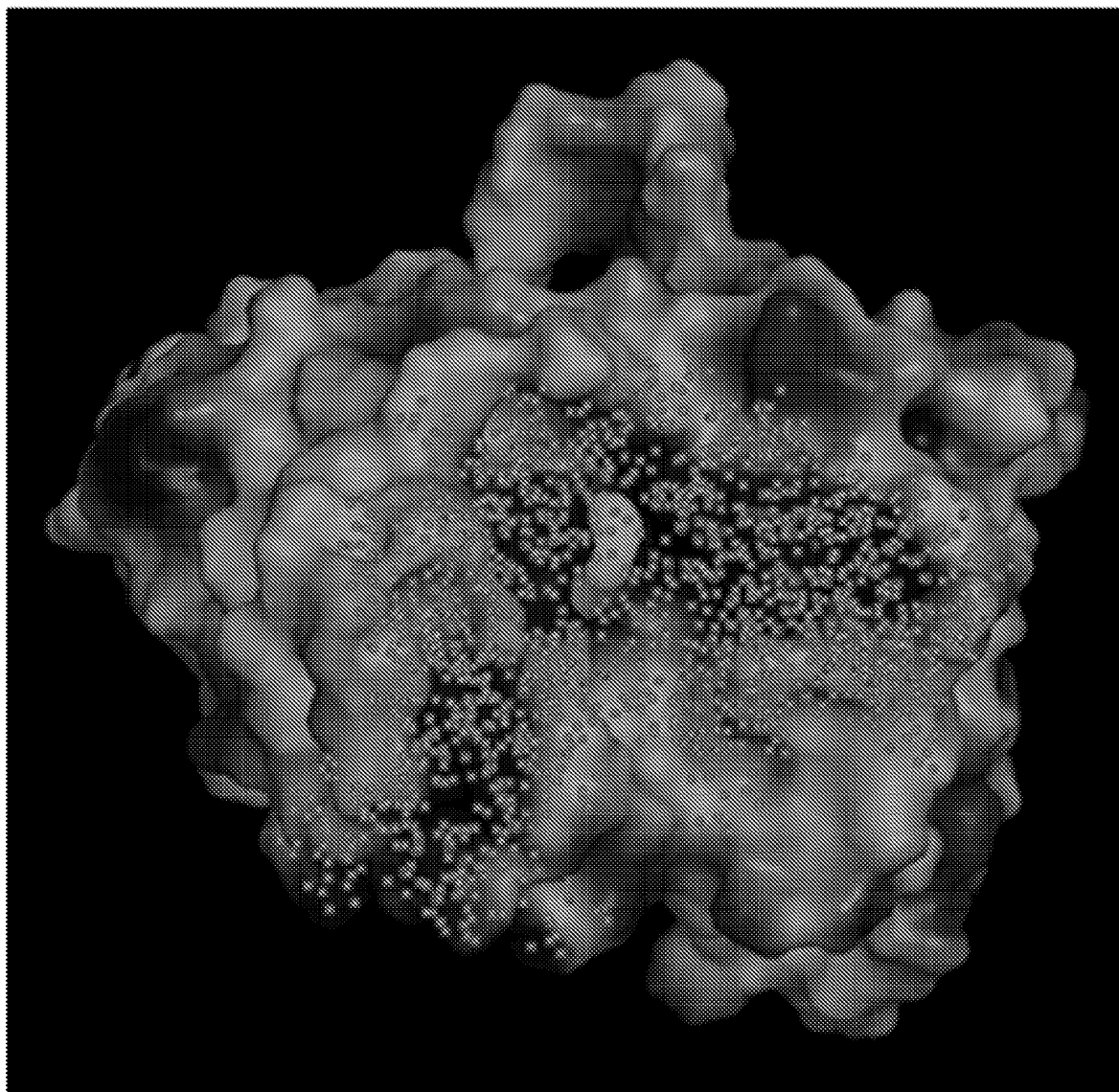


FIG. 11B

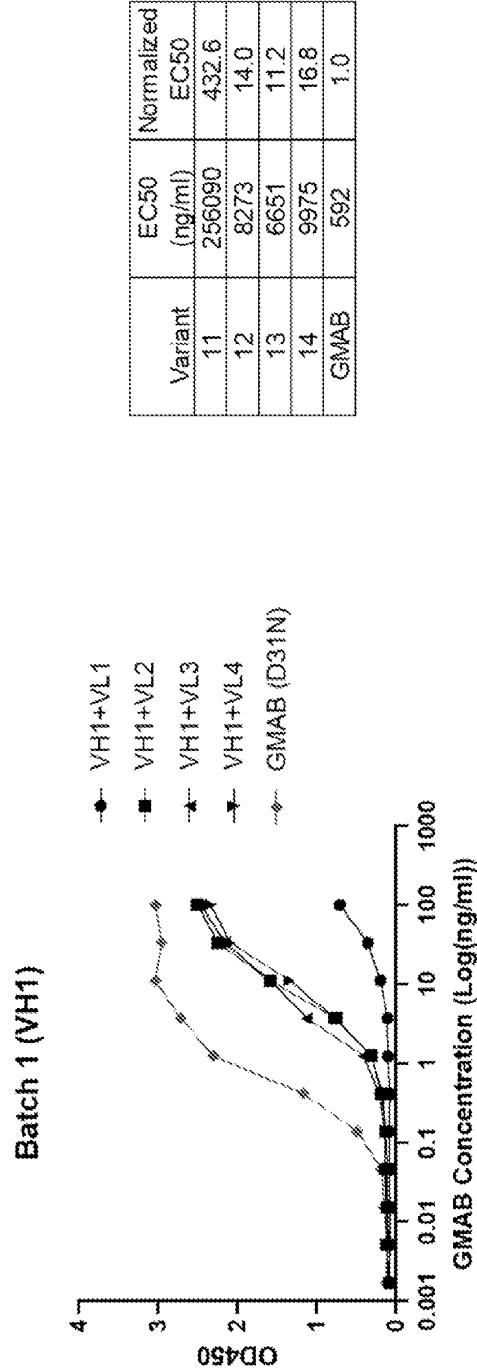


FIG. 12A

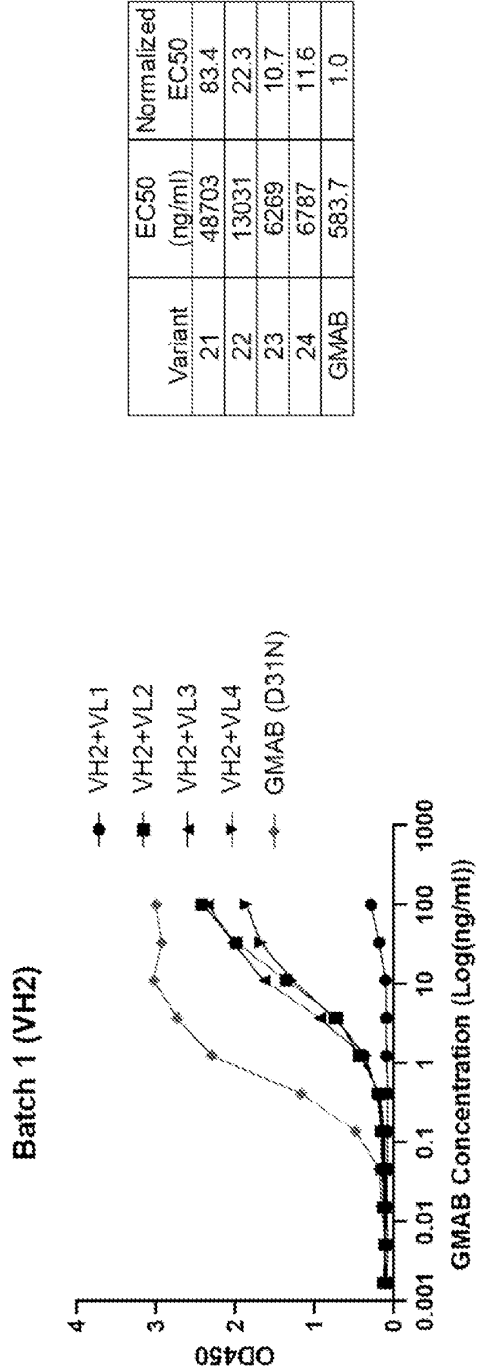


FIG. 12B

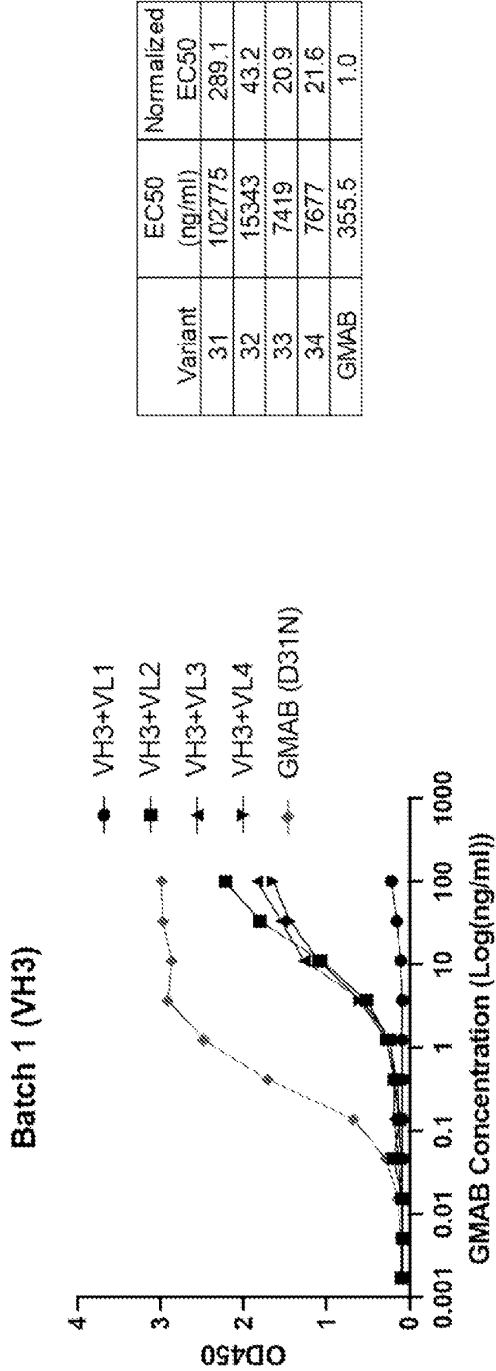


FIG. 12C

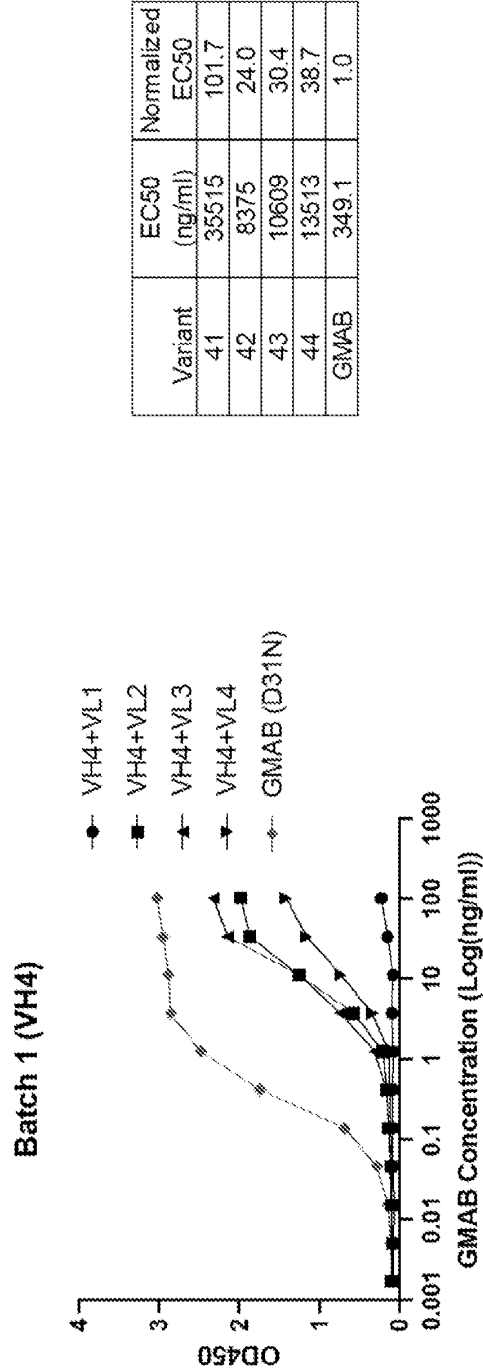
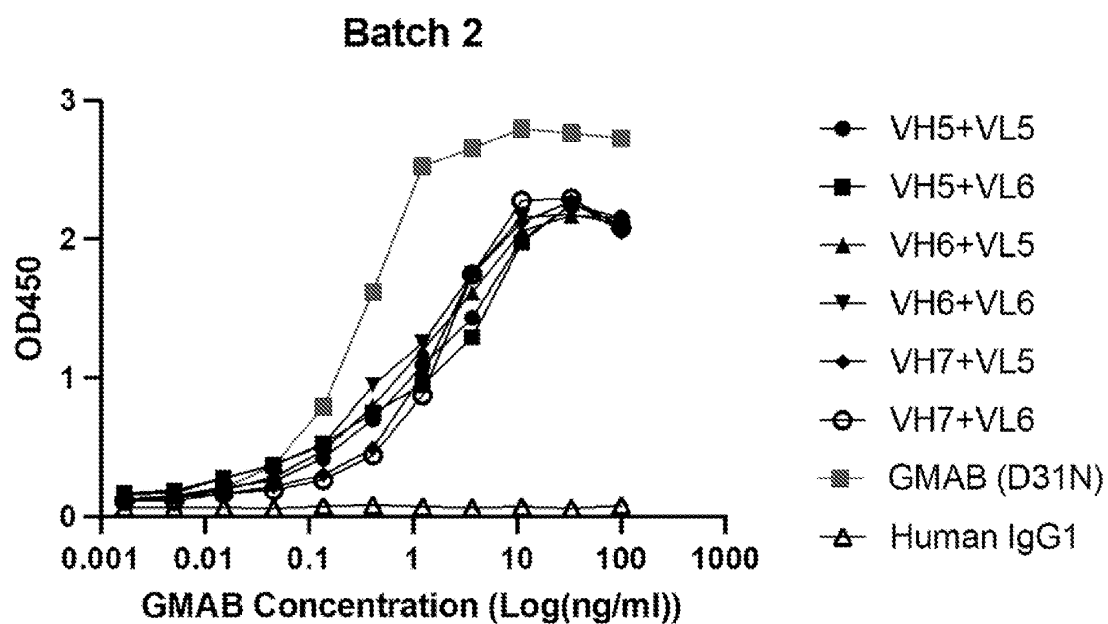


FIG. 12D



Variant	EC50 (ng/ml)	Normalized EC50
55	1815	5.7
56	2602	8.1
65	1157	3.6
66	893	2.8
75	1477	4.6
76	1766	5.5
GMAB	320	1

FIG. 12E

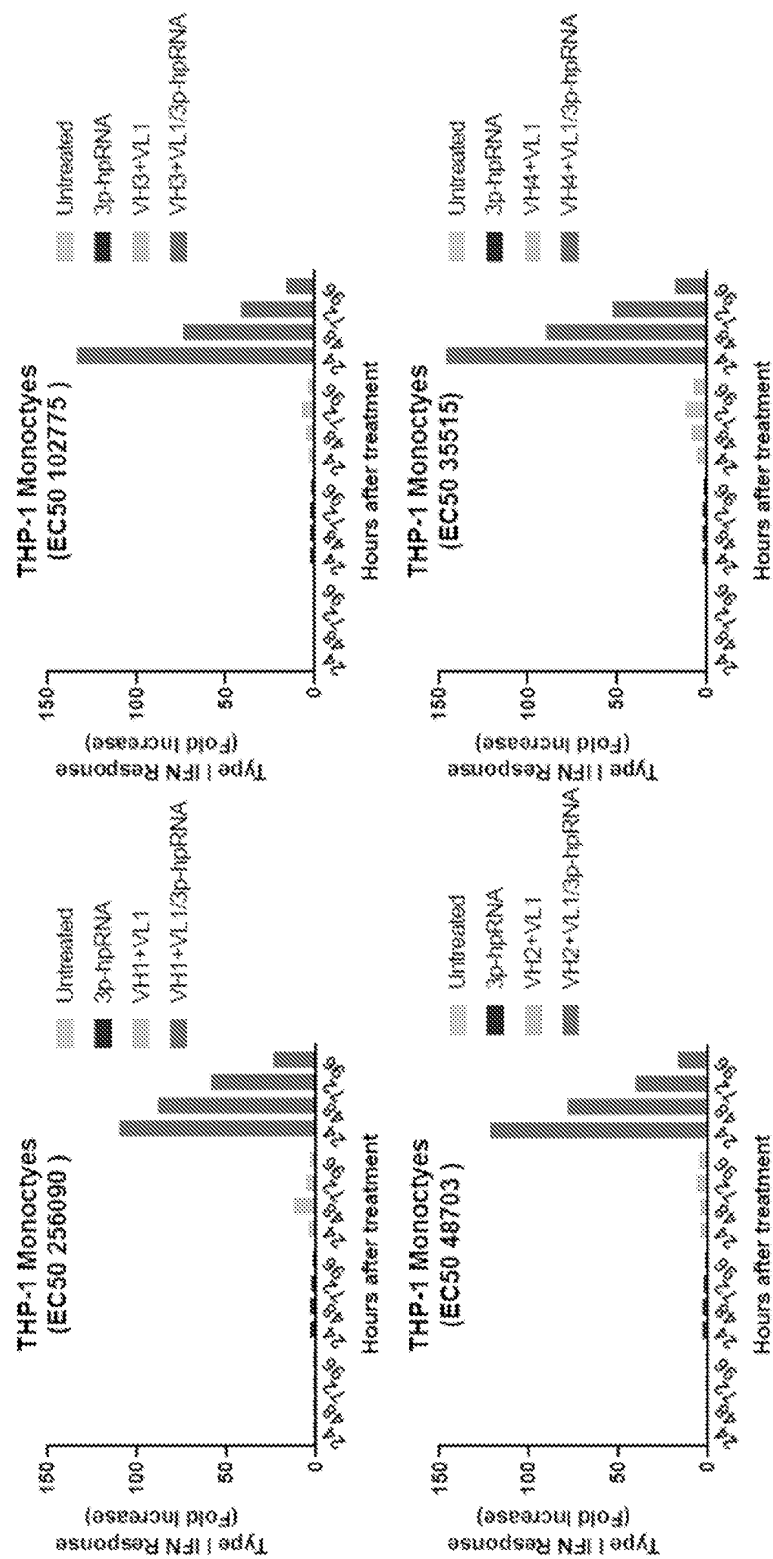


FIG. 13

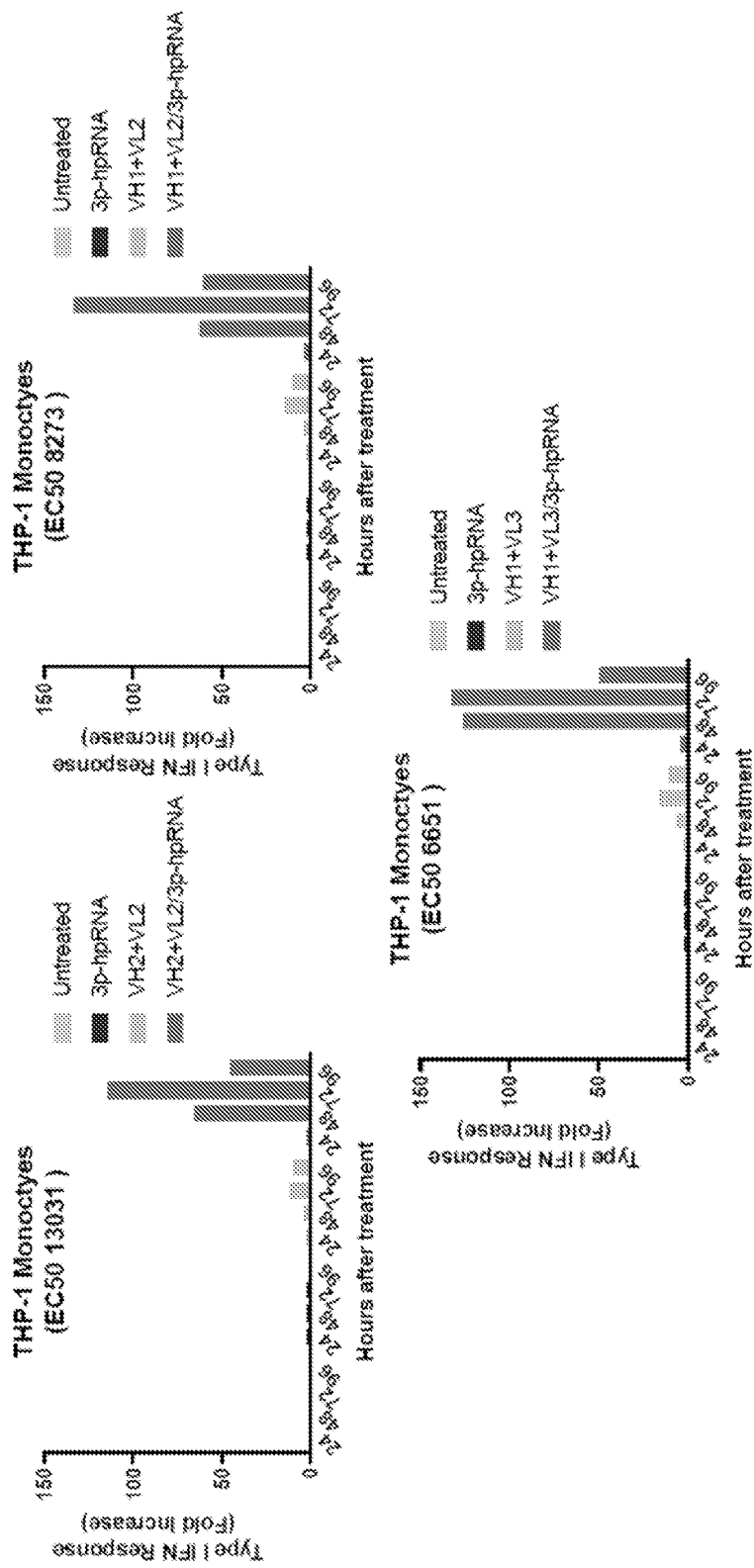


FIG. 14

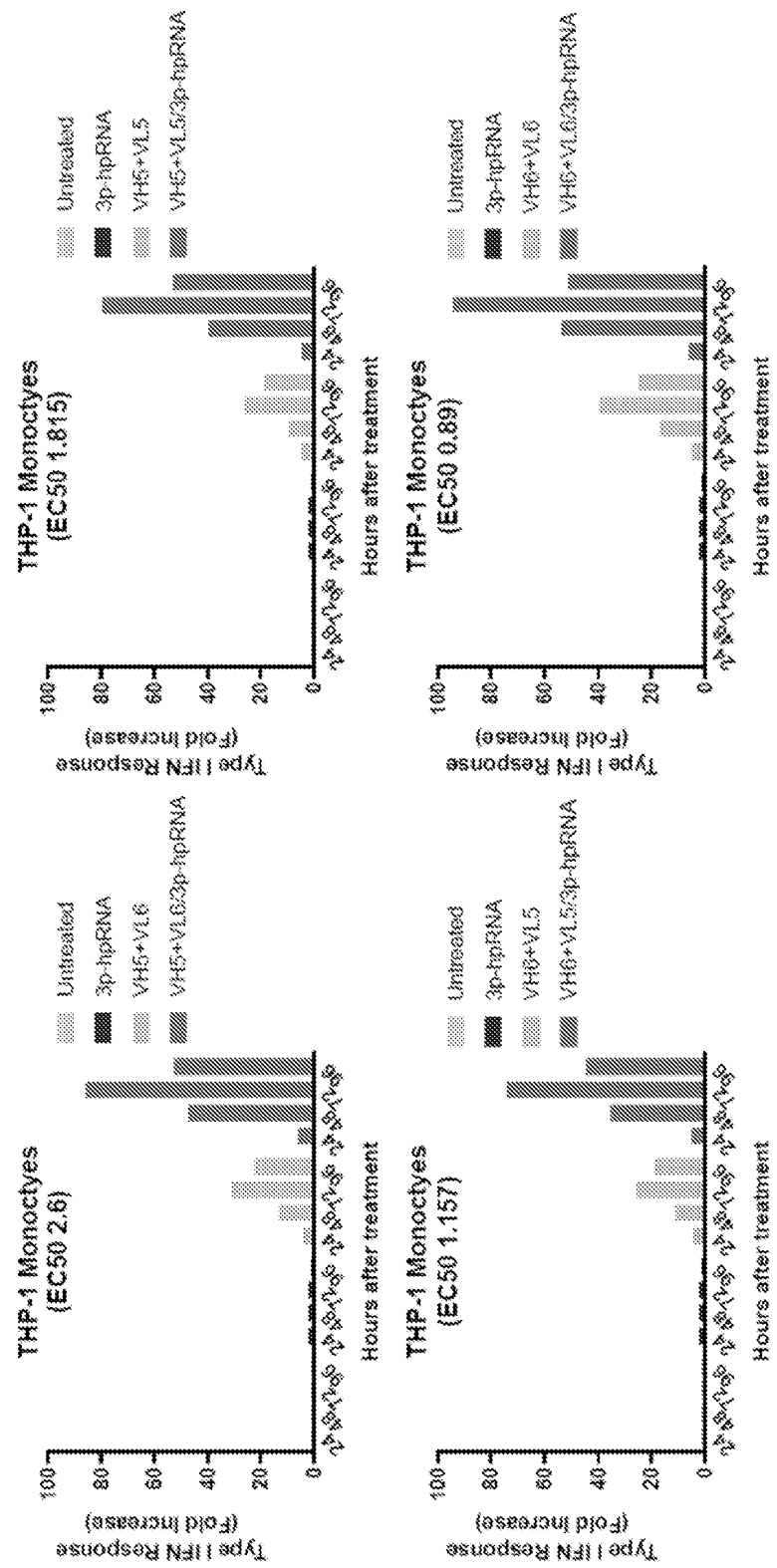


FIG. 15

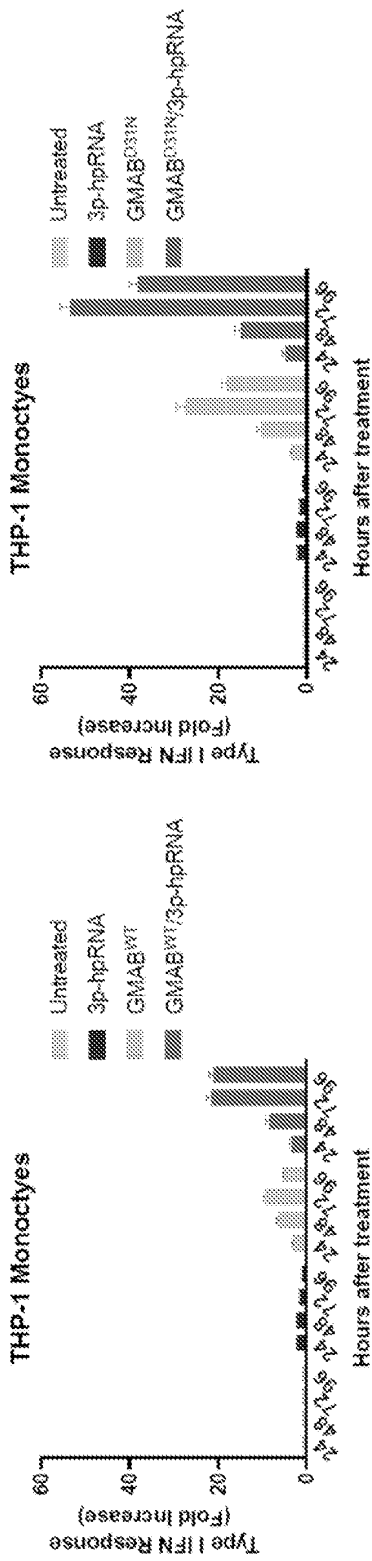


FIG. 16

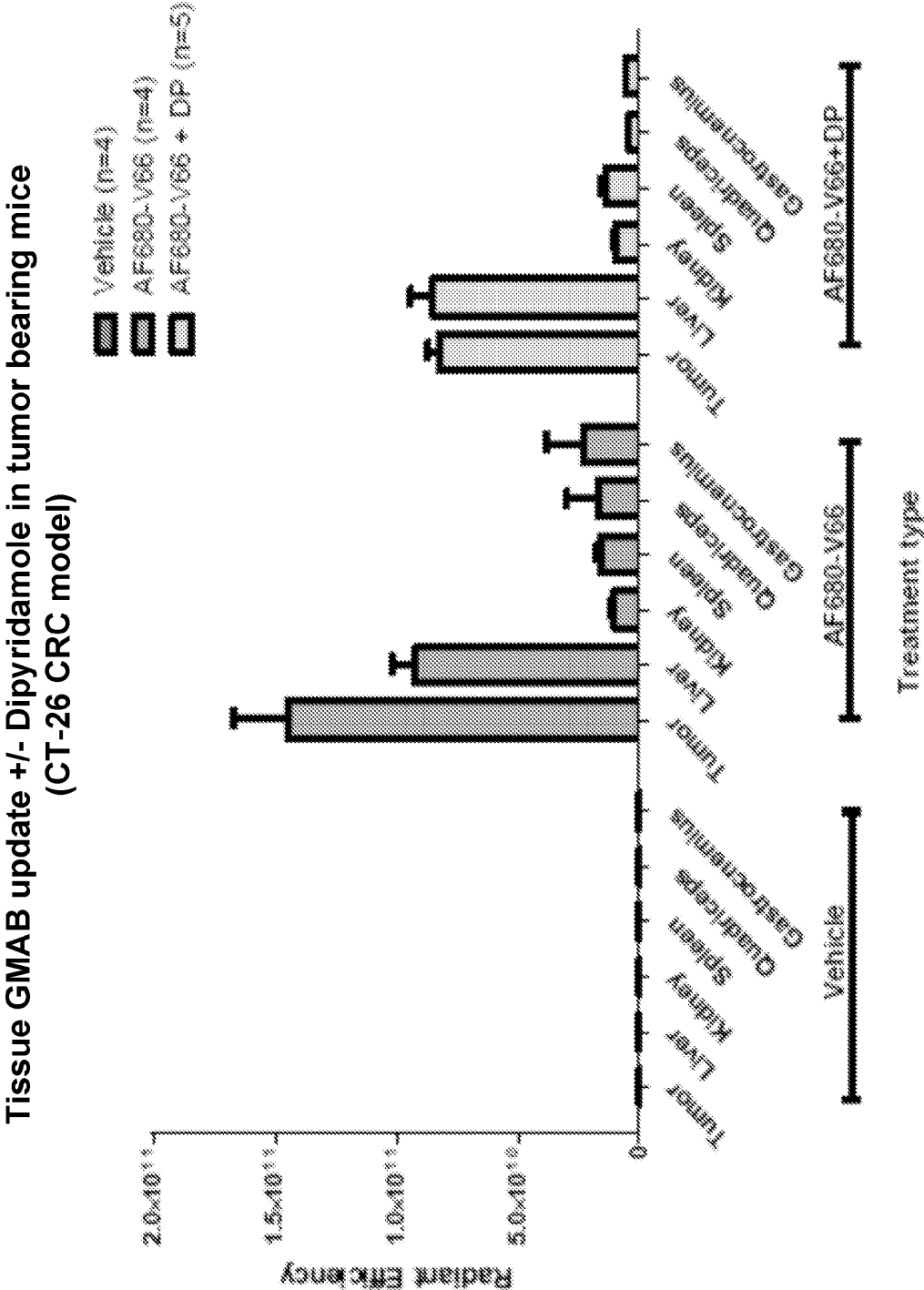


FIG. 17

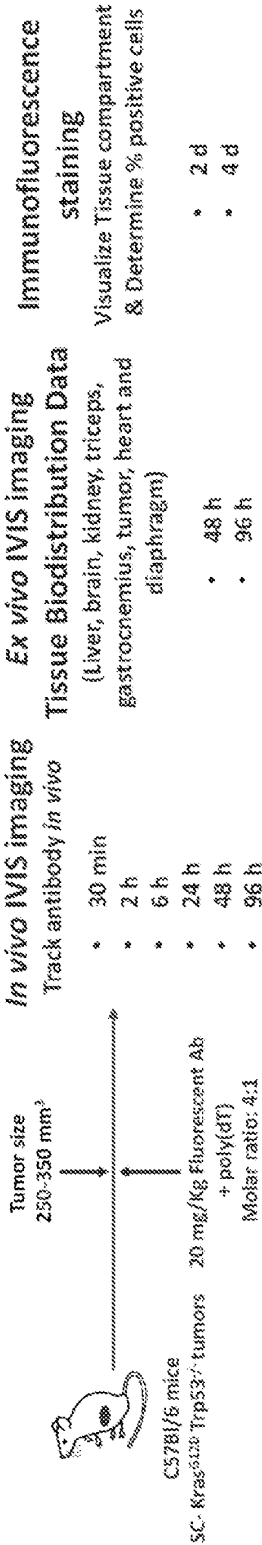


FIG. 18

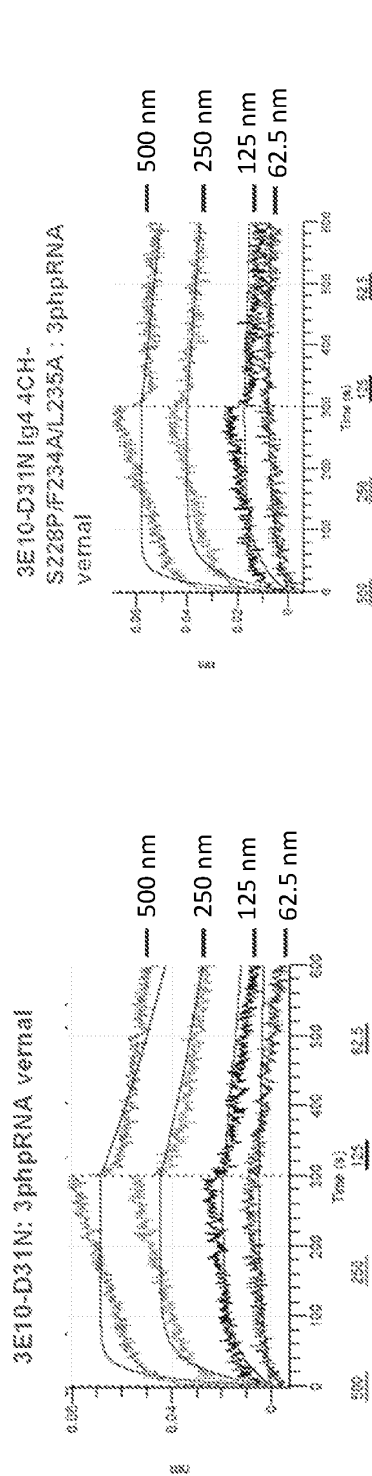


FIG. 19A

FIG. 19B

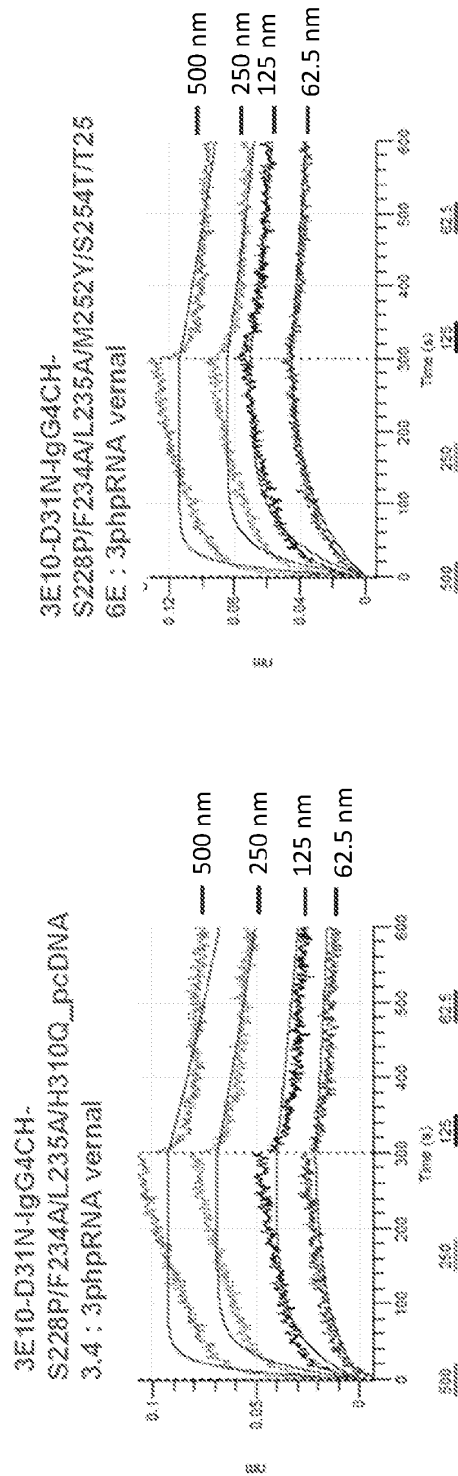


FIG. 19C

FIG. 19D

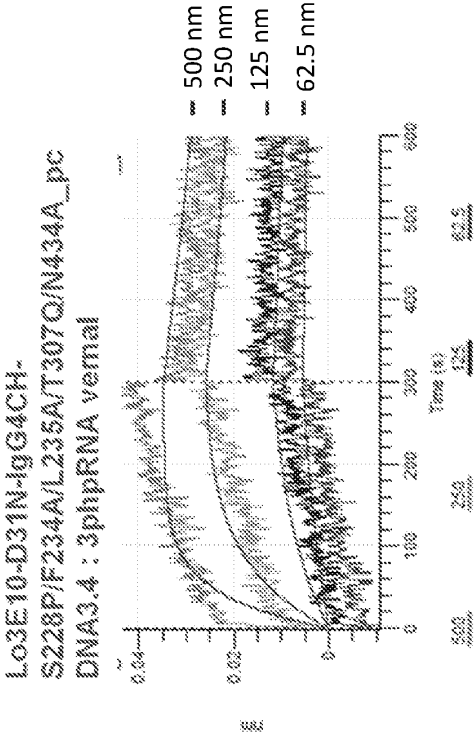


FIG. 19E

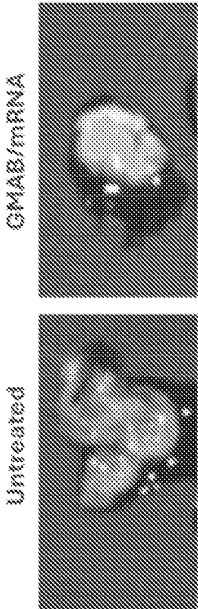


FIG. 20A

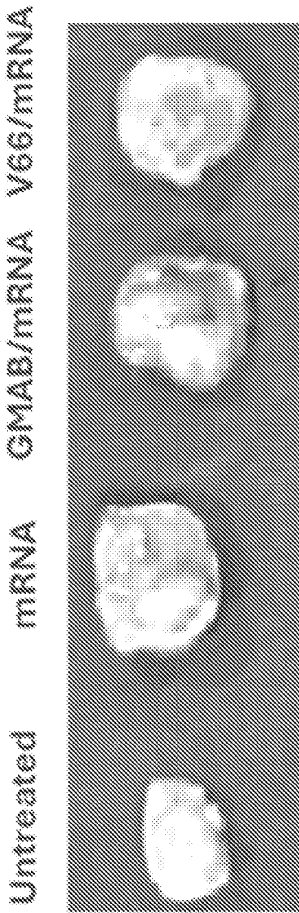


FIG. 20B

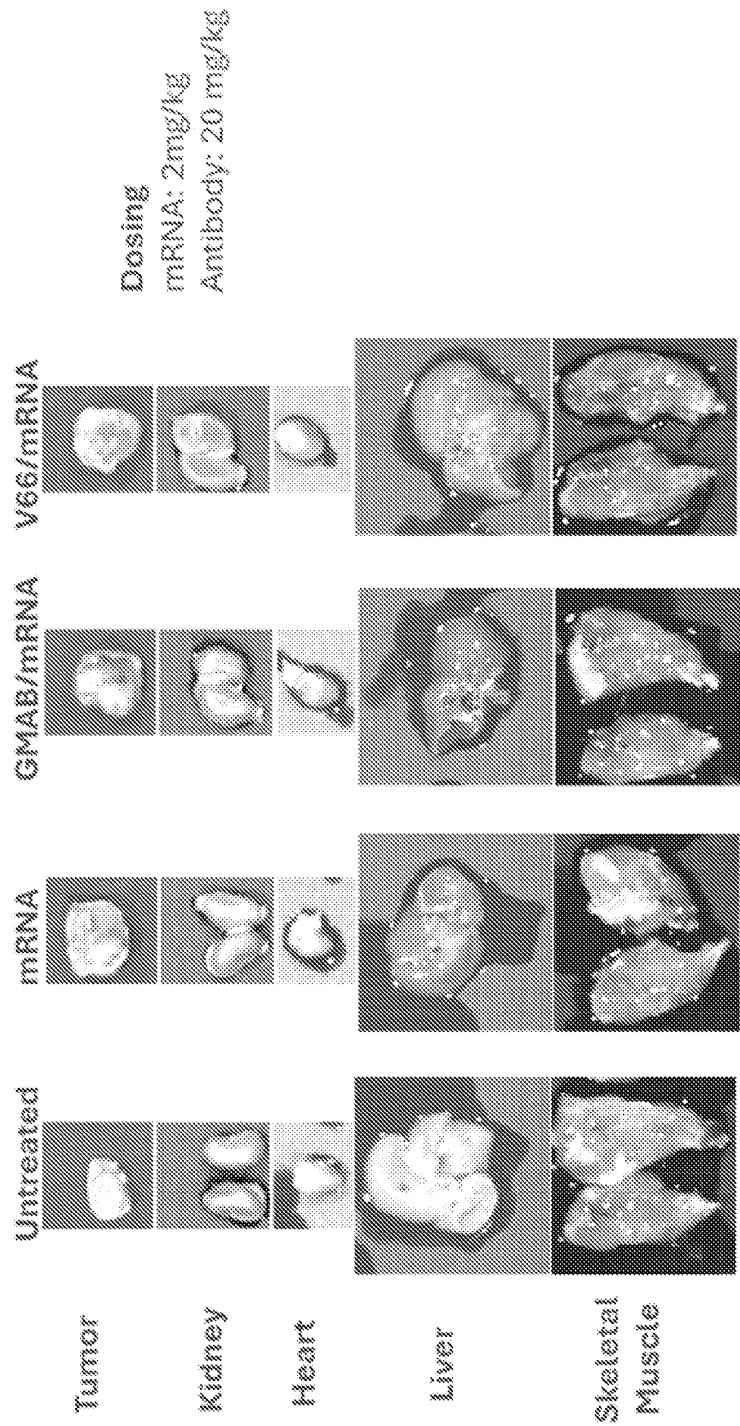


FIG. 21

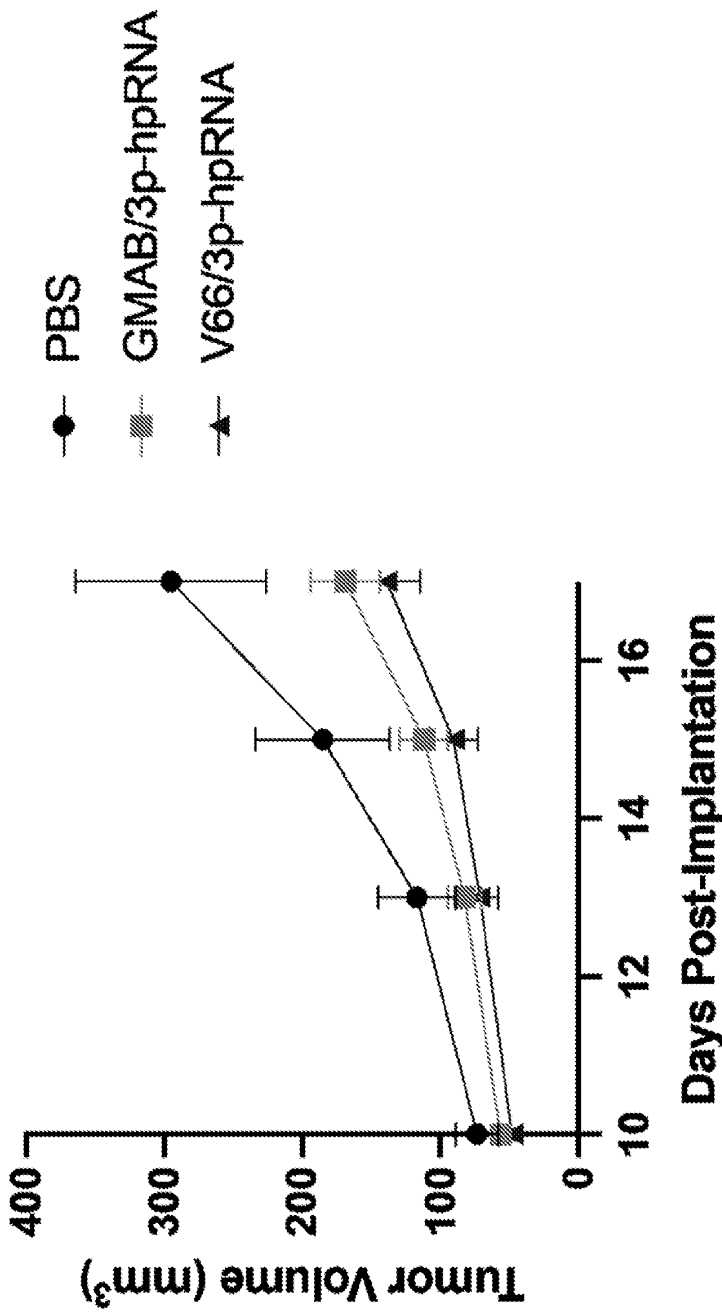


FIG. 22

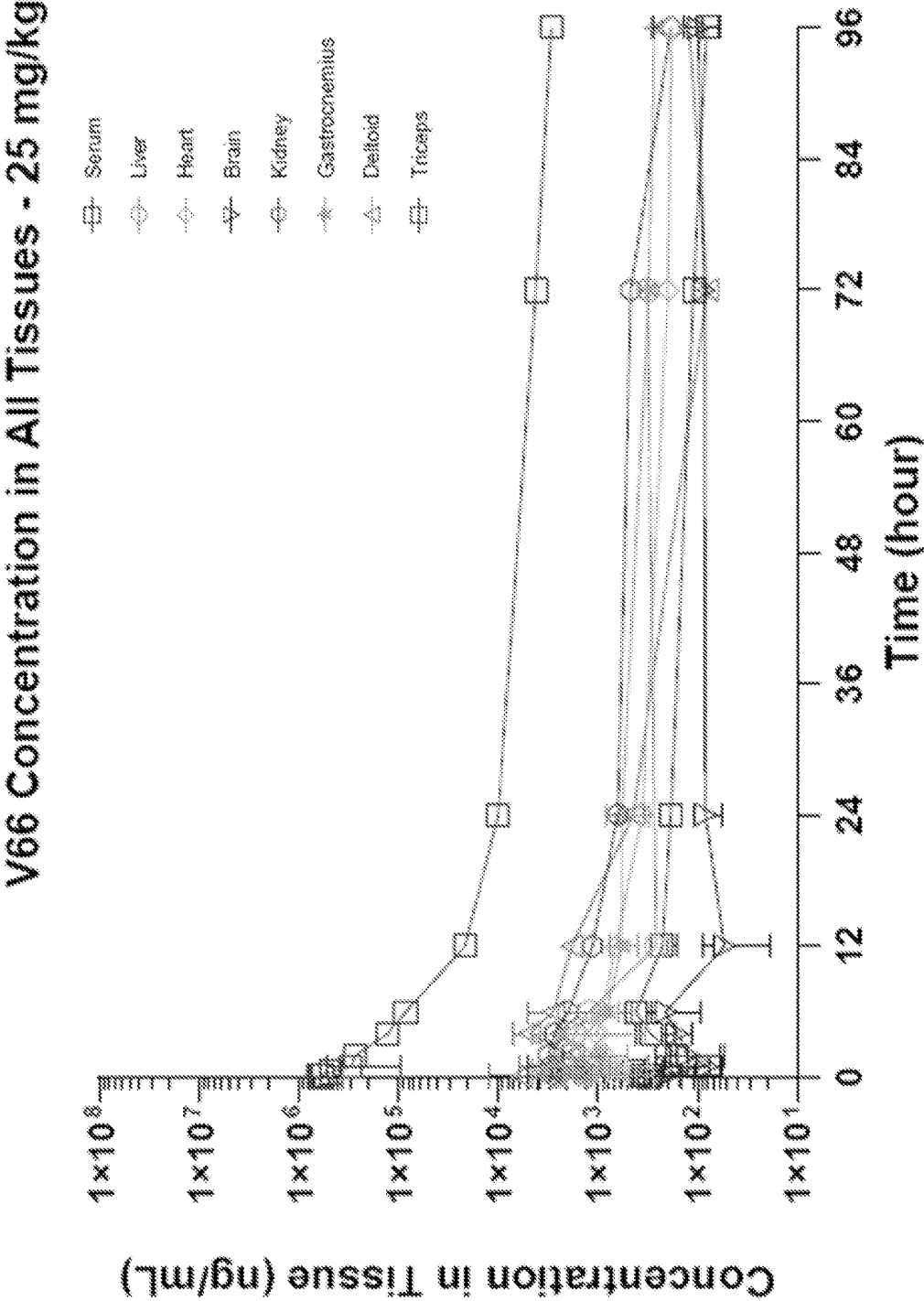


FIG. 23A

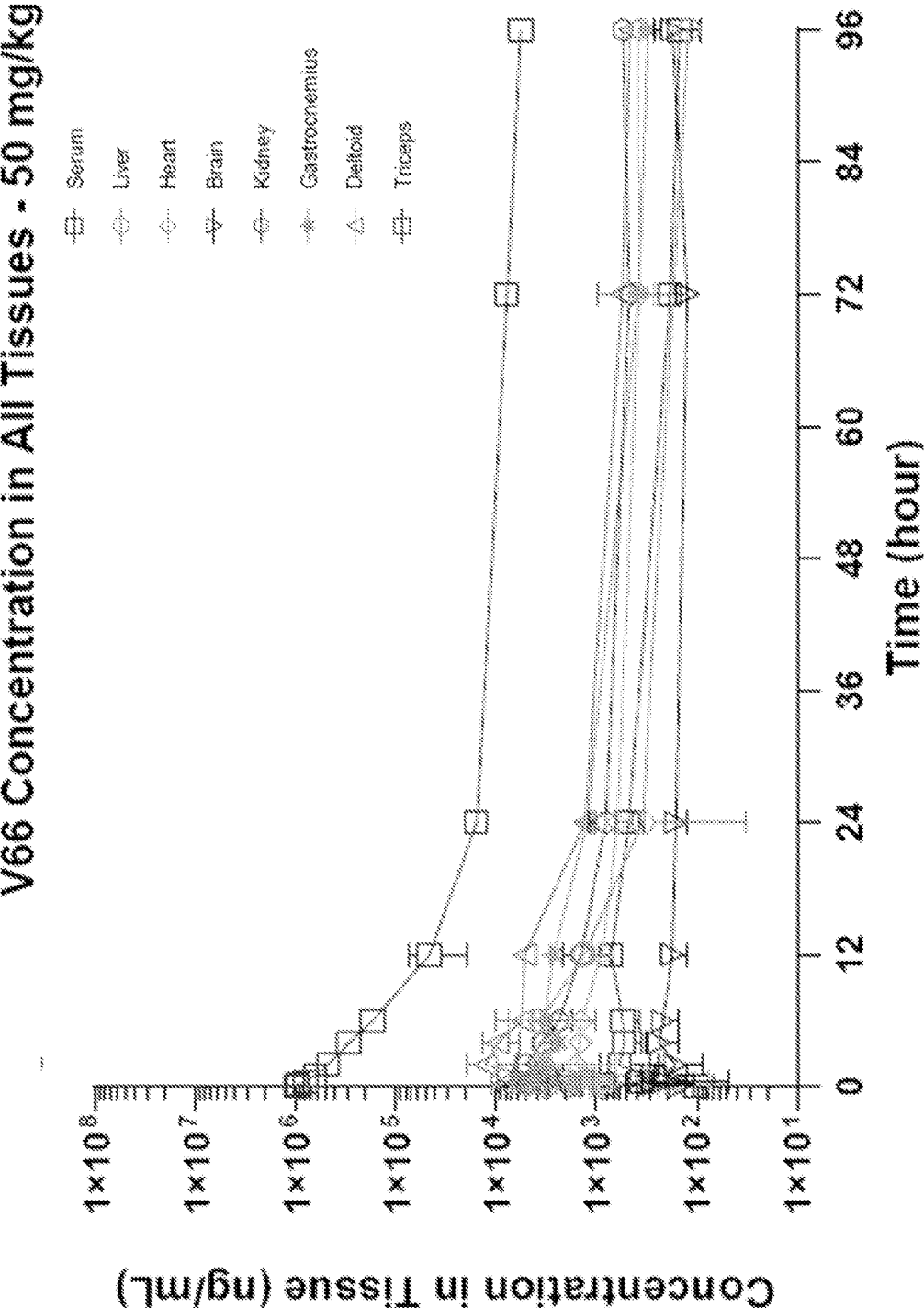


FIG. 23B

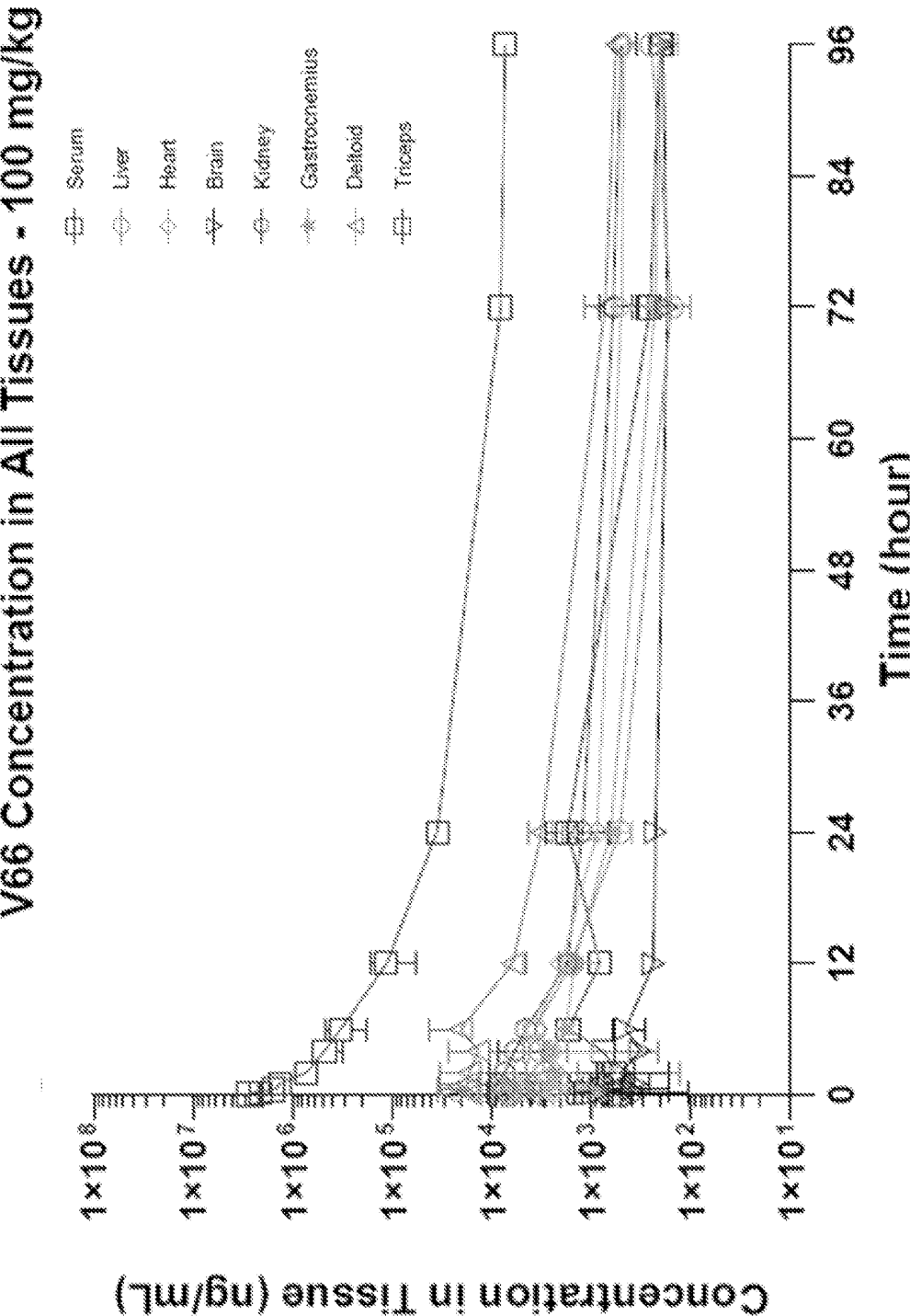


FIG. 23C

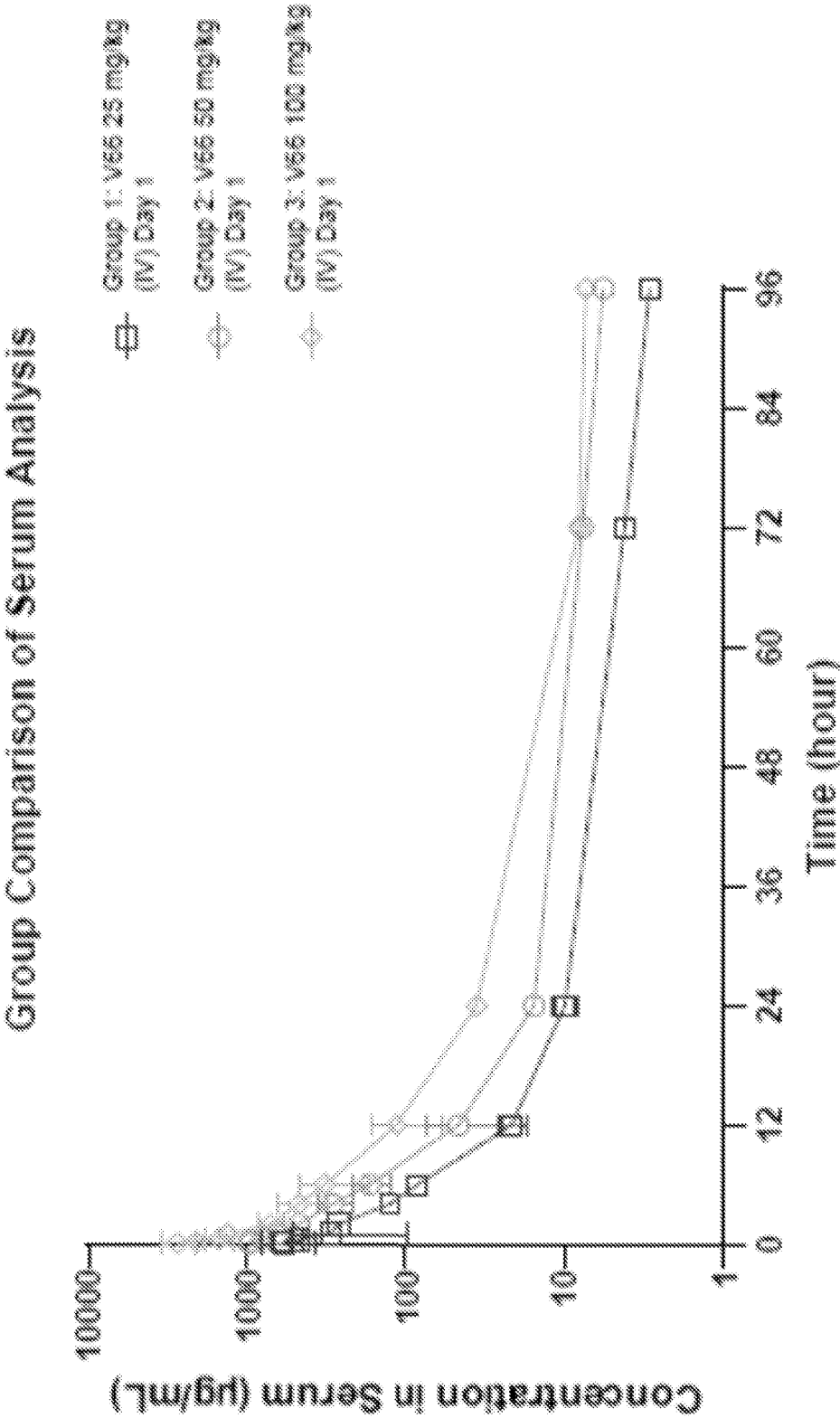


FIG. 23D

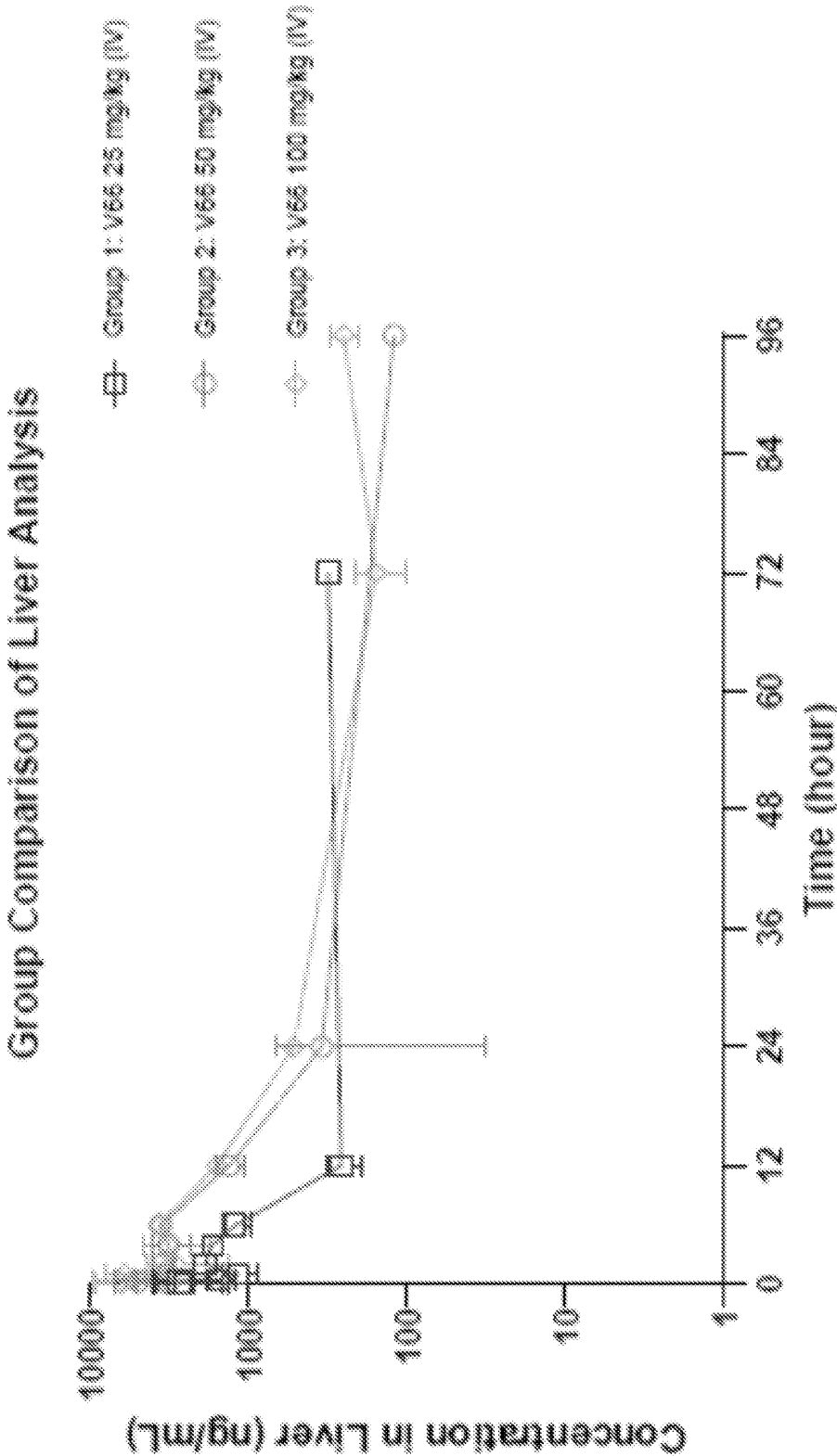


FIG. 23E

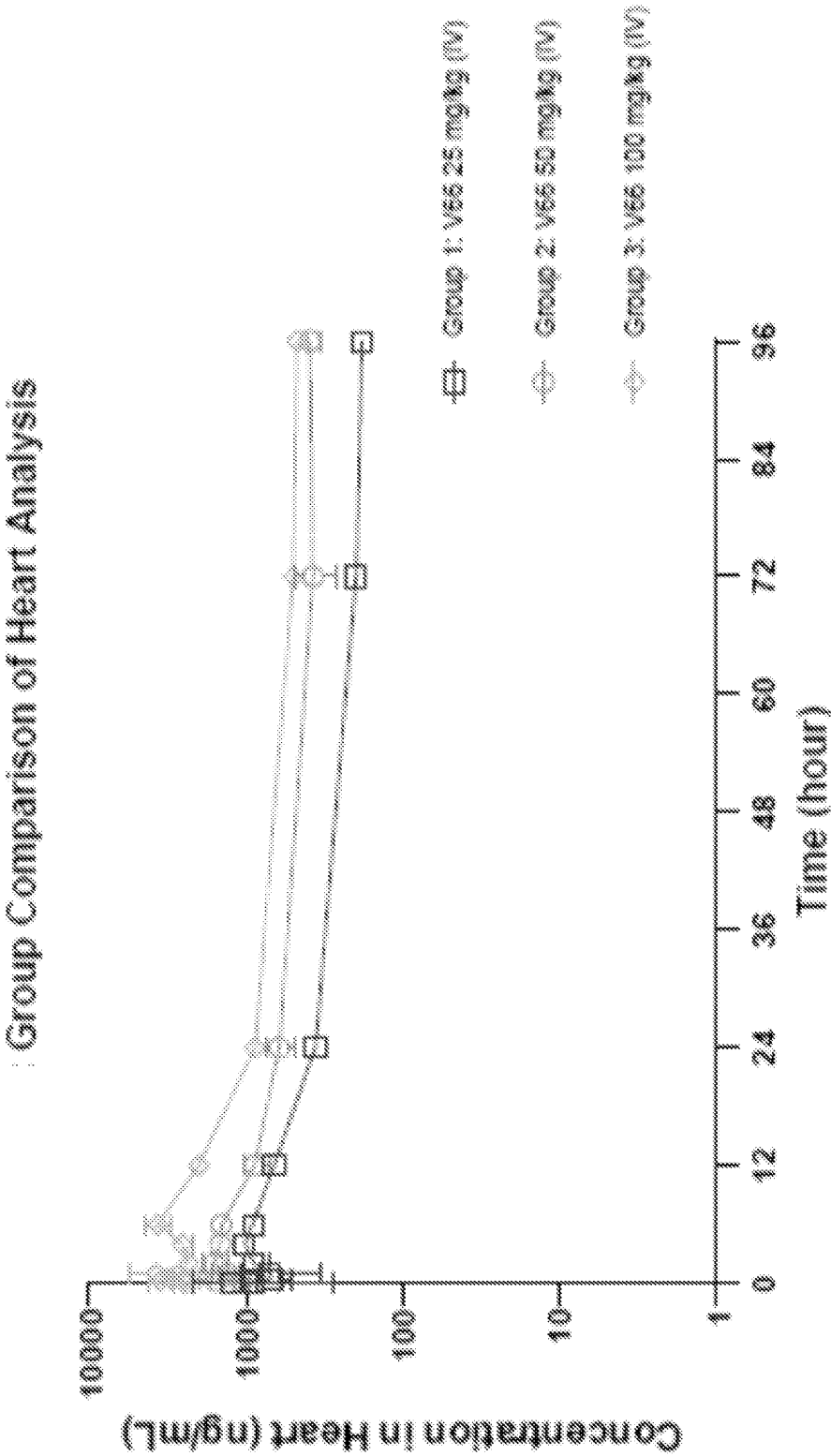


FIG. 23F

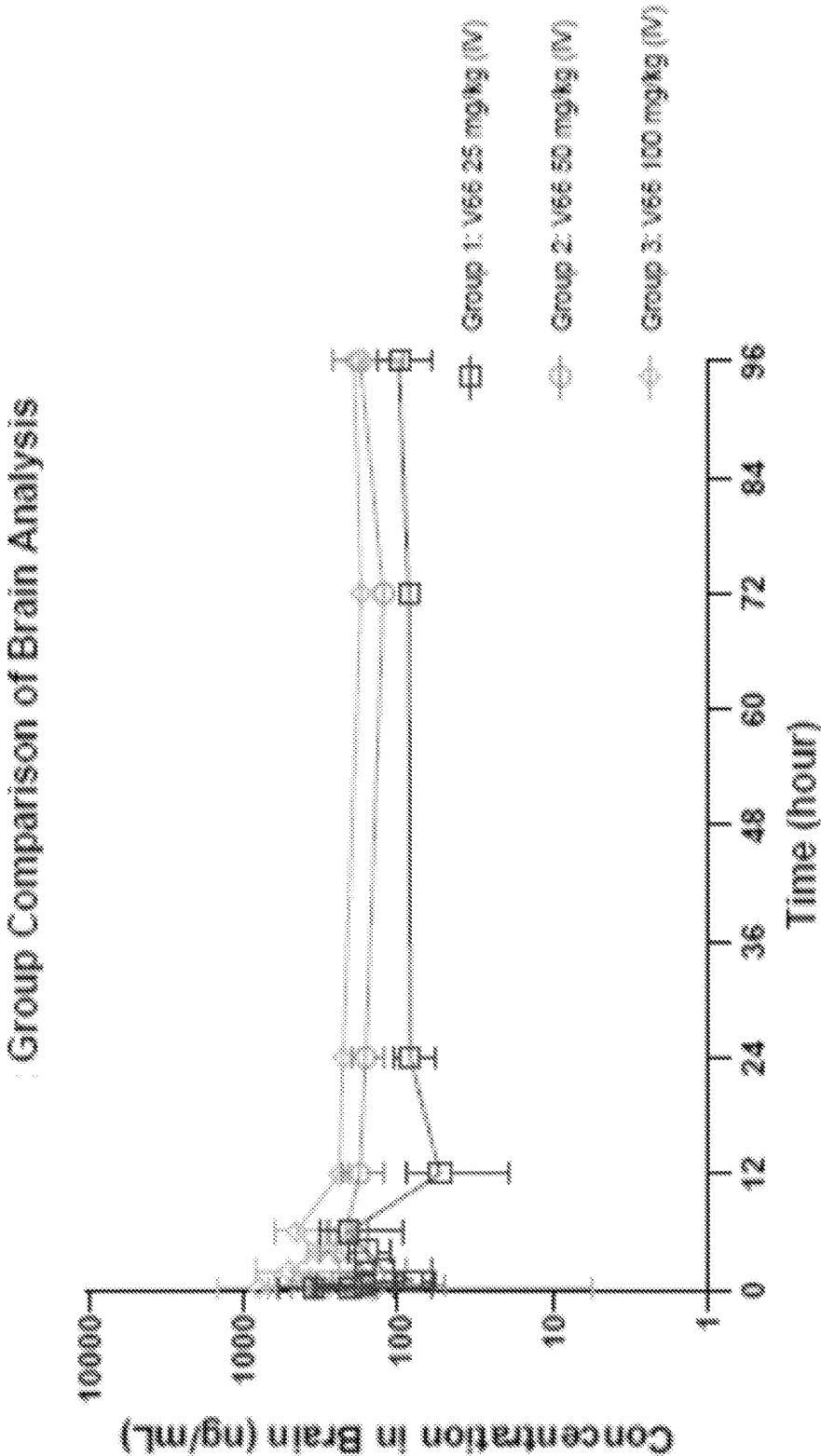


FIG. 23G

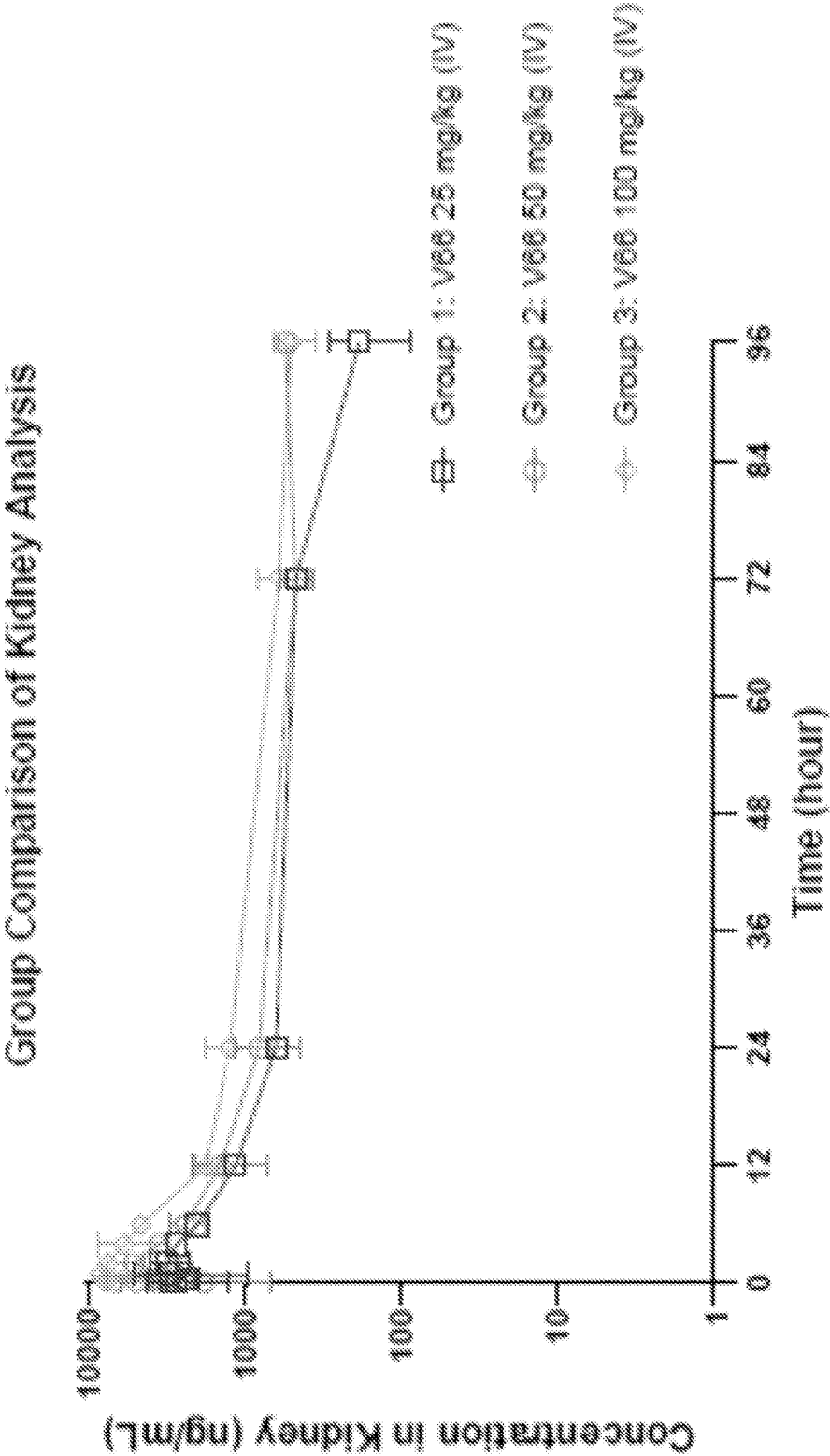


FIG. 23H

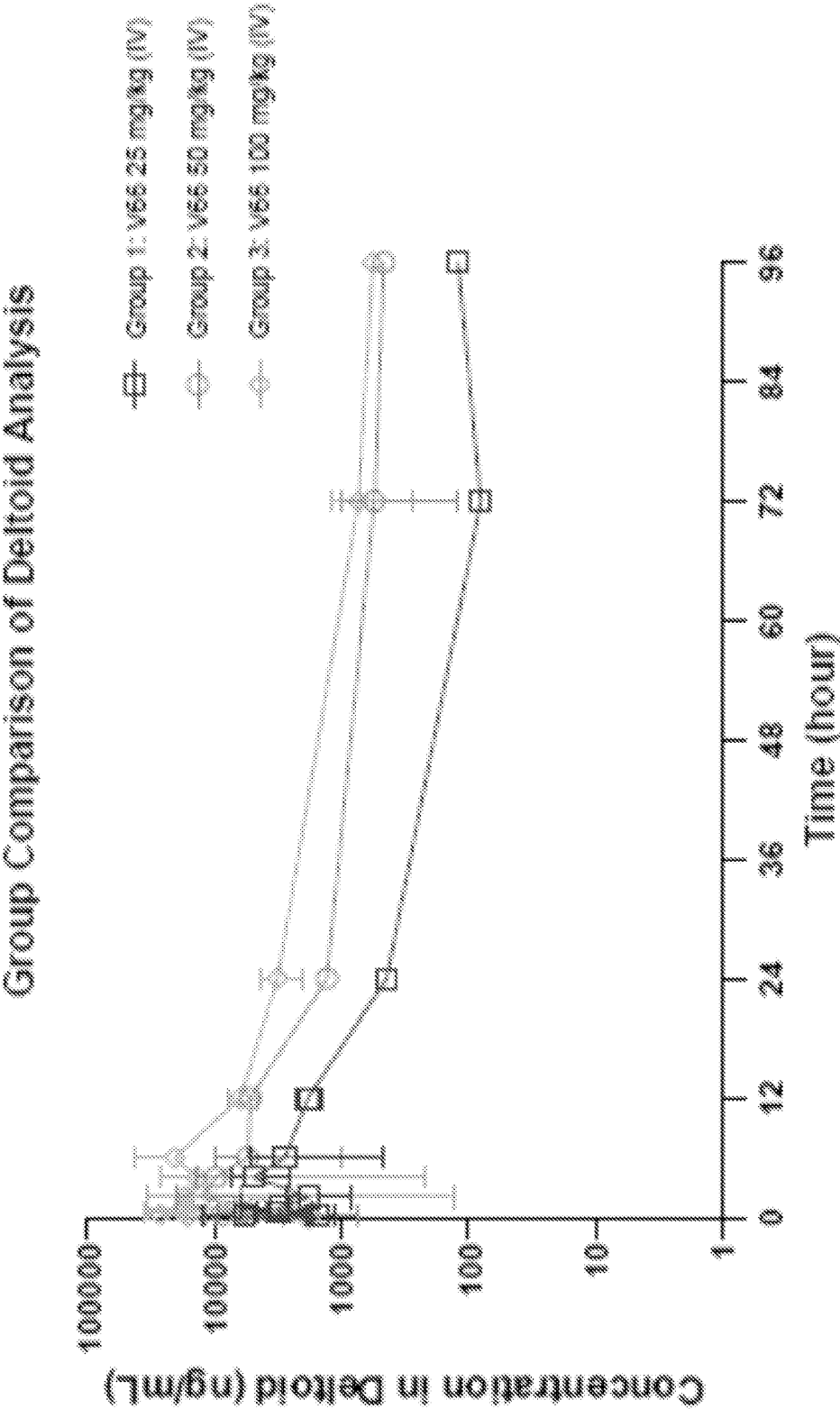


FIG. 23I

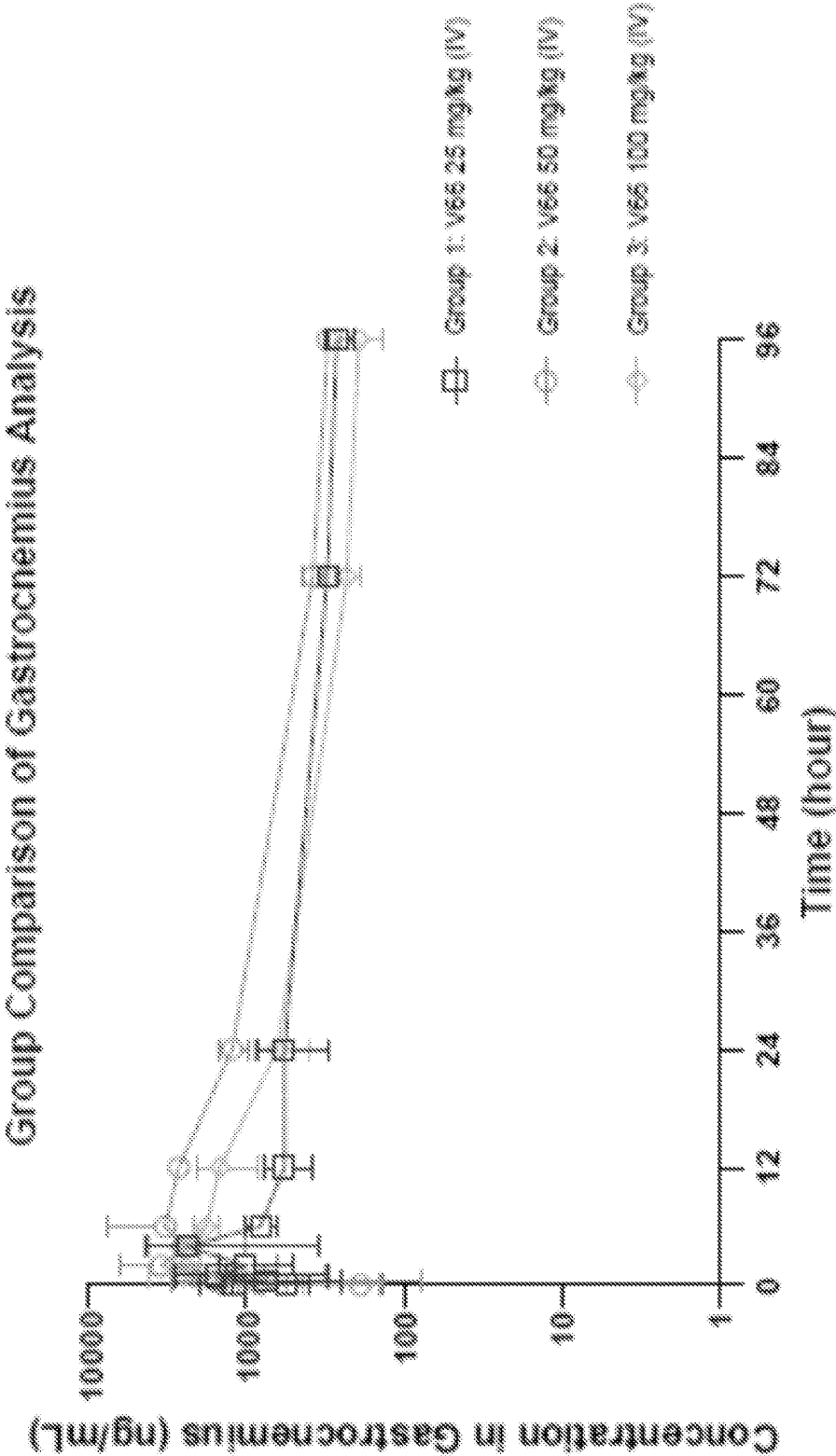


FIG. 23J

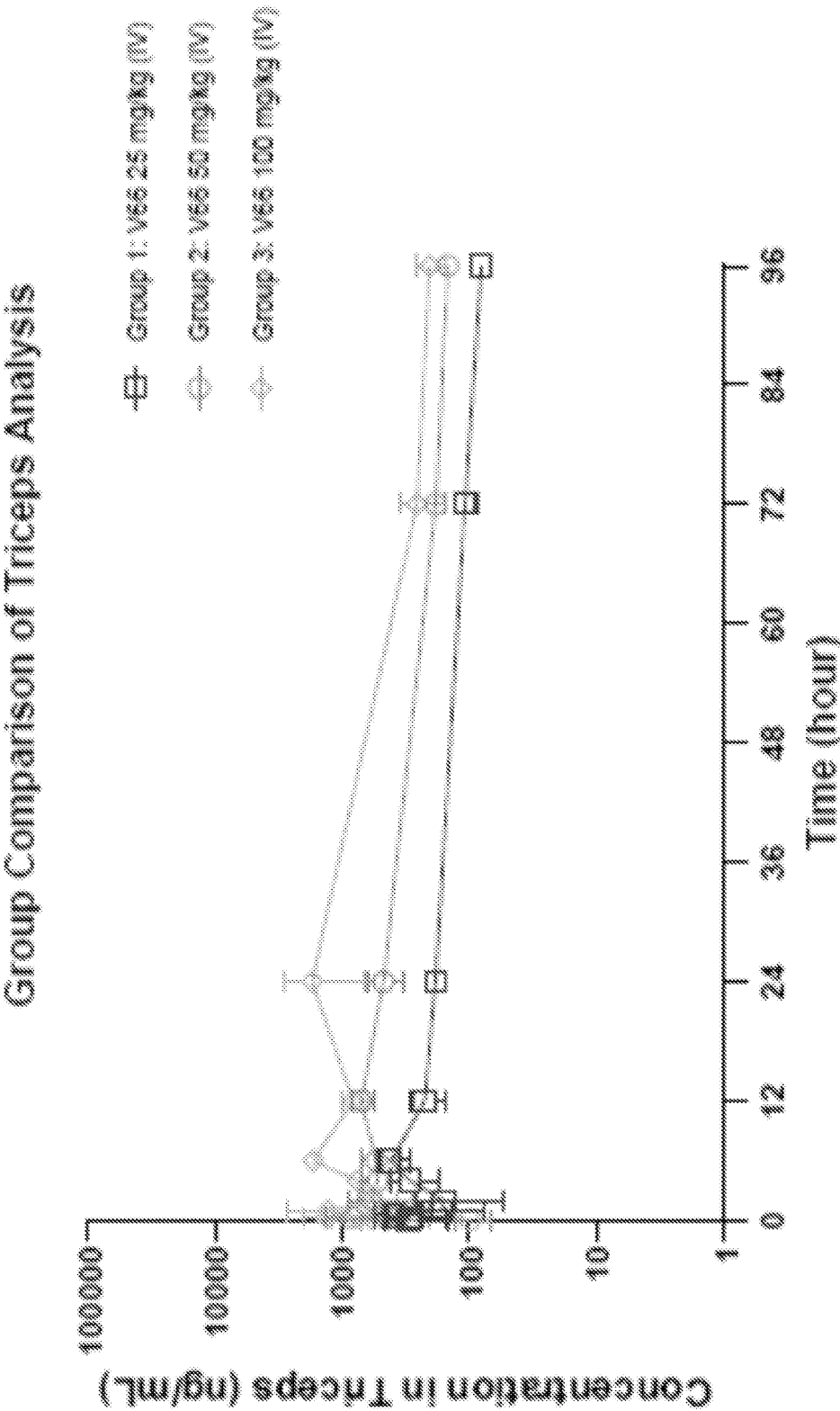


FIG. 23K

Group Comparison of Heart Analysis

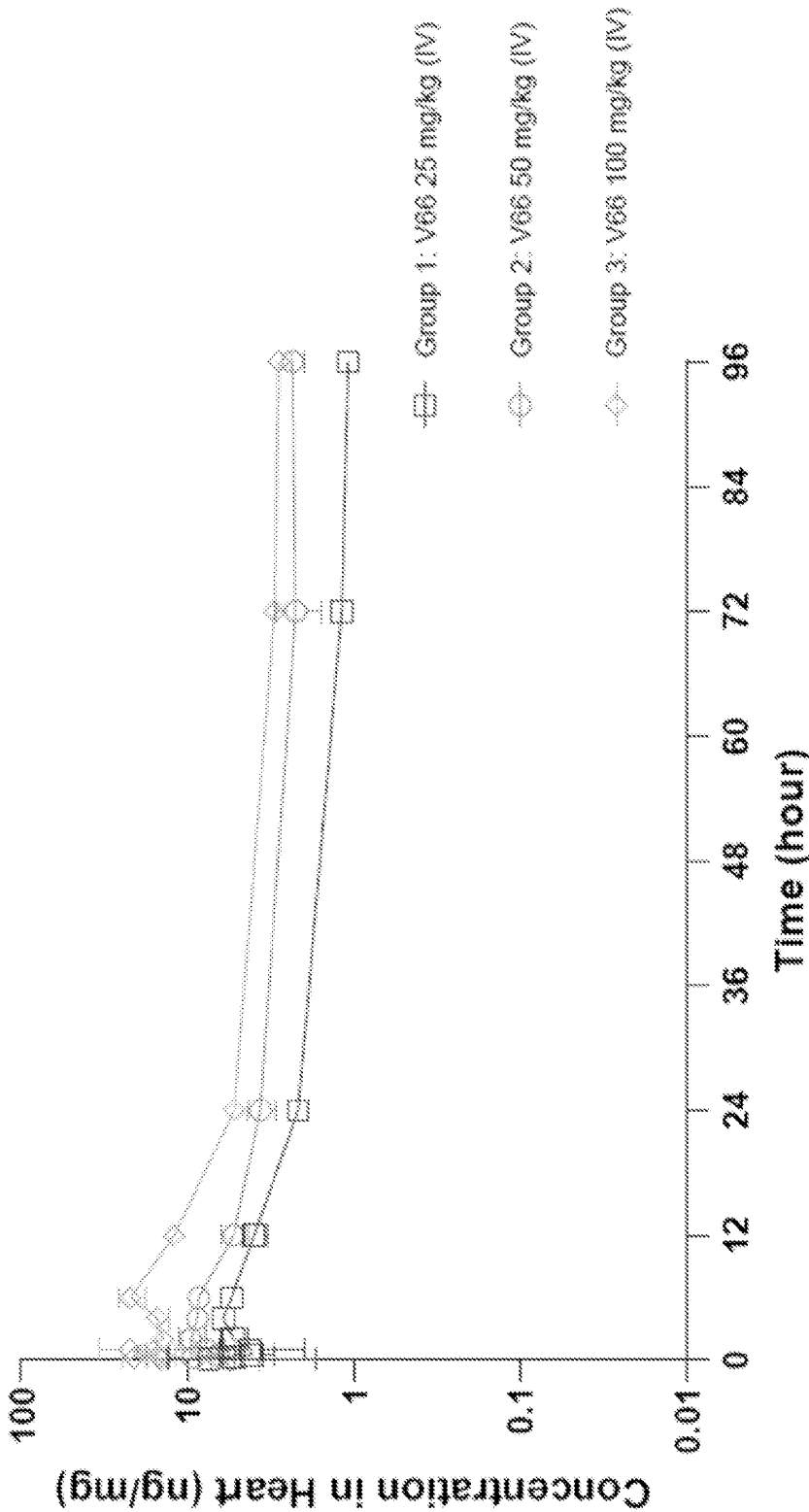


FIG. 23L

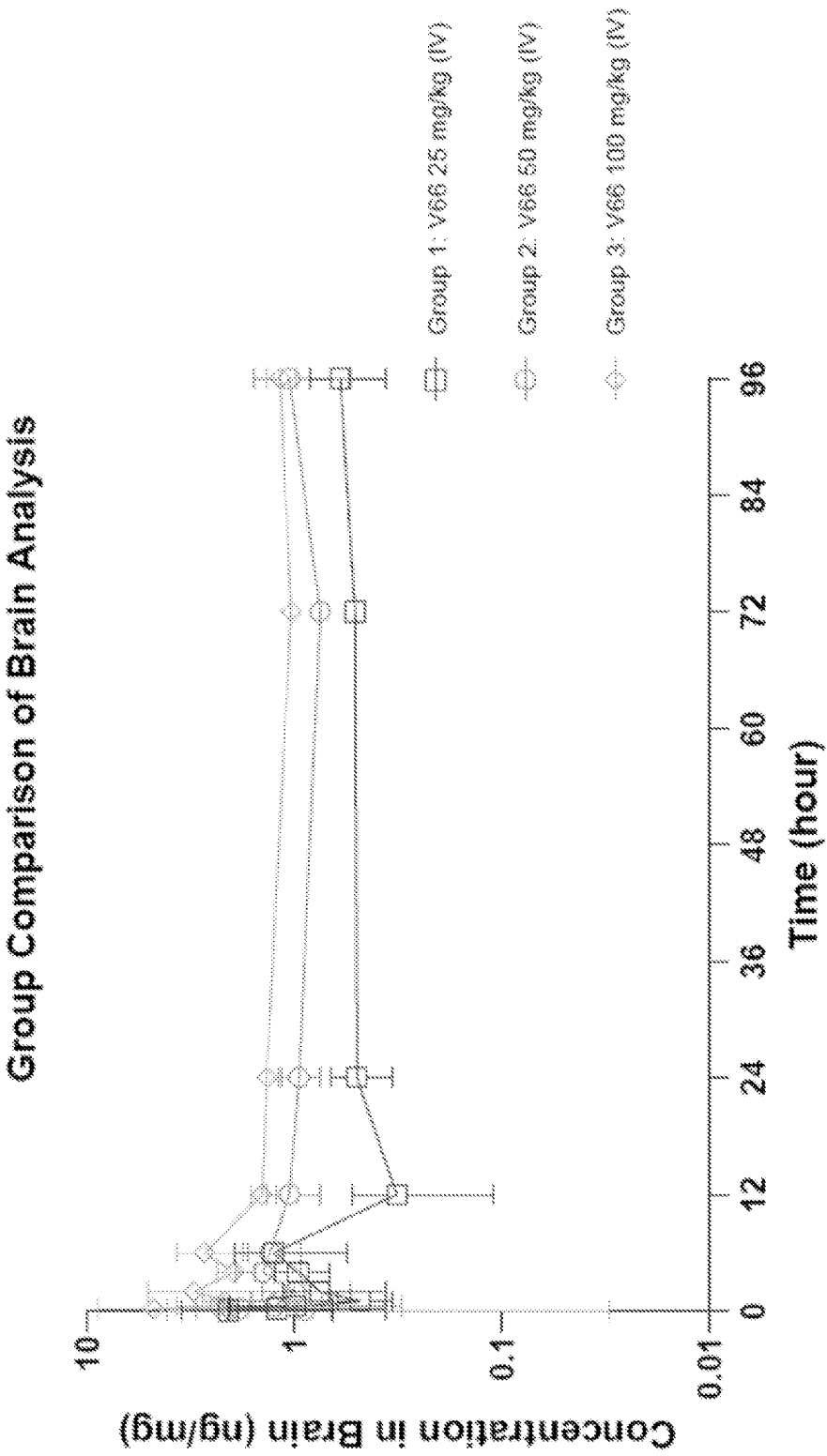


FIG. 23M

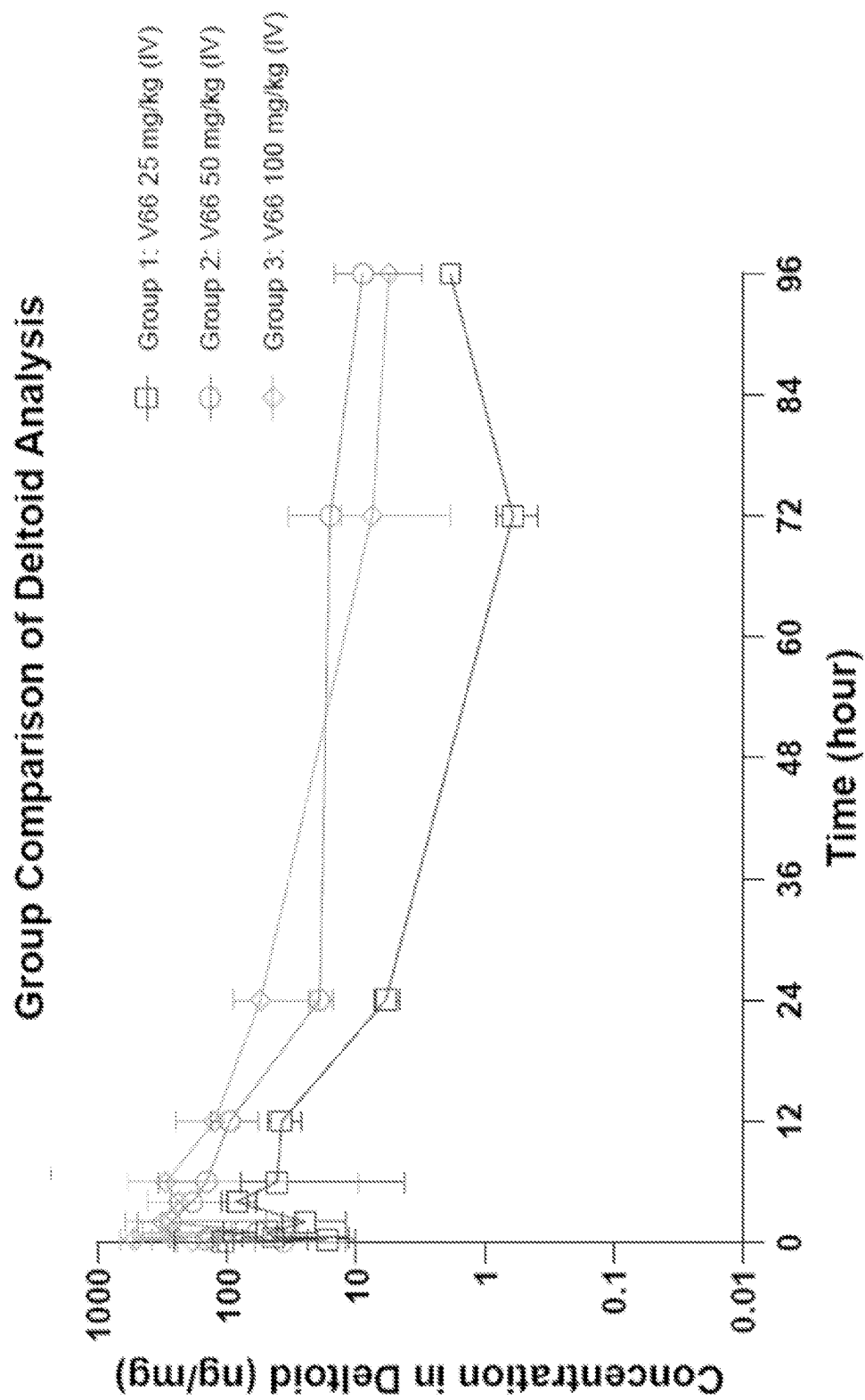


FIG. 23N

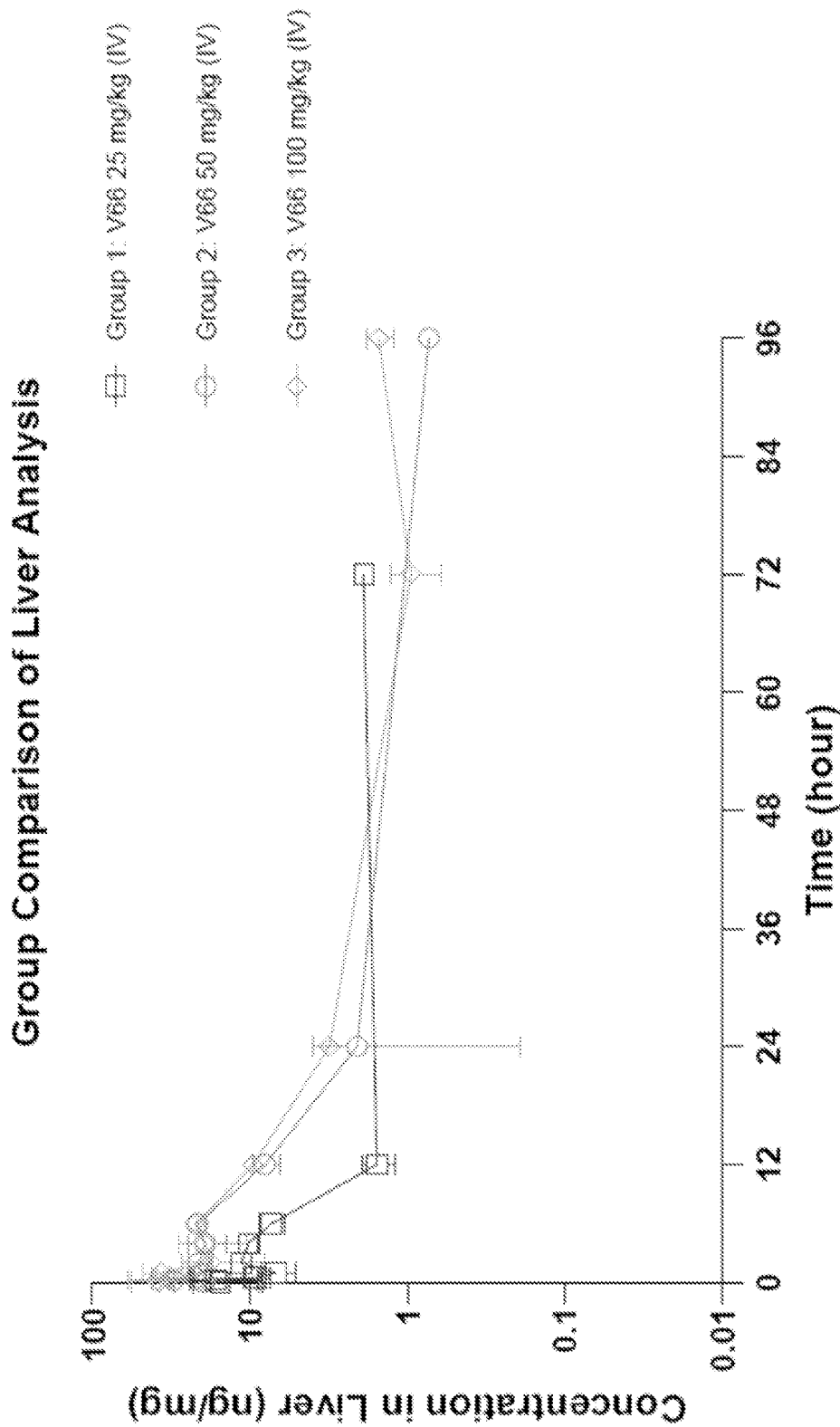


FIG. 230

Group Comparison of Kidney Analysis

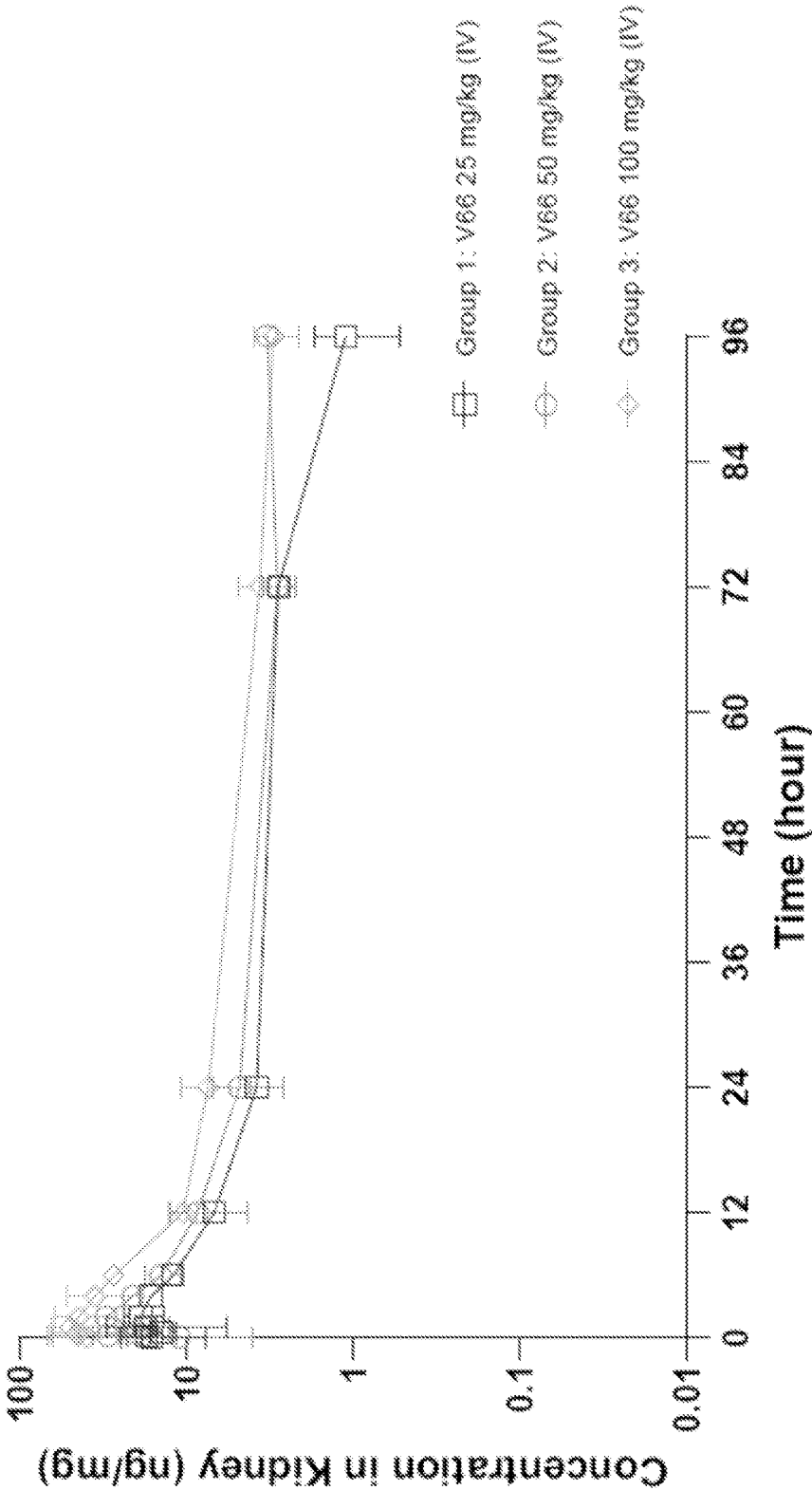


FIG. 23P

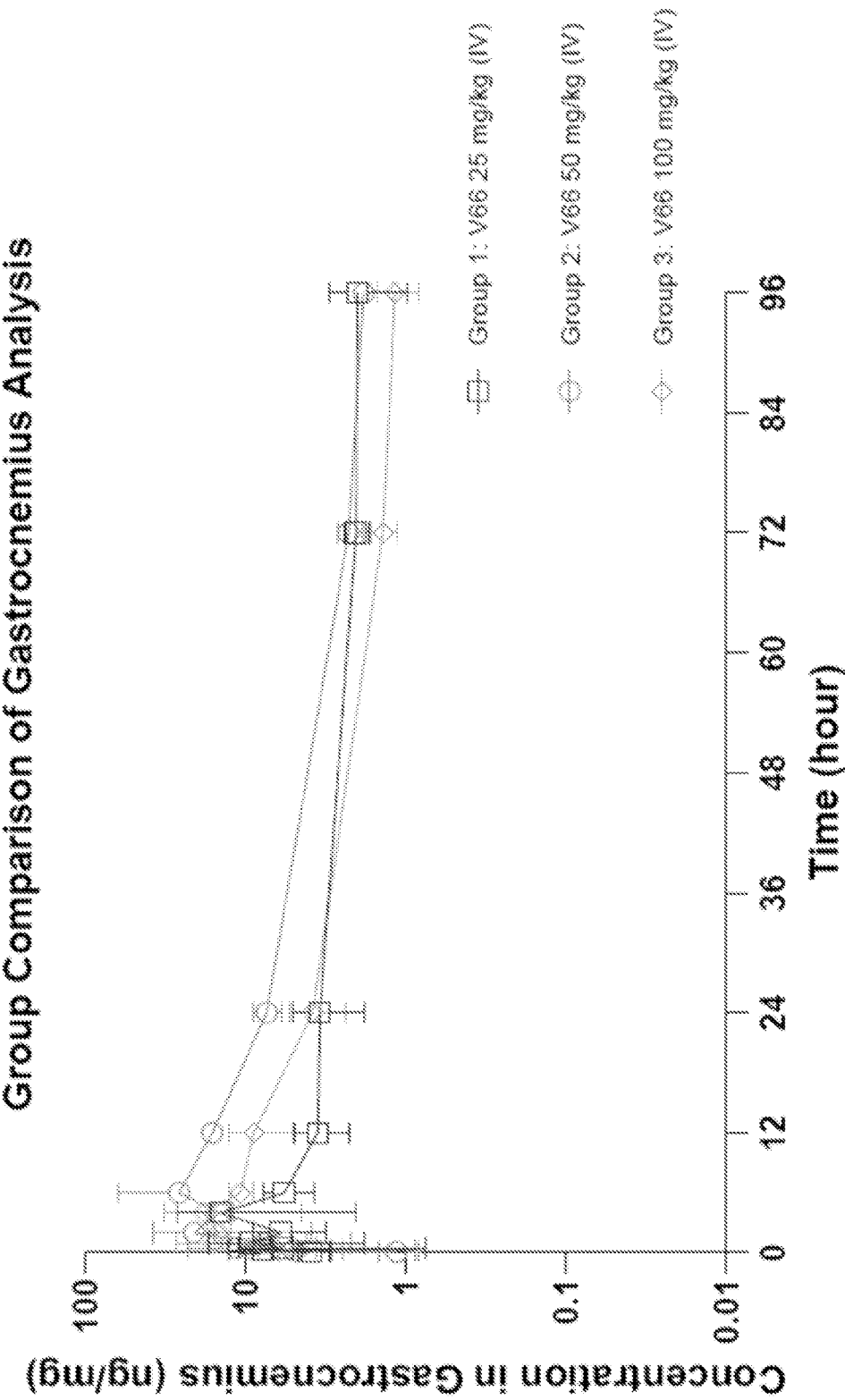


FIG. 23Q

PK Parameter	Group 1 - 25 mg/kg						
	Serum	Liver	Heart	Brain	Kidney	Gastrocnemius	Deltoid
Tmax (hr)	0.08	0.25	0.08	0.08	2.00	4.00	6.00
Cmax (ng/mL)	590176.88	2760.52	1139.35	349.01	3146.55	2396.34	414.75
AUClast (hr*ng/mL)	2204955.30	30862.41	33668.65	8691.21	69223.01	47182.90	15111.59
Rank of V66 Concentration by AUC	1	6	5	8	2	4	7
Group 2 - 50 mg/kg							
PK Parameter	Group 2 - 50 mg/kg						
	Serum	Liver	Heart	Brain	Kidney	Gastrocnemius	Deltoid
Tmax (hr)	0.08	0.25	2.00	0.25	2.00	2.00	2.00
Cmax (ng/mL)	968366.37	5082.91	1597.07	304.27	5074.80	3517.08	845.22
AUClast (hr*ng/mL)	4186886.10	58692.28	56674.19	14899.77	88008.07	98579.71	32556.60
Rank of V66 Concentration by AUC	1	5	6	8	4	3	7
Group 3 - 100 mg/kg							
PK Parameter	Group 3 - 100 mg/kg						
	Serum	Liver	Heart	Brain	Kidney	Gastrocnemius	Deltoid
Tmax (hr)	0.08	0.25	1.00	0.25	1.00	4.00	24.00
Cmax (ng/mL)	2767693.90	6577.94	3715.26	797.94	8360.64	2641.31	1737.15
AUClast (hr*ng/mL)	7890941.40	69311.08	93794.40	21269.60	129719.97	59432.86	71144.90
Rank of V66 Concentration by AUC	1	6	4	8	3	7	5

FIG. 24A

PK Parameter	Group 1 900 mg/kg (IV)									
	Serum	Liver	Heart	Brain	Kidney	Gastrocnemius	Thiceps	Deltoide		
r^2	1.00	0.95	0.91	0.01	0.83	0.96	1.00	0.85		
Half-Life (hr)	40.40	32.30	69.84	148.89	32.71	69.23	60.64	17.39		
T_{max} (hr)	0.08	0.25	0.08	0.08	2.00	4.00	6.00	0.08		
C_{max} (ng/mL)	590176.88	2760.52	1239.35	349.01	3146.55	2596.34	414.75	5842.34		
AUC_{0-100} (hr*ng/mL)	2204955.30	30882.41	33668.65	8693.21	69223.01	47182.90	15111.59	57226.66		
AUC_{0-100} (hr*ng/mL)	2376176.70	45674.88	52038.28	30001.37	77965.12	74019.29	22195.56	60261.76		
AUC_{0-100} (%)	7.21	91.39	95.30	71.02	11.21	86.26	31.92	5.04		
V_z Obs (mL/kg)	614.53	25504.36	48404.21	178991.81	15132.06	33733.98	98530.98	10407.77		
Cl Obs (mL/hr/kg)	10.52	547.35	480.42	823.90	320.66	337.75	1126.35	414.86		
Rank of V_{obs} Concentration by AUC_{0-100}	1	6	5	8	2	4	7	3		

FIG. 24B

PK Parameter	Group 2 V66 50 mg/kg (N)							
	Serum	Liver	Heart	Brain	Kidney	Gastrocnemius	Triceps	Deltoide
r^2	1.00	0.79	0.79	0.25	0.67	0.94	0.96	0.94
Half-Life (hr)	49.44	18.95	72.95	218.25	38.66	26.68	37.15	46.89
T_{max} (hr)	0.08	0.25	2.00	0.25	2.00	2.00	0.25	2.00
C_{max} (ng/mL)	962566.37	5082.91	1597.07	304.27	5074.80	3517.08	845.22	12698.33
AUC_{0-24} (hr*ng/mL)	4186886.10	59692.28	56674.19	14899.77	88008.07	98579.71	32556.60	179714.24
AUC_{0-24} (hr*ng/mL)	4593226.50	61999.71	97870.76	70398.68	118460.19	110387.77	40531.56	202041.79
$AUC\ %Extrap$ (%)	8.85	5.33	42.09	78.84	25.71	10.70	19.68	15.51
$V_z\ Obs$ (mL/kg)	776.45	22041.95	53766.64	223633.14	23540.01	17431.87	66115.30	16741.65
$Cl\ Obs$ (mL/hr/kg)	10.89	806.46	510.88	710.24	422.08	452.95	1233.61	247.47
Rank of V66 Concentration by AUC_{0-24}	1	5	6	8	4	3	7	2

FIG. 24C

PK Parameter	Group 3 V66 100 mg/kg (n)							
	Serum	Liver	Heart	Brain	Kidney	Gastrocnemius	Tripops	Deloid
r ²	0.85	0.79	0.88	0.58	0.96	0.92		0.94
Half-Life (hr)	28.95	19.87	77.07	79.71	54.02	40.45		34.30
T _{max} (hr)	0.08	0.25	1.00	0.25	1.00	4.00	24.00	0.25
C _{max} (ng/mL)	2767693.90	6577.94	3715.26	797.94	8260.64	3641.31	1737.15	26581.01
AUC _{0-∞} (hr*ng/mL)	7630941.40	69311.08	93794.40	21259.60	129719.97	59432.66	71144.90	321721.05
AUC _{0-∞} (hr*ng/mL)	8208006.10	76551.66	146447.65	43613.90	108828.66	70823.06		341559.83
AUC %Extrap (%)	9.86	9.86	33.95	51.23	23.16	16.08		5.81
V _d Obs (mL/kg)	526.39	37454.68	75928.43	283661.53	46165.10	82400.35		10263.84
Cl Obs (mL/hr/kg)	12.18	1306.31	662.84	2292.85	592.32	1411.97		292.77
Rank of V66 Concentration by AUC _{0-∞}	1	6	4	8	3	7	5	2

FIG. 24D