

Amino Acid Sequence of Human IDS (SEQ ID NO:1)

Iduronate-2-sulfatase (IDS)

→ Signal			→ Mature 42kD		
10	20	30	40	50	
MPPPRTGRGL	LWLGLVLSSV	CVALGSETQA	NSTTDALNVL	LIIVDDL RPS	
60	70	80	90	100	
LG CYGDKLVR	SPNIDQLASH	SLLFQNAFAQ	QAVCAPSRVS	FLTGRRPDTT	
110	120	130	140	150	
RLYDFNSYWR	VHAGNFSTIP	QYFKENGYVT	MSVGKVFHPG	ISSNHTDDSP	
160	170	180	190	200	
YWSFPPYHP	SSEKYENTKT	CRGPDGELHA	NLLCPVDVLD	VPEGTL PDKQ	
210	220	230	240	250	
STEQA IQLLE	KMKTSASPFF	LAVGYHKPHI	PFRYPKEFQK	LYPLENITLA	
260	270	280	290	300	
PDPEVPDGLP	PVAYNPWMDI	RQREDVQALN	ISVPYGPPIV	DFQRKIRQSY	
310	320	330	340	350	
FASVSYLDTQ	VGRLLSALDD	LQLANSTIIA	FTSDHGWALG	EHGEWAKYSN	
360	370	380	390	400	
FDVATHVPLI	FYVPGRTASL	PEAGEKLFPY	LDPFDSASQL	MEPGRQSM DL	
410	420	430	440	450	
VELVSLFPTL	AGLAGLQVPP	RCPVPSFHVE	LCREGKNLLK	HFRFRDLEED	
→ Mature 14kD					
460	470	480	490	500	
PYLPGNPREL	IAYSQYPRPS	DIPQWNSDKP	SLKDIKIMGY	SIRTIDYRYT	
510	520	530	540	550	
VWVGFN PDEF	LANFSDIHAG	ELYFVDS DPL	QDHNMYNDSQ	GGDLFQLLMP	

Italics = signal sequence (MPPPRTGRGL LWLGLVLSSV CVALG) (SEQ ID NO:46)

N = N-linked glycosylation sites (GlcNac...)

Boxed = Y-sulfation site (PSSEKYENTKTCRGPD) (SEQ ID NO:47)

Underscore = amino-terminal sequence of 42kD and 14kD peptides (Sleat 2005)

C⁸⁴ = formylglycine modification

N²⁸⁰ = M-6-P residue(s)

FIG. 1

CLUSTAL O(1.2.4) multiple sequence alignment of hIDS to orthologs

SP P22304 IDS_HUMAN	MPPRTGRGLLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR K6ZGI9 K6ZGI9_PANTR	MPPRTGRGLPWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR K7BKV4 K7BKV4_PANTR	MPPRTGRGLPWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR H9FTX2 H9FTX2_MACMU	MPTPGSGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR F7EJG2 F7EJG2_CALJA	MPPRTSRCLLLGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR U3DTL8 U3DTL8_CALJA	MPPRPSRCLLLGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR G7NRX7 G7NRX7_MACMU	MPTPGSGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR G7Q1V9 G7Q1V9_MACFA	MPTPGSGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR H2PX10 H2PX10_PONAB	MPPRTGRGLLWGLVLSVVCVALGSETQADSTTDGLNVLLIIVDDLPSLGCYGDKLVR	60
TR A0A0D9R4D1 A0A0D9R4D1_CHLSB	MPTPGSGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
TR G1RST8 G1RST8_NOMLE	MSPPRTGQGLLWGLVLSVVCVAXVTSKPPSFVDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I0000D9F625	MPTPGSGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I000274358B	MPPRTGRGLLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I00027F6FC5	MPTPGSGRGFLWGLVLSVVCVALGCEMQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I00027FAE03	MPPRTGLCLLLGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I0003ABBF28	MPTPGSGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I000533297F	MPTPASCGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60
UP I0005F40BD2	MPTPASCGRGFLWGLVLSVVCVALGSETQANSTTDALNVLLIIVDDLPSLGCYGDKLVR	60

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SP P22304 IDS_HUMAN	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR K6ZGI9 K6ZGI9_PANTR	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR K7BKV4 K7BKV4_PANTR	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR H9FTX2 H9FTX2_MACMU	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR F7EJG2 F7EJG2_CALJA	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR U3DTL8 U3DTL8_CALJA	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR G7NRX7 G7NRX7_MACMU	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR G7Q1V9 G7Q1V9_MACFA	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120
TR H2PX10 H2PX10_PONAB	SPNIDQLASHLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRL YDFNSYWRVHAGNFSTIP	120

FIG. 2

TR A0A0D9R4D1 A0A0D9R4D1_CHLSB	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLHNFNSYWRVHAGNFSTIP	120
TR G1RST8 G1RST8_NOMLE	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I0000D9F625	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I000274358B	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I00027F6FC5	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I00027FAE03	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I0003ABBF28	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I000533297F	SPNIDQLASHSLLFQNAFAQQAVCAPSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
UP I0005F40BD2	SPNIDQLASHSLLFQNAFAQQAVCTPSHVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIP	120
	*****:***:***** *****	
	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
SP P22304 IDS_HUMAN	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR K6ZG19 K6ZG19_PANTR	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR K7BKV4 K7BKV4_PANTR	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR H9FTX2 H9FTX2_MACMU	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR F7EJG2 F7EJG2_CALJA	QYFKDNGYYTMSVGKVFHPG SSNHSDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR U3DTL8 U3DTL8_CALJA	QYFKDNGYYTMSVGKVFHPG SSNHSDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR G7NRX7 G7NRX7_MACMU	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR G7Q1V9 G7Q1V9_MACFA	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR H2PX10 H2PX10_PONAB	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR A0A0D9R4D1 A0A0D9R4D1_CHLSB	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
TR G1RST8 G1RST8_NOMLE	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSXXXXXXKTCRGPDGELHA	180
UP I0000D9F625	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
UP I000274358B	QYFKENGYYTMSVGKVFHPG SSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
UP I00027F6FC5	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
UP I00027FAE03	QYFKDNGYYTMSVGKVFHPG SSNHSDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
UP I0003ABBF28	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
UP I000533297F	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
UP I0005F40BD2	QYFKENGYYTMSVGKVFHPG TSNHTDDSPYSWSFPPYHPSSSEKYENTKTCRGPDGELHA	180
	*****:***:***** *****	

FIG. 2 continued

SP	P22304	IDS_HUMAN	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	K6ZG19	K6ZG19_PANTR	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	K7BKV4	K7BKV4_PANTR	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	H9FTX2	H9FTX2_MACMU	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	F7EJG2	F7EJG2_CALJA	NLLCPVDVLDVPEGLPDKQSTEEAIRLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	U3DTL8	U3DTL8_CALJA	NLLCPVDVLDVPEGLPDKQSTEEAIRLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	G7NRX7	G7NRX7_MACMU	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	G7Q1V9	G7Q1V9_MACFA	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	H2PX10	H2PX10_PONAB	NLLAKKMCWMPRAPCCDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	A0A0D9R4D1	A0A0D9R4D1_CHLSB	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
TR	G1RST8	G1RST8_NOMLE	NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I0000D9F625		NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I000274358B		NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I00027F6FC5		NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I00027FAE03		NLLCPVDVLDVPEGLPDKQSTEEAIRLLKKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I0003ABBF28		NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I000533297F		NLLCPVDVLDVPEGLPDKQSTEQAVQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
UP	I0005F40BD2		NLLCPVDVLDVPEGLPDKQSTEQAIQLLEKMKTSASPFLLAVGYHKPHIPFRYPKEFQK	240
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SP	P22304	IDS_HUMAN	LYPLENITLAPDPEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	K6ZG19	K6ZG19_PANTR	LYPLENITLAPDPEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	K7BKV4	K7BKV4_PANTR	LYPLENITLAPDPEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	H9FTX2	H9FTX2_MACMU	LYPLENITLAPDSEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	F7EJG2	F7EJG2_CALJA	LYPLENITLAPDPEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	U3DTL8	U3DTL8_CALJA	LYPLENITLAPDPEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	G7NRX7	G7NRX7_MACMU	LYPLENITLAPDSEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	G7Q1V9	G7Q1V9_MACFA	LYPLENITLAPDSEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300
TR	H2PX10	H2PX10_PONAB	LYPLENITLAPDPEVPDGLPPVAYNPWMDIRQREDVQALNISVPYGP	300

FIG. 2 continued

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L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V D F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V D F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V D F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V F O R K I R Q S Y 300  
L Y P L E N I T L A P D S E V P D G L P P V A Y N P W M D I R Q R E D V Q A L N I S V P Y G P I P V D F O R K I R Q S Y 300
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[illegible]

FIG. 2 continued

TTR|A0A0D9R4D1|A0A0D9R4D1_CHL5B
TTR|G1RST8|G1RST8_NOMLE
UPI0000D9F625
UPI000274358B
UPI00027F6FC5
UPI00027FAE03
UPI0003ABBF28
UPI000533297F
UPI0005F40BD2

SP	P22304	IDS_HUMAN
TTR	K6ZG19	K6ZG19_PANTR
TTR	K7BKV4	K7BKV4_PANTR
TTR	H9FTX2	H9FTX2_MACMU
TTR	F7EJG2	F7EJG2_CALJA
TTR	U3DTL8	U3DTL8_CALJA
TTR	G7NRX7	G7NRX7_MACMU
TTR	G7Q1V9	G7Q1V9_MACFA
TTR	H2PX10	H2PX10_PONAB
TTR	AOA0D9R4D1	AOA0D9R4D1_CHLSB
TTR	G1RST8	G1RST8_NOMLE
UPI	I0000D9F625	
UPI	I000274358B	
UPI	I00027F6FC5	
UPI	I00027FAE03	
UPI	I0003ABBF28	
UPI	I000533297F	
UPI	I0005F40BD2	

SP	P22304	IDS_HUMAN	FYVPGRTASLPEAGEKLPYLDPFDSASQLMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	K6ZG19	K6ZG19_PANTR	FYVPGRTASLPEAGEKLPYLDPFDSASQLMEPGRQSMIDLVELVSLFPTLAGLAGLQAPP	420
TR	K7BKV4	K7BKV4_PANTR	FYVPGRTASLPEAGEKLPYLDPFDSASQLMEPGRQSMIDLVELVSLFPTLAGLAGLQAPP	420
TR	H9FTX2	H9FTX2_MACMU	FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	F7EJG2	F7EJG2_CALJA	FYVPGRTASLPEADEKLPYVDPFHSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	U3DTL8	U3DTL8_CALJA	FYVPGRTASLPEADEKLPYVDPFHSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	G7NRX7	G7NRX7_MACMU	FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	G7Q1V9	G7Q1V9_MACFA	FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	H2PX10	H2PX10_PONAB	FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	A0A0D9R4D1	A0A0D9R4D1_CHLSB	FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
TR	G1RST8	G1RST8_NOMLE	FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
UP	I0000D9F625		FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
UP	I000274358B		FYVPGRTASLPEAGEKLPYLDPFDSASQLMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
UP	I00027F6FC5		FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
UP	I00027FAE03		FYVPGRTASLPETGEKLPYVDPFHSASELMEPGRQSTDLVELVSLFPTLAGLAGLQVPP	420
UP	I0003ABBF28		FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
UP	I000533297F		FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
UP	I0005F40BD2		FYVPGRTASLPEAGEKLPYLDPFDSASELMEPGRQSMIDLVELVSLFPTLAGLAGLQVPP	420
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SP	P22304	IDS_HUMAN	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPSDIPQWNSDKP	480
TR	K6ZG19	K6ZG19_PANTR	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPSDIPQWNSDKP	480
TR	K7BKV4	K7BKV4_PANTR	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPSDIPQWNSDKP	480
TR	H9FTX2	H9FTX2_MACMU	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPADFPQWNSDKP	480
TR	F7EJG2	F7EJG2_CALJA	RCPVPSFHVLCREGKSLKHFRFHGLEEDPYLPGNPREL IAYSQYPRPADFPQWNSDKP	480
TR	U3DTL8	U3DTL8_CALJA	RCPVPSFHVLCREGKSLKHFRFHGLEEDPYLPGNPREL IAYSQYPRPADFPQWNSDKP	480
TR	G7NRX7	G7NRX7_MACMU	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPADFPQWNSDKP	480
TR	G7Q1V9	G7Q1V9_MACFA	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPADFPQWNSDKP	480
TR	H2PX10	H2PX10_PONAB	RCPVPSFHVLCREGKNLLKHFRFRDLEEDPYLPGNPREL IAYSQYPRPADFPQWNSDKP	480

FIG. 2 continued

SP	P22304	IDS_HUMAN	GGDLFQLLMP	550 (SEQ ID NO:27)
TR	K6ZG19	K6ZG19_PANTR	GGDLFQLLMP	550 (SEQ ID NO:28)
TR	K7BKV4	K7BKV4_PANTR	GGDLFQLLMP	550 (SEQ ID NO:29)
TR	H9FTX2	H9FTX2_MACMU	GGDLFQLLMP	550 (SEQ ID NO:30)
TR	F7EJG2	F7EJG2_CALJA	GGELFQSLMP	550 (SEQ ID NO:31)
TR	U3DTL8	U3DTL8_CALJA	GGELFQSLMP	550 (SEQ ID NO:32)
TR	G7NRX7	G7NRX7_MACMU	GGDLLQLLMP	550 (SEQ ID NO:33)
TR	G7Q1V9	G7Q1V9_MACFA	GGDLFQLLMP	550 (SEQ ID NO:34)
TR	H2PX10	H2PX10_PONAB	GGDLFQLLMP	550 (SEQ ID NO:35)
TR	AOA0D9R4D1	AOA0D9R4D1_CHLSB	GGDLFQLLMP	550 (SEQ ID NO:36)
TR	G1RST8	G1RST8_NOMLE	GGDLFQLLMP	550 (SEQ ID NO:37)
UP	I0000D9F625		GGDLLQLLMP	550 (SEQ ID NO:38)
UP	I000274358B		GGDLFQLLMP	550 (SEQ ID NO:39)
UP	I00027F6FC5		GGDLFQLLMP	550 (SEQ ID NO:40)
UP	I00027FAE03		GGELFQSLMP	550 (SEQ ID NO:41)
UP	I0003ABBF28		GGDLFQLLMP	550 (SEQ ID NO:42)
UP	I000533297F		GGDLFQLLMP	550 (SEQ ID NO:43)
UP	I0005F40BD2		GGDLFQLLMP	550 (SEQ ID NO:44)
***: * ***				
Species Legend:				
SP	P22304	IDS_HUMAN	[Homo sapiens]	
TR	K6ZG19	K6ZG19_PANTR	[Pan troglodytes (Chimpanzee)]	
TR	K7BKV4	K7BKV4_PANTR	[Pan troglodytes (Chimpanzee)]	
TR	H9FTX2	H9FTX2_MACMU	[Macaca mulatta (Rhesus macaque)]	
TR	F7EJG2	F7EJG2_CALJA	[Callithrix jacchus (White-tufted-ear marmoset)]	
TR	U3DTL8	U3DTL8_CALJA	[Callithrix jacchus (White-tufted-ear marmoset)]	
TR	G7NRX7	G7NRX7_MACMU	[Macaca mulatta (Rhesus macaque)]	
TR	G7Q1V9	G7Q1V9_MACFA	[Macaca fascicularis (Crab-eating macaque; Cynomologous monkey)]	

FIG. 2 continued

TR|H2PX10|H2PX10_PONAB

TR|A0A0D9R4D1_CHLSB

TR|G1RST8|G1RST8_NOMLE

UPI0000D9F625

UPI000274358B

UPI00027F6FC5

UPI00027FAE03

UPI0003ABBF28

UPI000533297F

UPI0005F40BD2

[Pongo abelii (Sumatran orangutan)]

[Chlorocebus sabaeus (Green monkey)]

[Nomascus leucogenys (Northern white-cheeked gibbon)]

[Macaca mulatta (Rhesus macaque)]

[Pan paniscus (Pygmy chimpanzee; Bonobo)]

[Papio Anubis (Olive baboon)]

[Saimiri boliviensis (Bolivian squirrel monkey)]

[Macaca fascicularis (Crab-eating macaque; Cynomologous monkey)]

[Rhinopithecus roxellana (Golden snub-nosed monkey; Pygathrix roxellana)]

[Colobus angolensis palliatus (Peters' Angolan colobus)]

FIG. 2 continued

hIDS MPS II Variants

L41P (mild); 41X (intermediate); D45N (MPS2); R48P (mild); Y54D (severe); N63D (mild/intermediate); A68E (severe); S71N (mild); S71R (severe); L73F (severe); A79E (mild); A82E (MPS2); A82V (no significant enzyme activity); A85S (severe); A85T (mild to severe forms); P86L (intermediate to severe forms); P86Q (MPS2); P86R (severe); S87N (mild); R88C (severe);	E125V (mild); S132W (severe); G134R (severe); K135N (intermediate); K135R (intermediate); H138D (mild/intermediate); G140V (MPS2; no significant enzyme activity); S143F (MPS2); D148H (intermediate); H159P (severe); 159X (missing in MPS2; intermediate form); P160R (MPS2); N181I (mild); L182P (intermediate); C184F (mild/intermediate); C184W (MPS2); L196S (mild/intermediate); D198G (mild); A205P (intermediate); L221P (intermediate);	D334G (severe); D334N (mild); H335R (intermediate); G336E (severe); G336R (severe); W337R (intermediate); L339R (severe); G340D (mild); E341K (severe); H342Y (mild); W345C (mild/severe); A346D (mild/severe); A346V (mild/severe); K347I (MPS2); K347Q (severe); K347T (severe); Y348H (MPS2); S349I (severe); P358R (severe); L403R (intermediate); L410P (MPS2); C422G (mild);
--	--	---

FIG. 3

R88G (severe); R88H (intermediate/severe form); R88L (severe); R88P (severe—total absence of residual activity); V89F (MPS2); L92P (severe); G94D (mild); R95G (intermediate); R95T (mild); 95X (severe); L102R (mild); Y108C (mild); Y108S (mild); N115Y (MPS2); S117Y (severe); 117X (missing in MPS2; severe form; deleterious mutation); T118I (mild to severe; greatly reduced activity); 118X (missing in MPS2; severe form); P120H (mild); P120R (severe); Q121H (severe); Q121R (severe);	G224E (severe); Y225D (intermediate); K227M (intermediate); K227Q (severe); P228L (MPS2); P228T (severe); H229R (intermediate/severe); H229Y (severe); P231L (mild); D252N (MPS2); L259P (severe); Y264N (MPS2); N265I (intermediate; deleterious mutation); P266H (mild); P266R (MPS2); D269V (MPS2); Q293H (mild); S299I (mild); D308E (mild); D308N (intermediate); T309A (severe); R313C (MPS2; unknown pathological significance); L314P (severe); S333L (severe);	C422R (severe); C432Y (severe); E434K (MPS2); Q465P (severe); P467L (severe); R468G (mild/severe); R468L (mild/severe); R468Q (severe/intermediate; greatly reduced activity); R468W (mild/severe); P469H (mild); D478G (mild); D478Y (severe); P480L (mild); P480Q (mild); P480R (severe); I485K (MPS2); I485R (severe); MG488–489IA (intermediate); Y490S (intermediate); S491F (mild); W502C (severe); W502S (MPS2); E521K (severe); E521V (severe); Y523C (mild).
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FIG. 3 continued

Human IDS Processing Steps

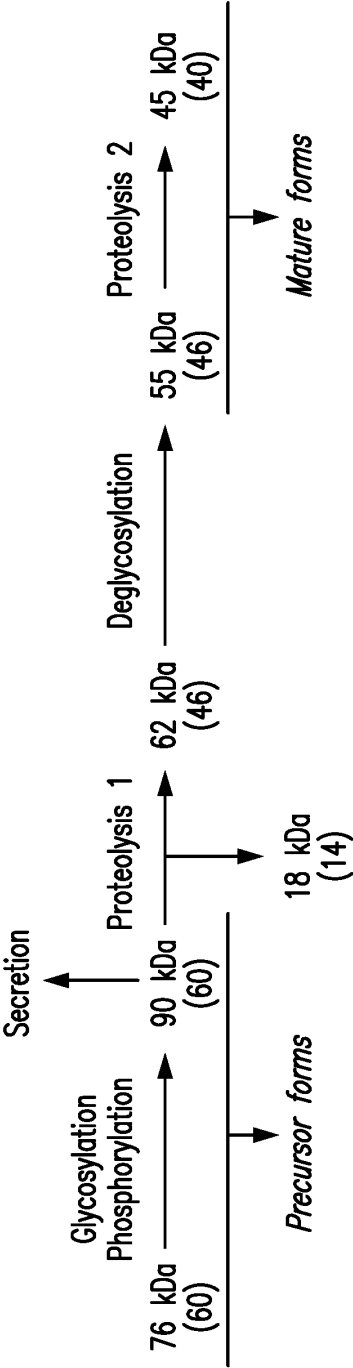


FIG. 7. IDS processing. Molecular mass of deglycosylated polypeptides is indicated in parentheses.

(From, Millat et al., 1997, Exp. Cell. Res. 230: 362–367 ("Millat 1997") Fig. 7).

FIG. 4

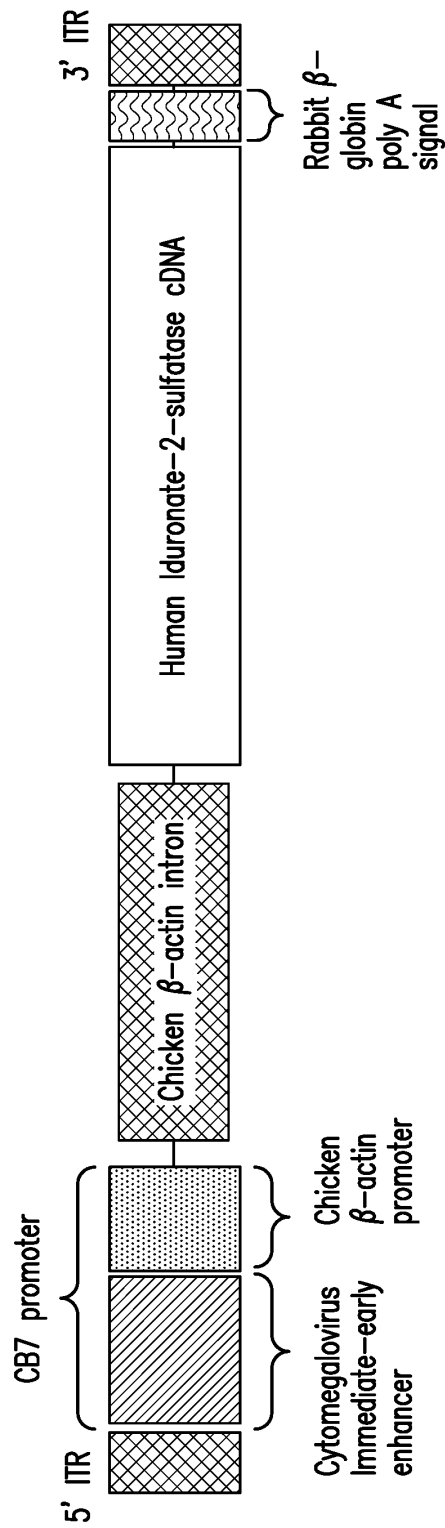


FIG. 5

VP11-736 →

AAV1	MAADGYLPDWLEDNLSEGIREW WDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD	60
AAV2	MAADGYLPDWLEDTLSEGI RQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD	60
AAV3-3	MAADGYLPDWLEDNLSEGIREW WALKPGVPQPKANQQHQDNRRGLVLPGYKYLGPGNGLD	60
AAV4-4	- MTDGYLPDWLEDNLSEGIREWWALQPGAPKPKANQQHQDNARGLVLPGYKYLGPGNGLD	59
AV5	MSFVDHPPDWLEEF-VGEGLREFLGLEAGPPKPKPNQQHQDQARGVLVPGYNYLGPGNGLD	59
AAV6	MAADGYLPDWLEDNLSEGIREW WDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD	60
AAV7	MAADGYLPDWLEDNLSEGIREW WDLKPGAPKPKANQQKQDNGRGLVLPGYKYLGPFNGLD	60
AAV8	MAADGYLPDWLEDNLSEGIREW WALKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD	60
hu31	MAADGYLPDWLEDTLSEGI RQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPGNGLD	60
hu32	MAADGYLPDWLEDTLSEGI RQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPGNGLD	60
AAV9	MAADGYLPDWLEDNLSEGIREW WALKPGAPQPKANQQHQDNARGLVLPGYKYLGPGNGLD	60
SUBS	-STVDHP-----ETVG-V-QFLK-QA-P-K-PAERKK-DG-----N-F----- MF L D E V P QS G Q R	

AAV1	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV2	KGEPVNEADAALAEHDKAYDRQLDSGDNPYLKYNHADADEFQERLKEDTSFGGNLGRAVFQ	120
AAV3-3	KGEPVNEADAALAEHDKAYDQQLKAGDNPYLKYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV4-4	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLKYNHADADEFQRRLQGDTSFSGGNLGRAVFQ	119
AV5	RGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADADEFQEKLADDTSFGGNLGKAVFQ	119
AAV6	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV7	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
AAV8	KGEPVNAADAALAEHDKAYDQQLQAGDNPYLRYNHADADEFQERLQEDTSFGGNLGRAVFQ	120
hu31	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLKYNHADADEFQERLKEDTSFGGNLGRAVFQ	120
hu32	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLKYNHADADEFQERLKEDTSFGGNLGRAVFQ	120
AAV9	KGEPVNAADAALAEHDKAYDQQLKAGDNPYLKYNHADADEFQERLKEDTSFGGNLGRAVFQ	120
SUBS	R-----E-EV-R-----IS-NE-DS-----R-----QK-QD-----K----- R R E AG Q	

FIG. 6

	VP2-138→ ₁ ---HVR1--- ₁	
AAV1	AKKRVLEPLGLVEEGAKTAPGKKRPVEQSPQ-EPDSSSGIGK TGQQ PAKKRLNFGQTGDS	179
AAV2	AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPV-EPDSSSGTGK AGQQ PARKRLNFGQTGDA	179
AAV3-3	AKKRILEPLGLVEEAAKTAPGKK GAVD QSPQ-EPDSSSGVGKSGK QPA RKRLNFGQTGDS	179
AAV4-4	AKKRVLEPLGLVE QAG ETAPGKKRPLIESPQ- Q PDSS TGIGKKGKQ PAKK KL V FEDETGA	178
AV5	AKKRVLEPFGLVEEGAKTAP TGKR IDDHFP----- KRKKARTEEDSKPSTSSDA	168
AAV6	AKKRVLEPFGLVEEGAKTAPGKKRPVEQSPQ-EPDSSSGIGK TGQQ PAKKRLNFGQTGDS	179
AAV7	AKKRVLEPLGLVEEGAKTAPAKKRPVEPSPQRS PD SS TGIGKKGQ QPAKKRLNFGQTGDS	180
AAV8	AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQRS PD SS TGIGKKGQ QPAKKRLNFGQTGDS	180
hu31	AKKRILLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSG SQ PAKK KL NFGQTGDT	179
hu32	AKKRILLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSG SQ PAKK KL NFGQTGDT	179
AAV9	AKKRILLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGAQPAKKRLNFGQTGDT	179
SUBS	---V---F--- QGGE ---TG---GID HF ---V---S---S---T--- KKQARTREKSVPEDETGA	
	I PV A ALIP Q T V T K E D K STSS S	
	E AS	
	RA	

FIG. 6 continued

HVR3

AAV1 VITTSTRTWALPTYNNHLYKQIS-SASTGASNDNHYFGYSTPWGYDFNRFHCHFSRDPW 297
AAV2 VITTSTRTWALPTYNNHLYKQIS--SQSGASNDNHYFGYSTPWGYDFNRFHCHFSRDPW 296
AAV3-3 VITTSTRTWALPTYNNHLYKQIS--SQSGASNDNHYFGYSTPWGYDFNRFHCHFSRDPW 296
AAV4-4 VTTTSTRTWVLPTYNNHLYKRLG-----ESLQSNNTYNGFSTPWGYDFNRFHCHFSRDPW 287
AV5 VVTKSTRTWVLPSYNNHQQYREIKS-GSVDGSNANAYFGYSTPWGYDFNRFHSHWSRDPW 287
AAV6 VITTSTRTWALPTYNNHLYKQISSAST-GASNDNHYFGYSTPWGYDFNRFHCHFSRDPW 297
AAV7 VITTSTRTWALPTYNNHLYKQISS-ETAGSTNDNTYFGYSTPWGYDFNRFHCHFSRDPW 298
AAV8 VITTSTRTWALPTYNNHLYKQISNGTSGGATNDNTYFGYSTPWGYDFNRFHCHFSRDPW 299
hu31 VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYDFNRFHCHFSRDPW 298
hu32 VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYDFNRFHCHFSRDPW 298
AAV9 VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYDFNRFHCHFSRDPW 298
SUBS -T-K-----V-S-----Q-RRLGSGSQSDATQA-T-----S-W-----
V E K AATTEGL S H
G V
E A

FIG. 6 continued

AAV1	QRLINNNWGFRPKRLNFKLFNIQVKEVTTNDGVTTIANNLTSTVQVFSDEYQLPYVLGS	357
AAV2	QRLINNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS	356
AAV3-3	QRLINNNWGFRPKLSFKLFNIQVRGVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS	356
AAV4-4	QRLINNNWGMRPKAMRVKIFNIQVKEVTTSNGETTVANNLTSTVQVIFADSSYELPYVMDA	347
AV5	QRLINNYWGFRPRLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDYQLPYVVG	347
AAV6	QRLINNNWGFRPKRLNFKLFNIQVKEVTTNDGVTTIANNLTSTVQVFSDEYQLPYVLGS	357
AAV7	QRLINNNWGFRPKRLRFKLFNIQVKEVTTNDGVTTIANNLTSTIQVFSDEYQLPYVLGS	358
AAV8	QRLINNNWGFRPKRLSFKLFNIQVKEVTQNEGTCTIANNLTSTIQVFTDSEYQLPYVLGS	359
hu31	QRLINNNWGFRPKRLNFKLFNIQVKEVTDNNGVKTIANNTSTVQVFTDSYQLPYVLGS	358
hu32	QRLINNNWGFRPKRLNFKLFNIQVKEVTDNNGVKTIANNTSTVQVFTDSYQLPYVLGS	358
AAV9	QRLINNNWGFRPKRLNFKLFNIQVKEVTDNNGVKTIANNTSTVQVFTDSYQLPYVLGS	358
SUBS	M RAMRV I VQDSTT I I S DE E MDA	
	K S QSE E A S	
	S	

FIG. 6 continued

HVR4

AAV1 AHQGCCLPPFPADVFMI PQYGYL TLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
AAV2 AHQGCCLPPFPADVFMPV PQYGYL TLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
AAV3-3 AHQGCCLPPFPADVFMPV PQYGYL TLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
AAV4-4 GQEGSLPPFPNDVFMPV PQYGYCGLVTGNTSQQQTDRNAFYCLEYFPSQMLRTGNNFEITY 407
AV5 GTEGCLPAFPQP VTL PQYGYATLN RD-NTENPTERSSFFCLEYFPSKMLRTGNNFEITY 406
AAV6 AHQGCCLPPFPADVFMI PQYGYL TLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
AAV7 AHQGCCLPPFPADVFMI PQYGYL TLNNG---SQSVGRSSFYCLEYFPSQMLRTGNNFEFSY 415
AAV8 AHQGCCLPPFPADVFMI PQYGYL TLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFTY 416
hu31 AHEGCLPPFPADVFMI PQYGYL TLNDG---GQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
hu32 AHEGCLPPFPADVFMI PQYGYL TLNDG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
AAV9 AHEGCLPPFPADVFMI PQYGYL TLNDG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
SUBS GQQ-S-A-PQ-TL-----CG-VND-GNPTD-NA-F-----EIT-
T N V A T Q Q E T
R E S

-----HVR5-----

AAV1 TFEEVPFHSSYAHSQSLDRLMNPL IDQYL YYLNRTQ-NQSGSAQNKDLLFSRGSPAGMSV 473
AAV2 TFEDVPFHSSYAHSQSLDRLMNPL IDQYL YYLSRTN-TPSGTTTQSRLQFSQAGASDIRD 472
AAV3-3 TFEDVPFHSSYAHSQSLDRLMNPL IDQYL YYLNRTQGCTTS GTTNQSRL LFSQAGPQSM SL 473
AAV4-4 SF EKVPFHSMYAHSQSLDRLMNPL IDQYL WGLQSTTTGTTLNAGTATTNFKLRPTNFSN 467
AV5 NFEEVPFHSSFA PSQNL FKL ANPLVDQYL YRFVSTN-----NTGGVQFNKNLAGRYAN 459
AAV6 TFEDVPFHSSYAHSQSLDRLMNPL IDQYL YYLNRTQ-NQSGSAQNKDLLFSRGSPAGMSV 473
AAV7 SFEDVPFHSSYAHSQSLDRLMNPL IDQYL YYLARTQSNPGGTAGNRELQFYQGGPSTMAE 475
AAV8 TFEDVPFHSSYAHSQSLDRLMNPL IDQYL YYLSRTQT-TGGTANTQTLGFSQGGPNTMAN 475
hu31 EFENVPFHSSYAHSQSLDRLMNPL IDQYL YYLSKTINGSG--QNQQTLKFSVAGPSNMAV 473
hu32 EFENVPFHSSYAHSQSLDRLMNPL IDQYL YYLSKTINGSG--QNQQTLKFSVAGPSNMAV 473
AAV9 EFENVPFHSSYAHSQSLDRLMNPL IDQYL YYLSKTINGSG--QNQQTLKFSVAGPSNMAV 473
SUBS T-D-MF-----A-V-WGFNR-QTNTS-AGTKRTQ-TQCSAATFSN
S E QS NSTPT TQNSDVN NK NL QGYRD
N K V TG Q T AE L YRLR TRI L
A RG G GS E
ND

FIG. 6 continued

	HVR9										HVR10									
AAV1	DDEDKFFPMSGVMIFGKESA--GASNTALD-NVMITDEEEIKATNPVATERFGTVAVN										FQ 585									
AAV2	DDEEKFFPQSGVLIFGKQGS--EKTNDVIE-KVMITDEEEIRTTNPVATEQYQGSVSTNL										Q 584									
AAV3-3	DDEEKFFPMHGNLIFGKEGT--TASNAELD-NVMITDEEEIRTTNPVATEQYQTVANNL										Q 585									
AAV4-4	PADSKFS-NSQLIFAGPKQN--GNTATVPG-TLIFTSEEELAATNATDTDMWGNLPGGD										Q 583									
AV5	LQGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNN										Q 574									
AAV6	DDKDKFFPMSGVMIFGKESA--GASNTALD-NVMITDEEEIKATNPVATERFGTVAVNL										Q 585									
AAV7	DDEDRFFPSSGVLIFGKTGA--TN-KTLE-NVLMTNEEEIRPTNPVATEEYGI										VSSNLQ 586									
AAV8	DDEERFFPSNGILIFGKQNA--ARDNADYS-DVMLTSEEEIKTTNPVATEEYGI										VADNLQ 587									
hu31	EGEDRFFPLSGSLIFGKQGT--GRDNVDAD-KVMITNEEEIKTTNPVATESY										GQVATNHQ 585									
hu32	EGEDRFFPLSGSLIFGKQGT--GRDNVDAD-KVMITNEEEIKTTNPVATESY										GQVATNHQ 585									
AAV9	EGEDRFFPLSGSLIFGKQGT--GRDNVDAD-KVMITNEEEIKTTNPVATESY										GQVATNHQ 585									
SUBS	LQGSNTYAMENTMFANPKQN--TNTATVPG-TLIF-S-S-TQPV-ATDYDMW-NLPGGD-																			
	PADEK S QHQLI		SESA		EASKAALE-NMLM D		RA R		NVF TMSN L											
	DDK		NN V		TPS		AK KTY		L		A		QG I V N							
	S I		N		EI						E S S F									
	N				Y						R		D							

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      --HVR10--
AAV1  SSSTDPATGDVVHAMGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKNPPP 645
AAV2  RGNRQAATADVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPP 644
AAV3-3 SSNTAPTTGTVNHQGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPP 645
AAV4-4 SNSNLPTVDRLTALGAVPGMVWQNRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKHPPP 643
AV5    SSTTAPATGTYNLQEIVPGSVMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPP 634
AAV6  SSSTDPATGDVVHVMGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPP 645
AAV7  AANTAAQTQVVNNQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPP 646
AAV8  QQNTAPQIGTVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPP 647
hu31  SAQAQAQTGWVQNQGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
hu32  SAQAQAQTGWVQNQGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
AAV9  SAQAQAQTGWVQNQGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKHPPP 645
SUBS  RNSNLPTVDRLTALEAV—S—ME—I—————E-GAH—AI—L-N—
      ASNTA AIADYHTM V          N
      QGTRD   QT NH
      Q       V  L
              V
              S

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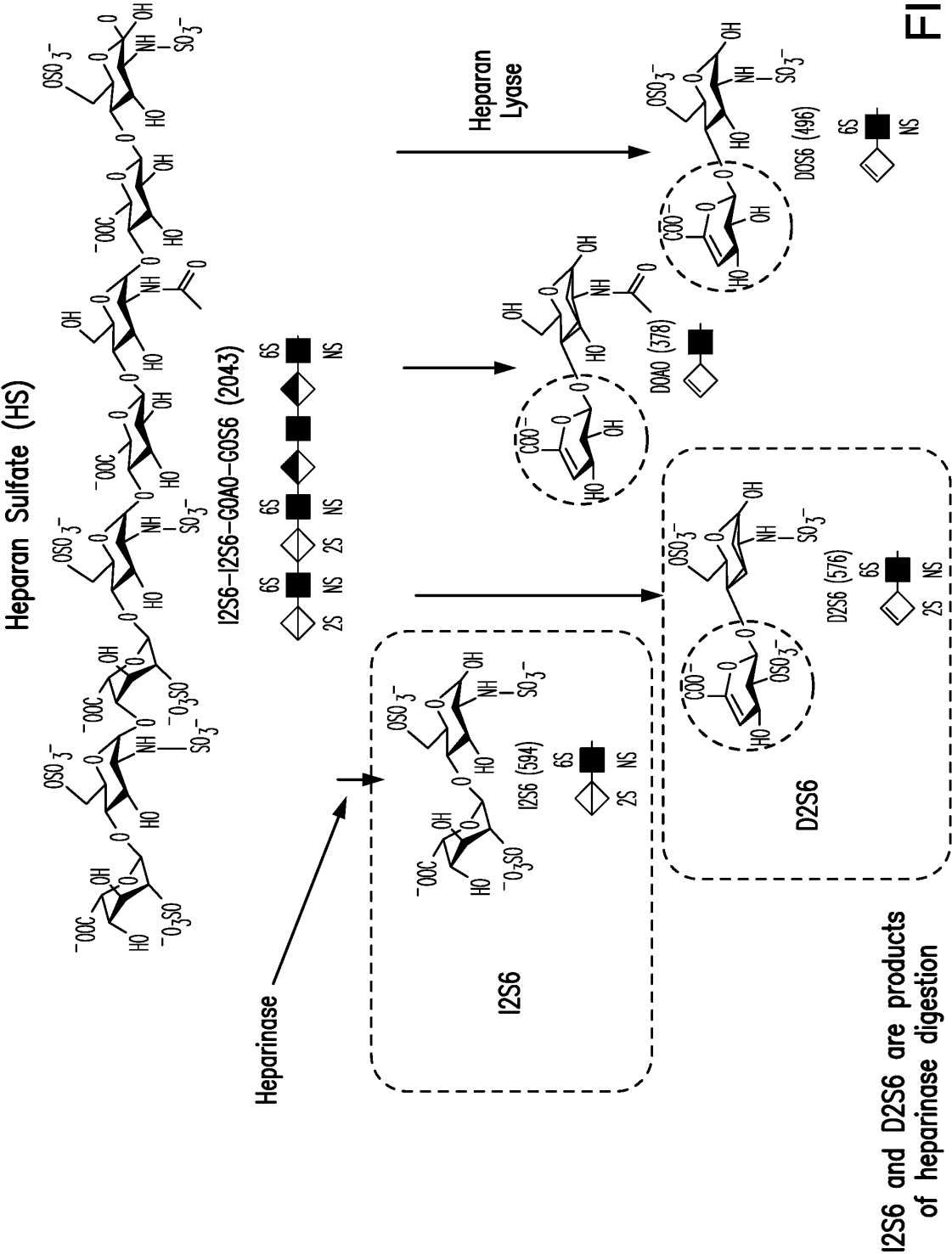
FIG. 6 continued

		┌--HVR11--┐	
AAV1	QILIKNTPVPANPPAEFSATKFASFITQYSTGQVSVEIEWELQKENS	SKRWNPEVQYTSNY	705
AAV2	QILIKNTPVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNY	704
AAV3-3	QIMIKNTPVPANPPTTFSPAKFASFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNY	705
AAV4-4	QIFIKNTPVPANPATTFSSTPVNSFITQYSTGQVSVQIDWEIQKERS	SKRWNPEVQYTSNY	703
AV5	MMLIKNTPVPCNI-TSFSDPVSSFITQYSTGQVTVEMEWELKKENS	SKRWNPEIQYTNNY	693
AAV6	QILIKNTPVPANPPAEFSATKFASFITQYSTGQVSVEIEWELQKENS	SKRWNPEVQYTSNY	705
AAV7	QILIKNTPVPANPPEVFTPAKFASFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNF	706
AAV8	QILIKNTPVPADPPTTFNQSKLNSFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNY	707
hu31	QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNY	705
hu32	QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNY	705
AAV9	QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENS	SKRWNPEIQYTSNY	705
SUBS	MM-----G-IAAE-SDVPVS-----QMD-IK-R-----V-----		
	F	SET TAA FA	
		S PT	
		V QS	
		S	

FIG. 6 continued

	,-----HVR12-----,	
AAV1	AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL	736 (SEQ ID NO. 16)
AAV2	NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL	735 (SEQ ID NO. 17)
AAV3-3	NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL	736 (SEQ ID NO. 18)
AAV4-4	GQQNSLLWAPDAAGKYTEPRAIGTRYLTHHL	734 (SEQ ID NO. 19)
AV5	NDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL	724 (SEQ ID NO. 20)
AAV6	AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL	736 (SEQ ID NO. 21)
AAV7	EKQTGVDFAVDSQGVYSEPRPIGTRYLTRNL	737 (SEQ ID NO. 22)
AAV8	YKSTSVDFAVNTEGVYSEPRPIGTRYLTRNL	738 (SEQ ID NO. 23)
hu31	YKSNNVEFAVSTEGVYSEPRPIGTRYLTRNL	736 (SEQ ID NO. 24)
hu32	YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL	736 (SEQ ID NO. 25)
AAV9	YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL	736 (SEQ ID NO. 26)
SUBS	GQQVSLWTPDAA-K-RTT-A-----HP-	(SEQ ID NO:48)
	NDPQF D SSN E T H	(SEQ ID NO:49)
	A TG NQ L	(SEQ ID NO:50)
	E A T	(SEQ ID NO:51)
		(SEQ ID NO:52)
		(SEQ ID NO:53)

FIG. 6 continued



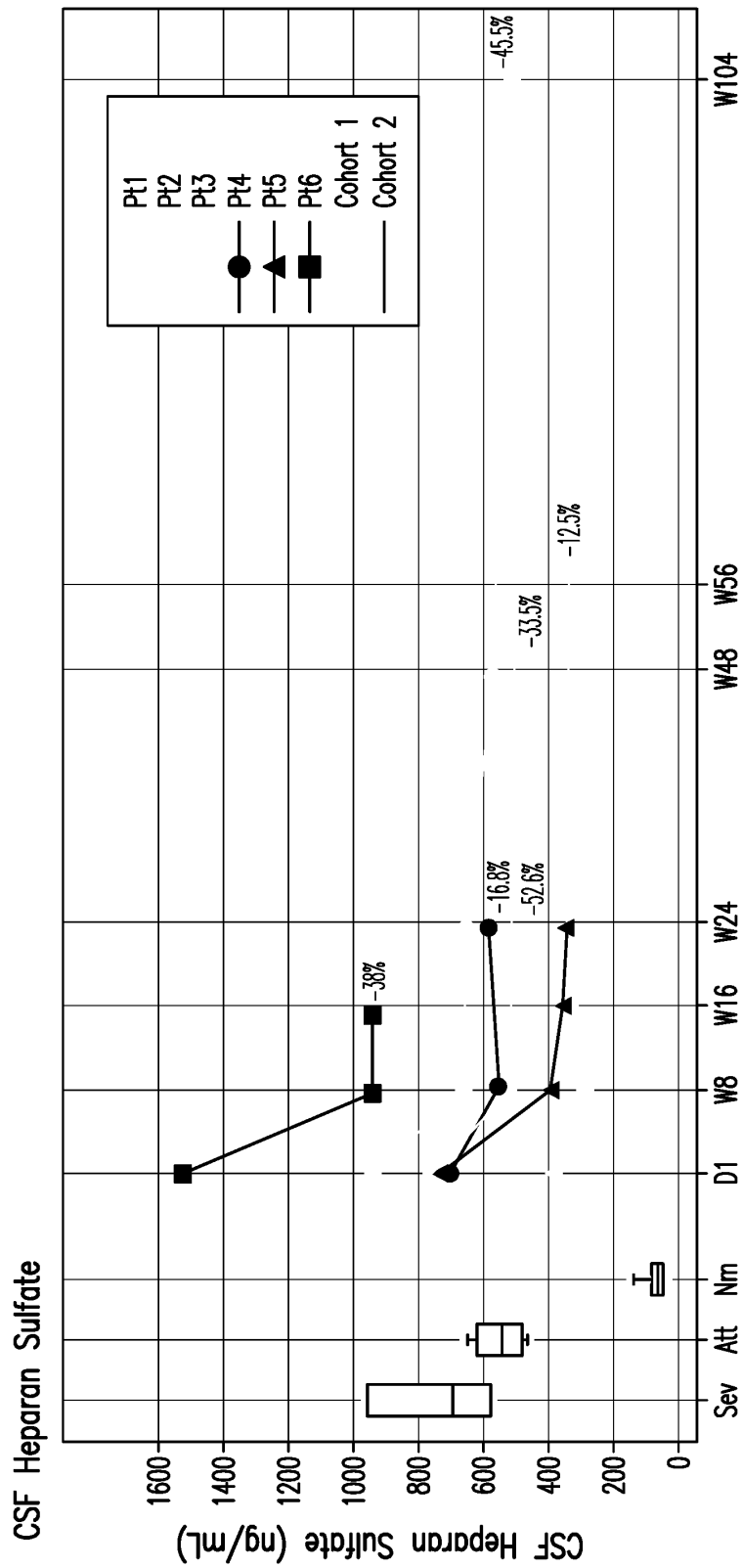


FIG. 8

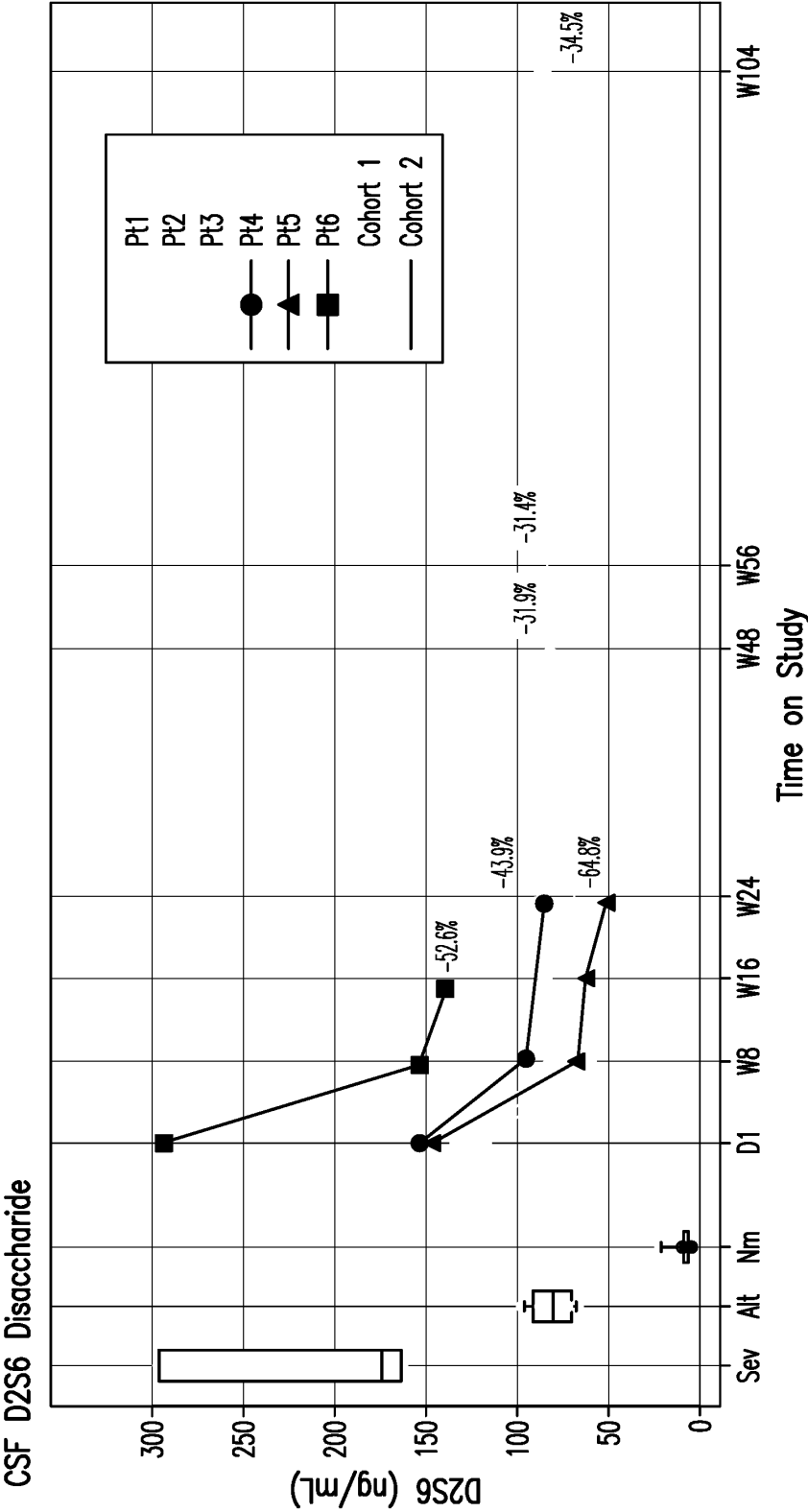


FIG. 9

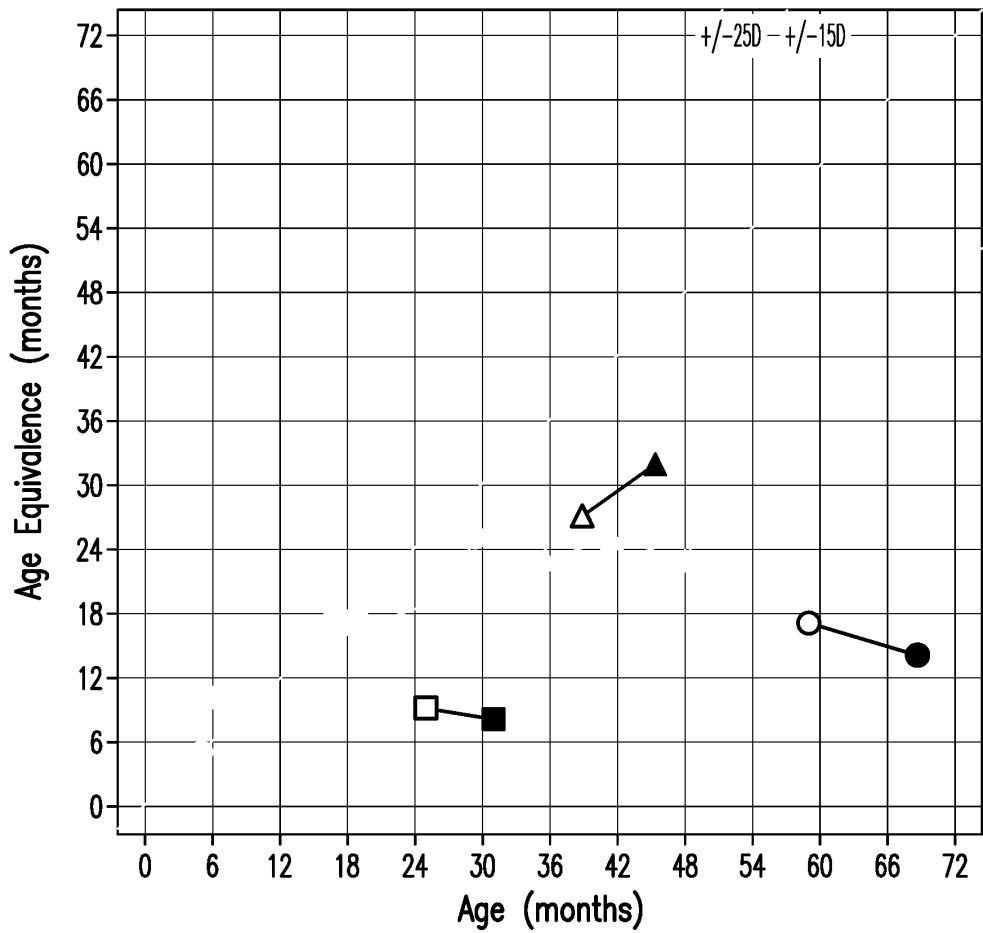
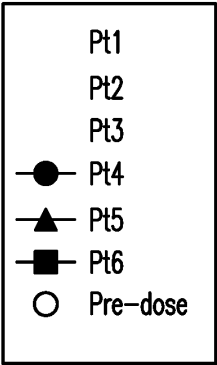


FIG. 10A



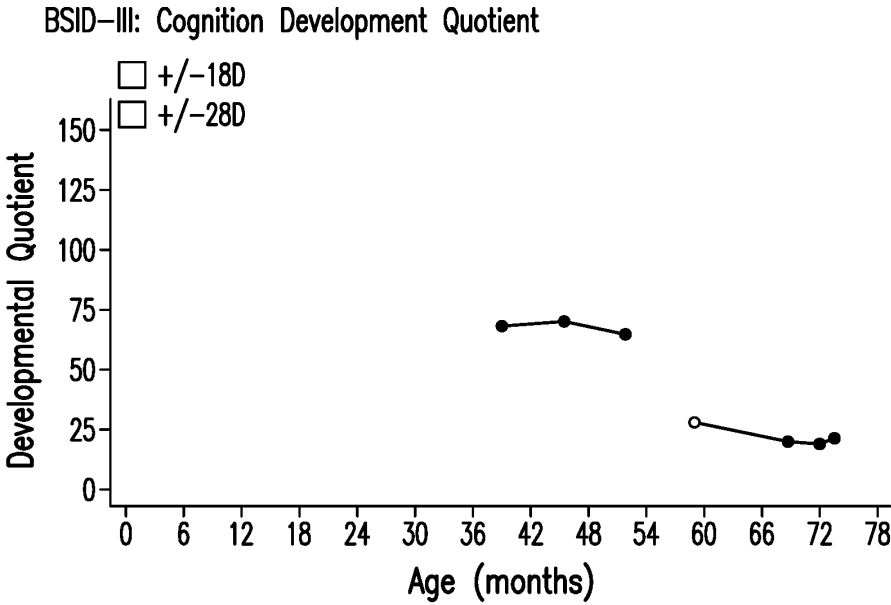


FIG. 10B

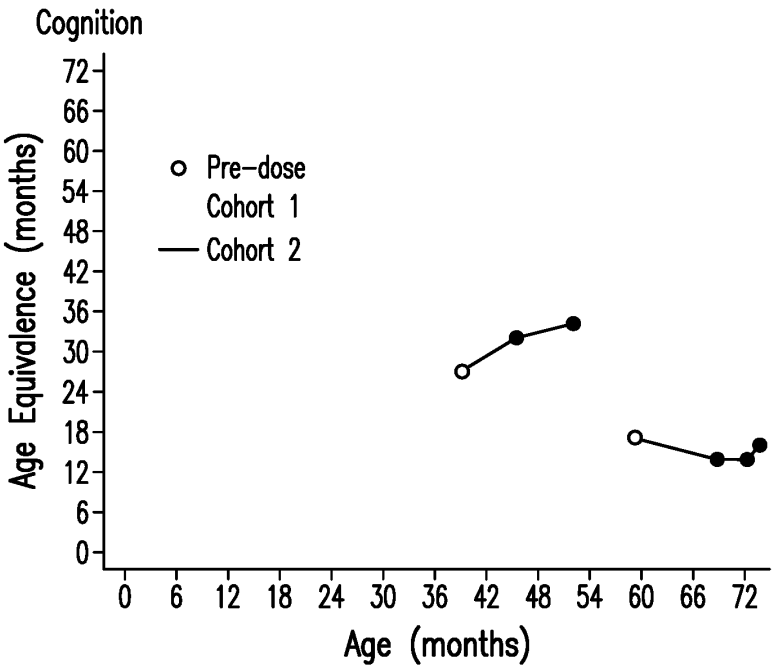


FIG. 10C

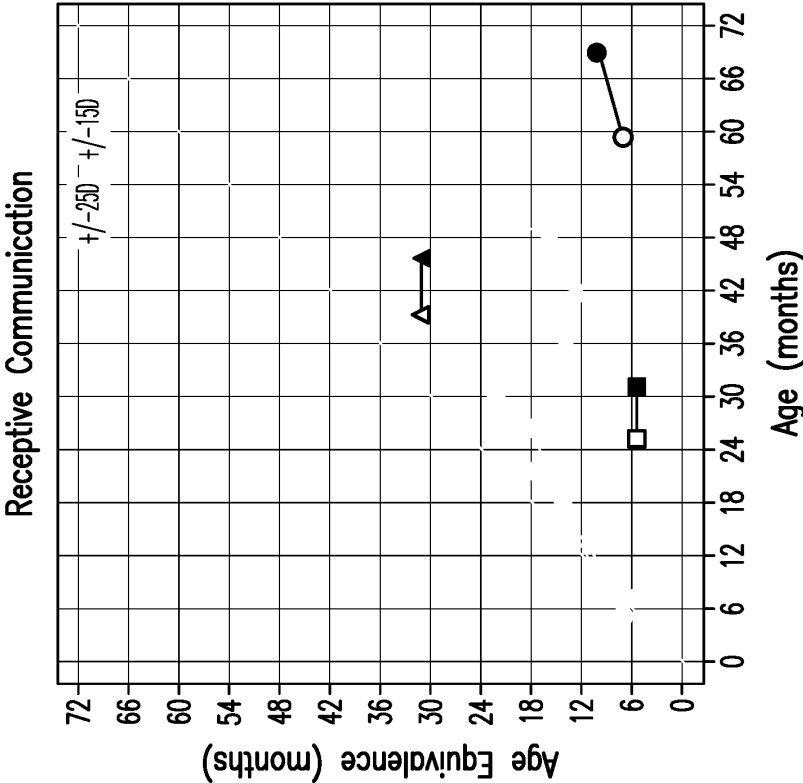


FIG. 11B

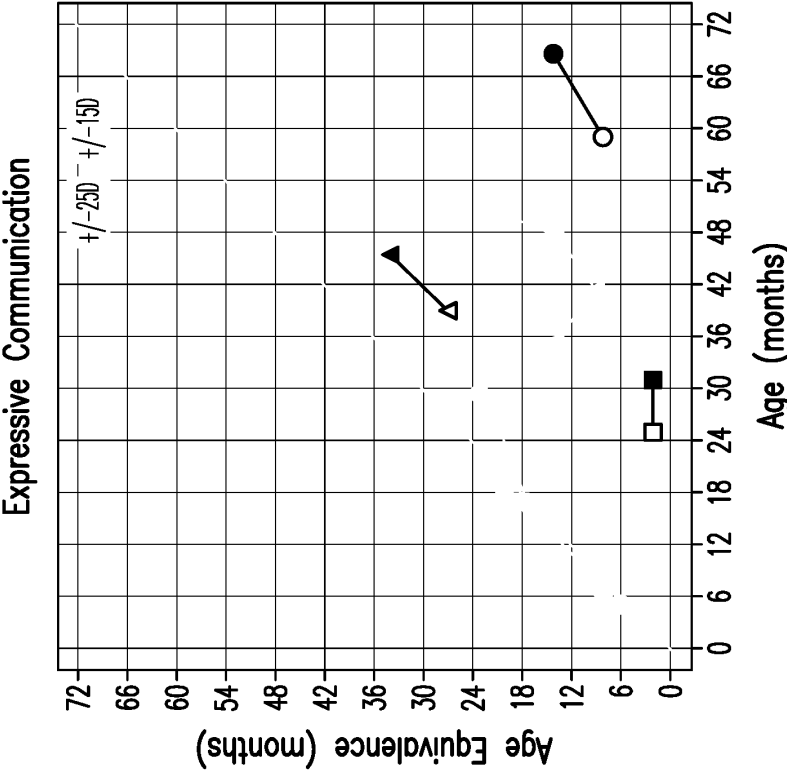
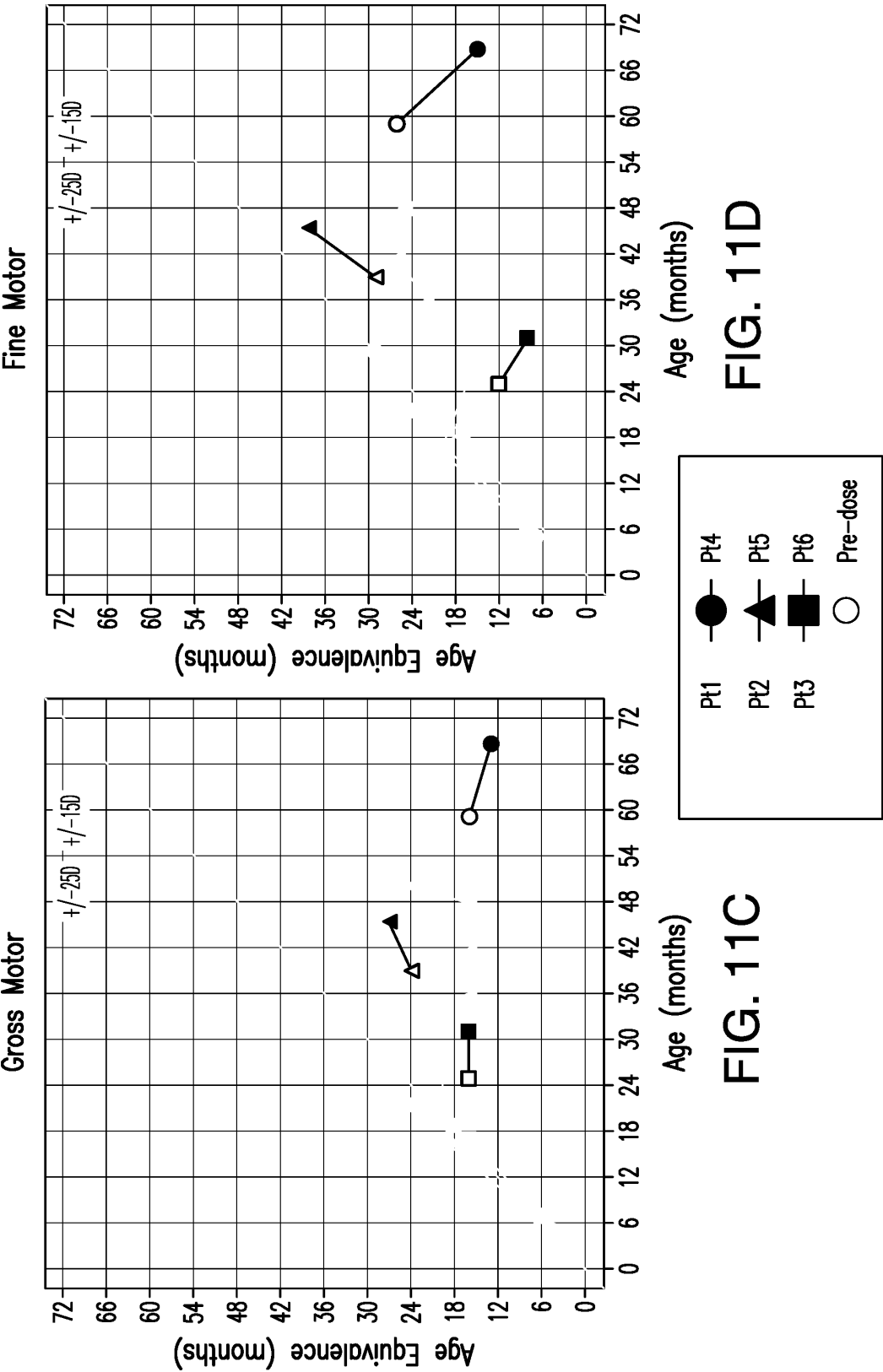
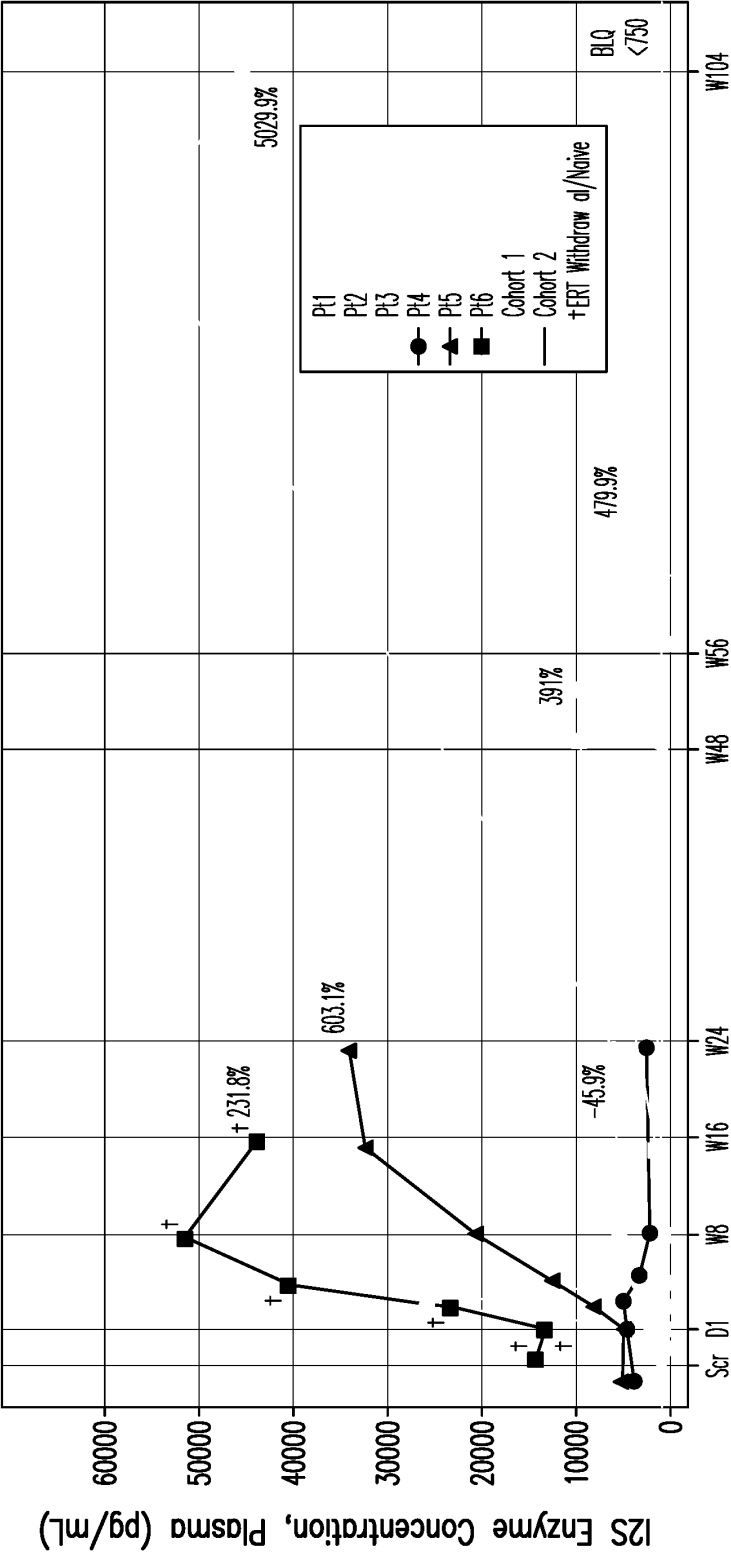


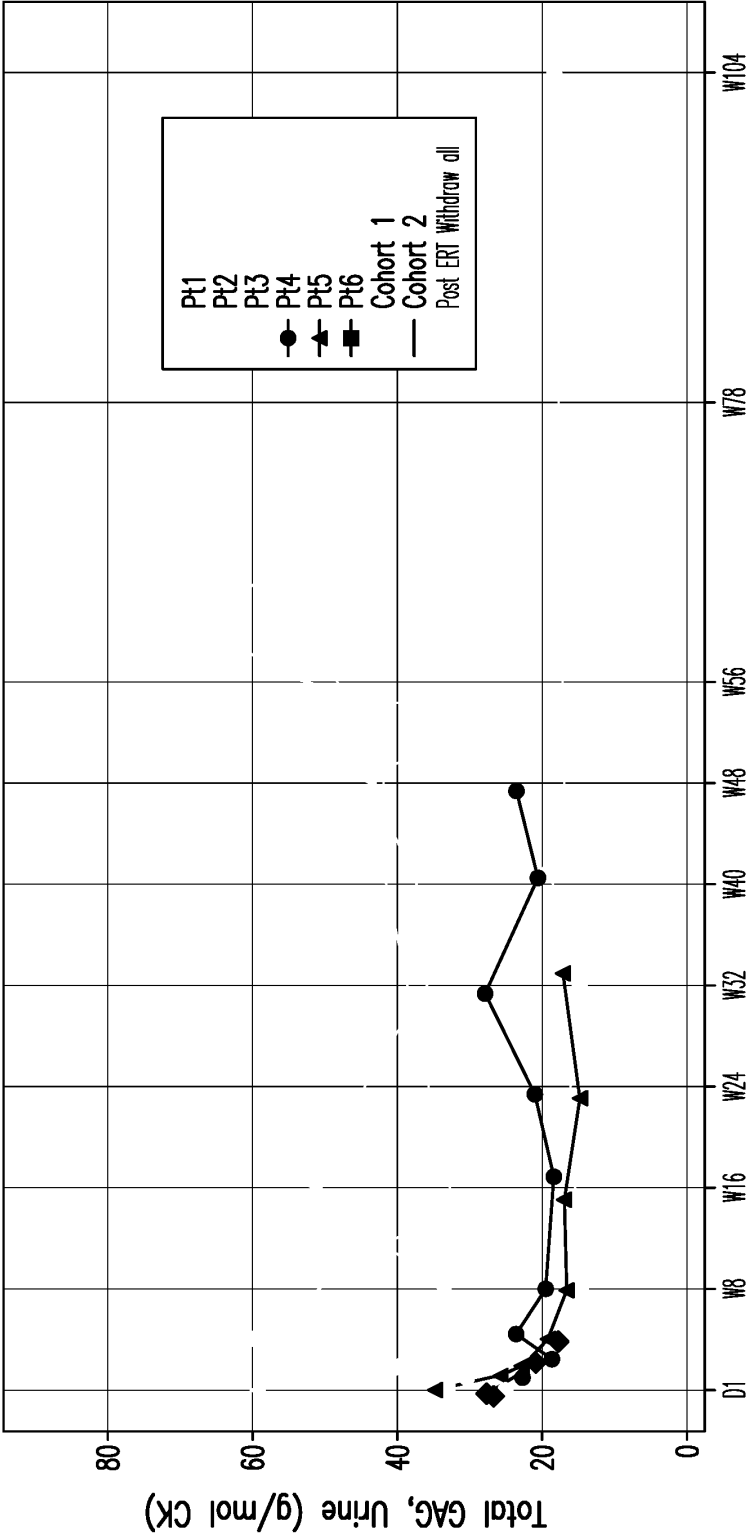
FIG. 11A





Time on Study

FIG. 12



Time on Study

FIG. 13

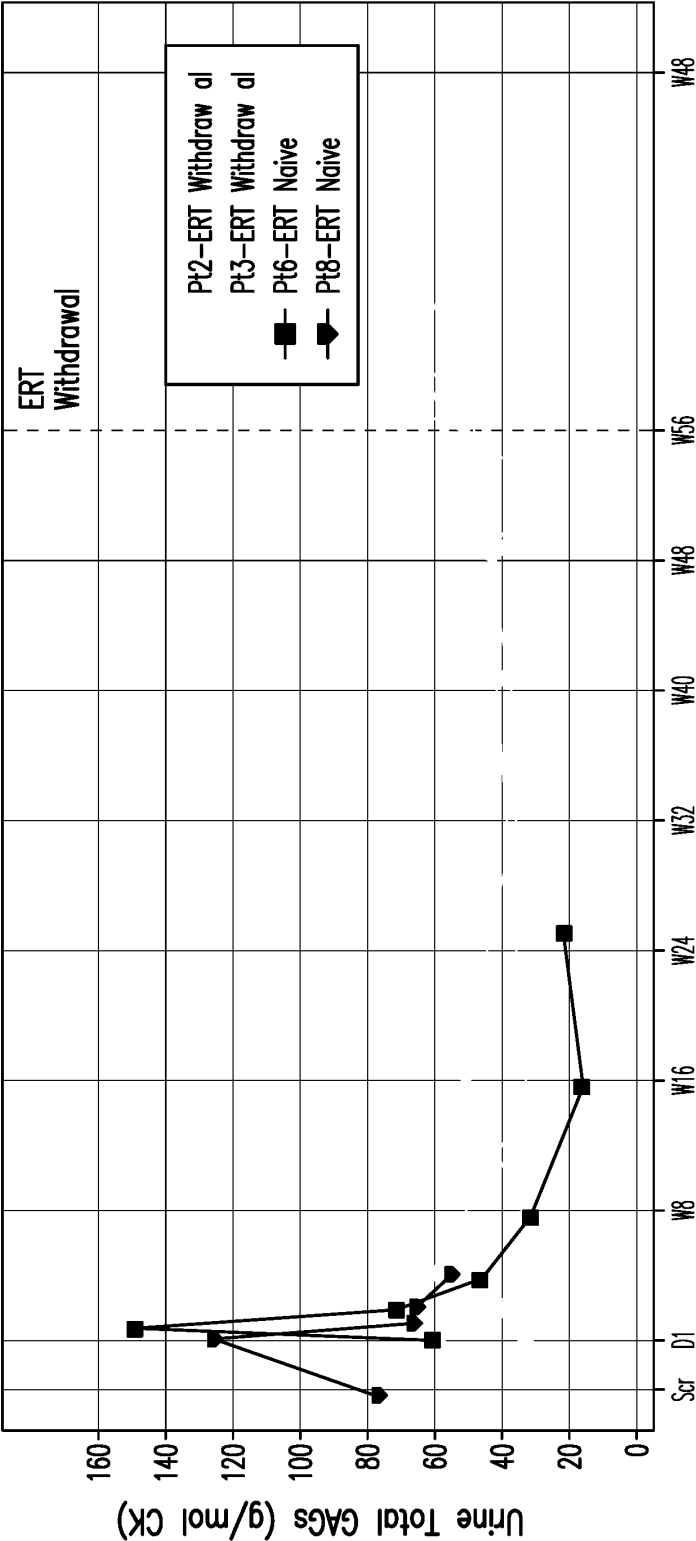


FIG. 14

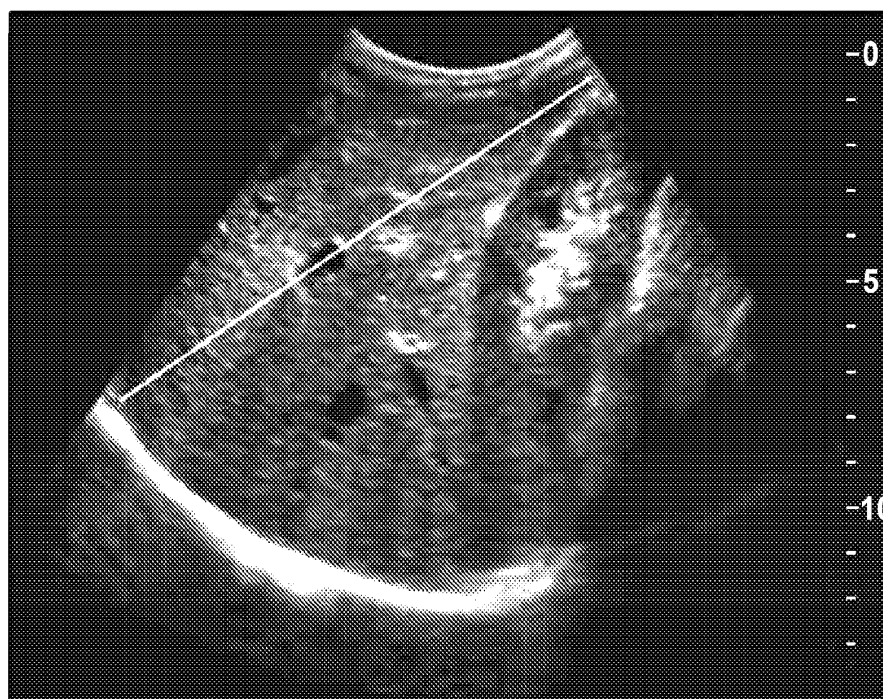


FIG. 15

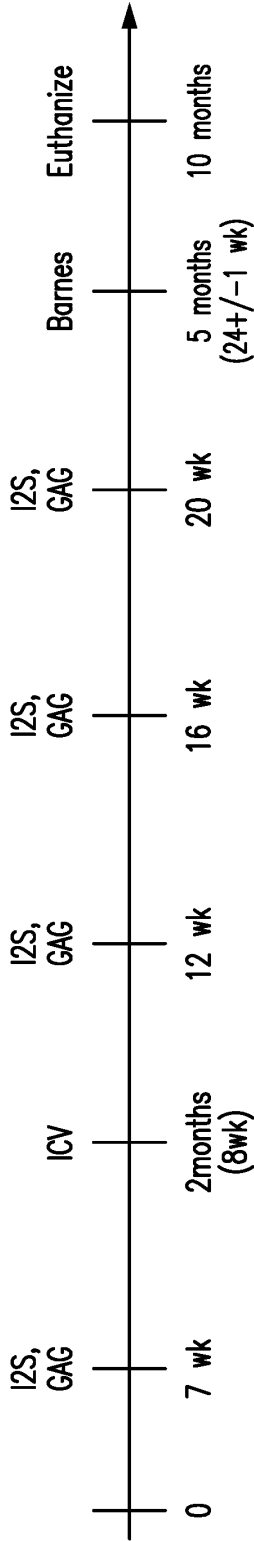


FIG. 16

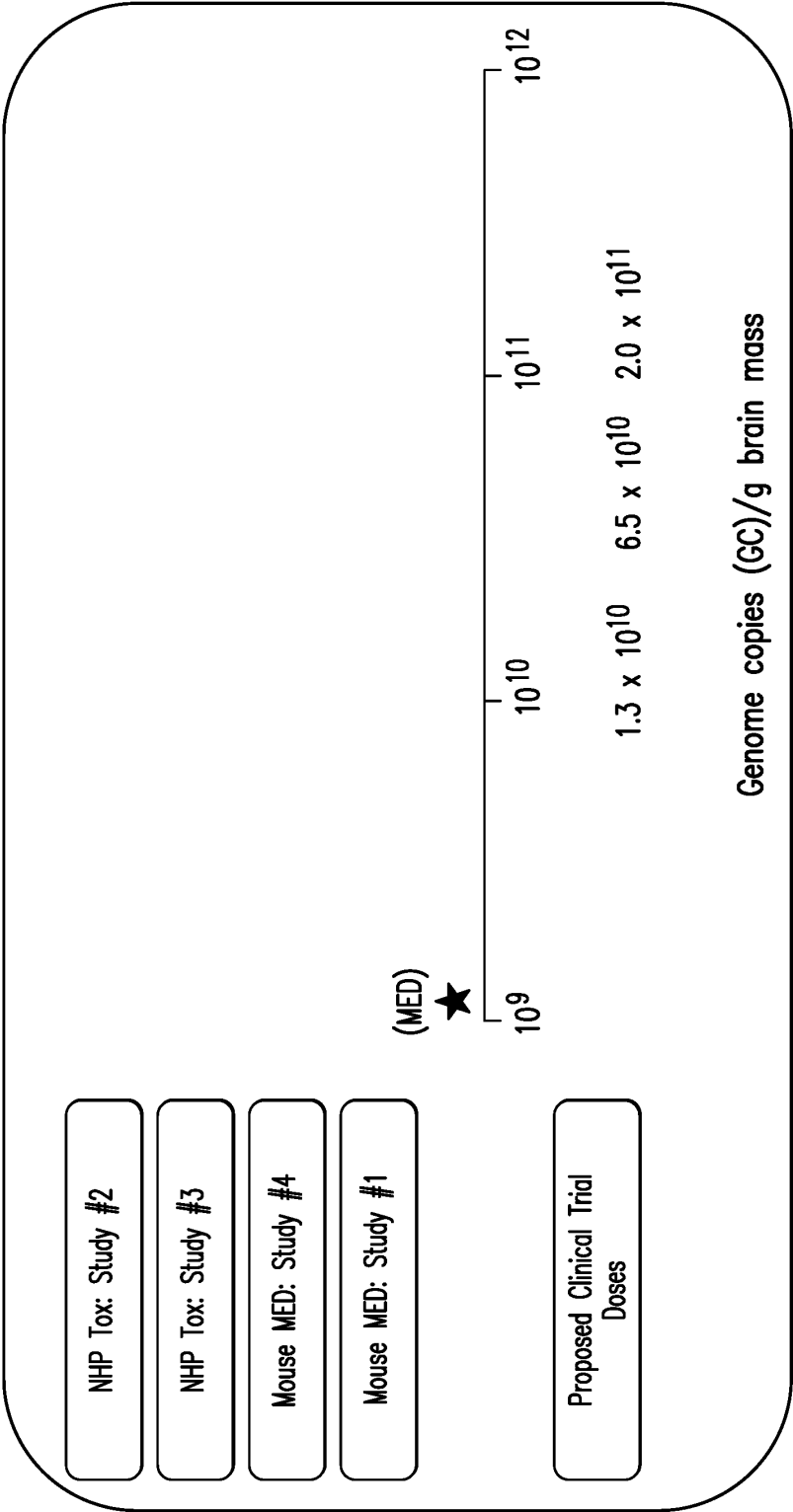


FIG. 17

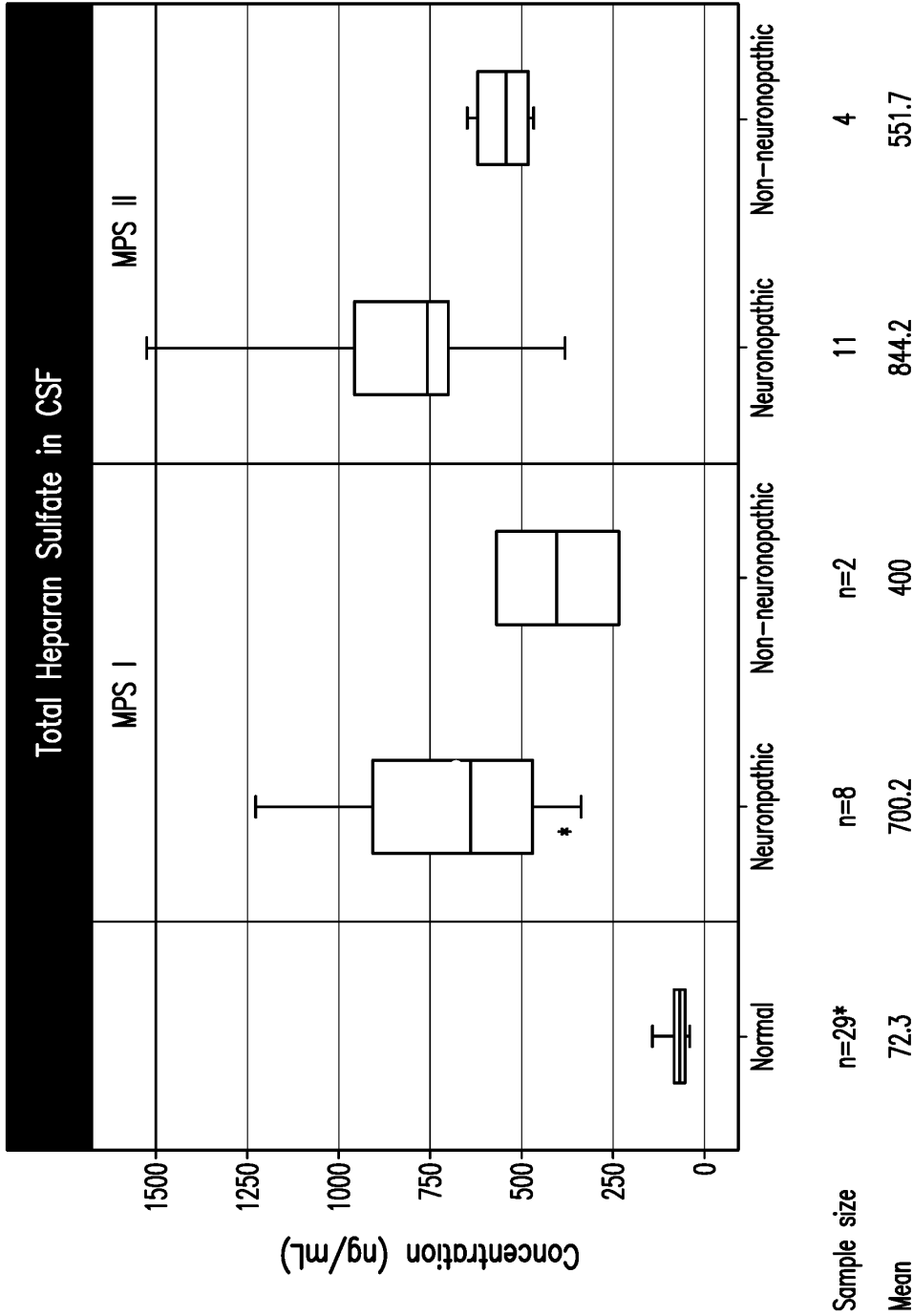


FIG. 18

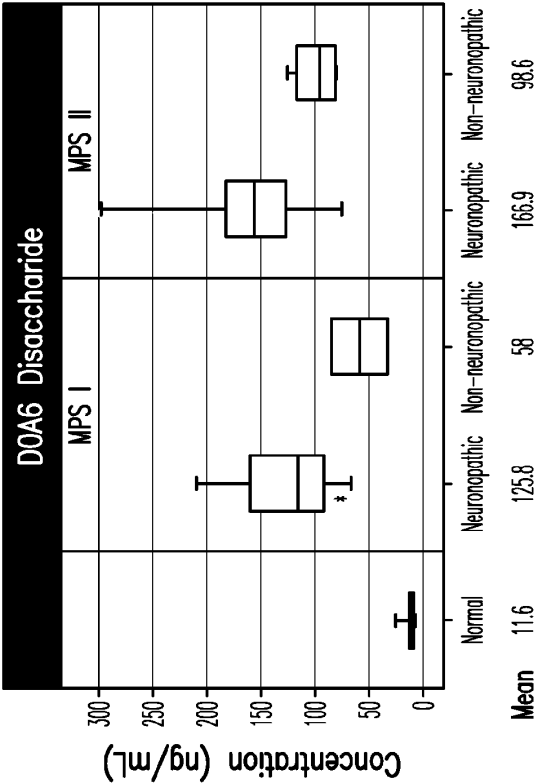


FIG. 19B

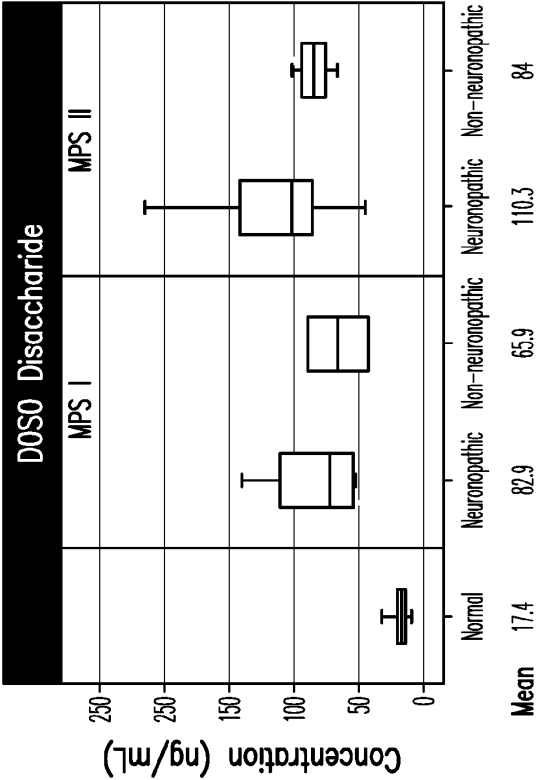


FIG. 19A

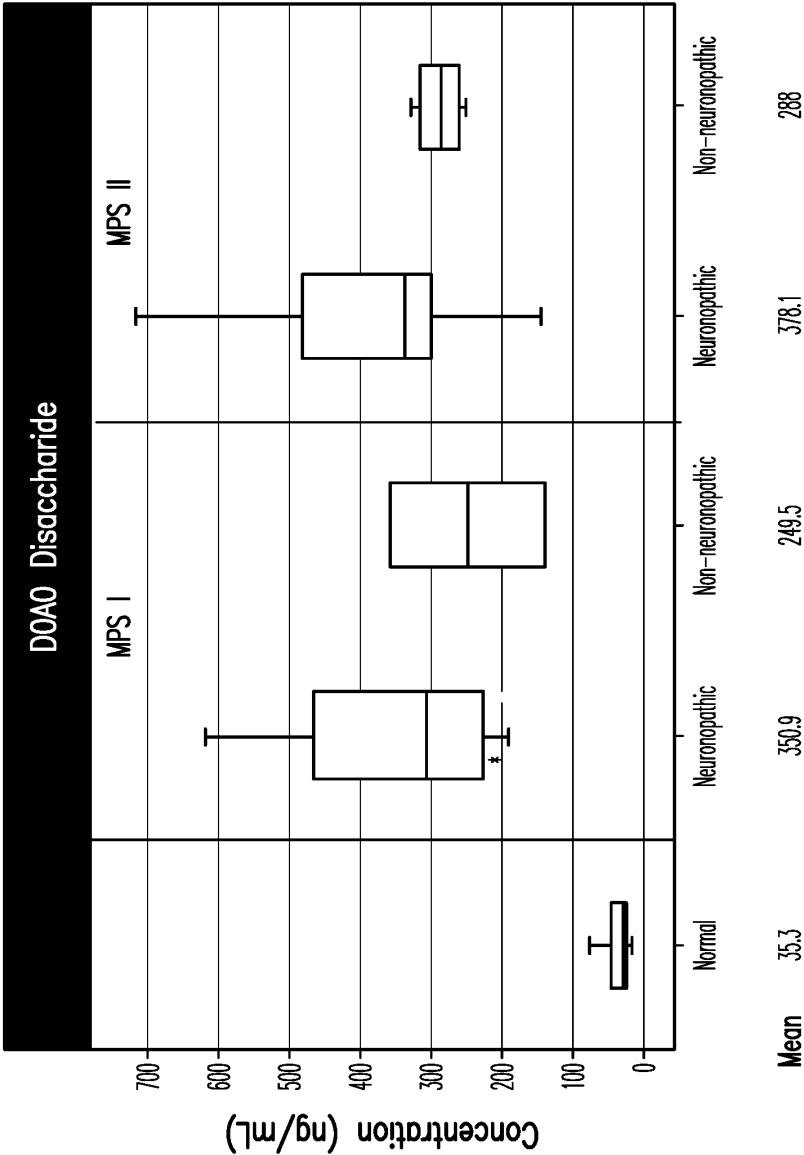


FIG. 19C

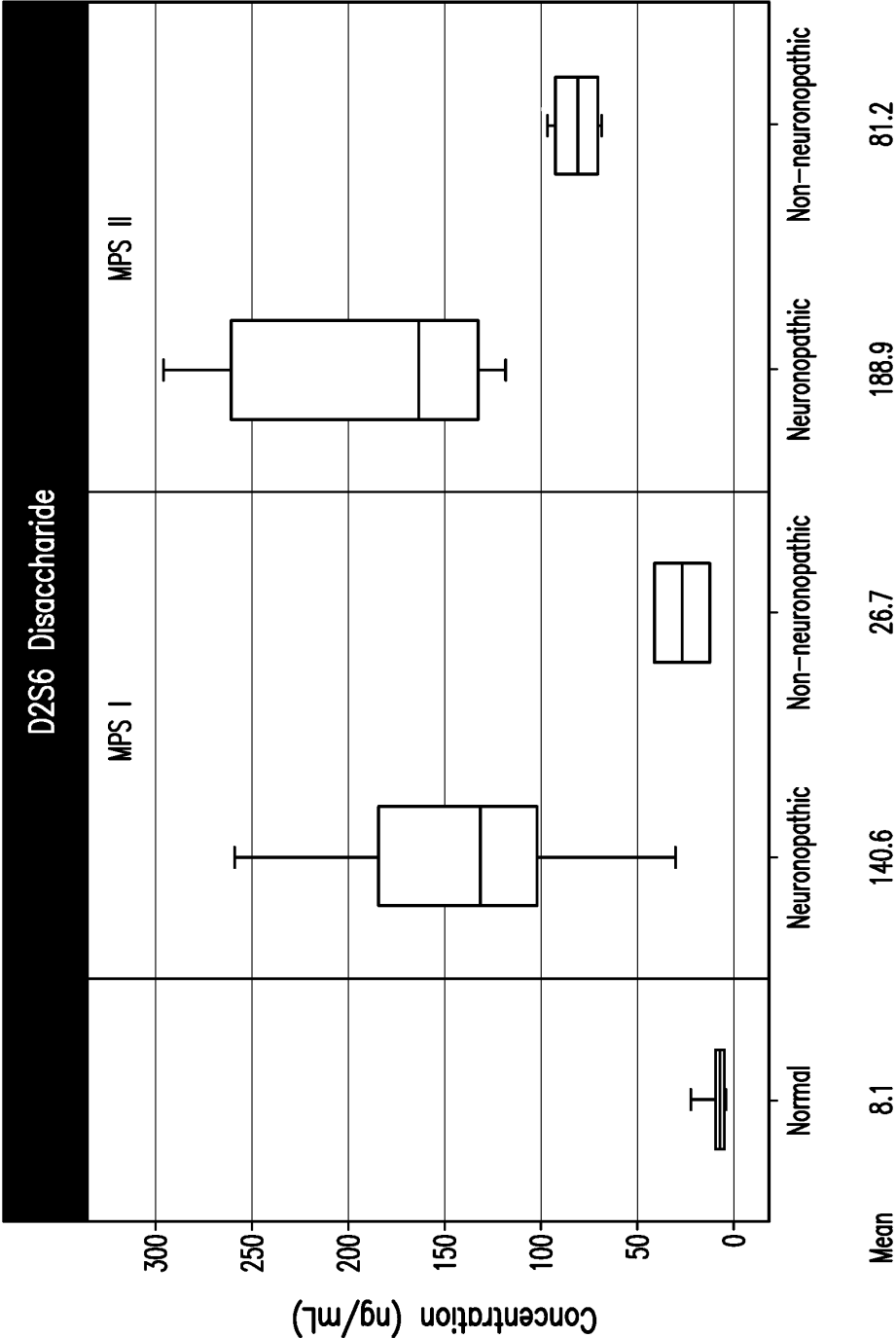


FIG. 20

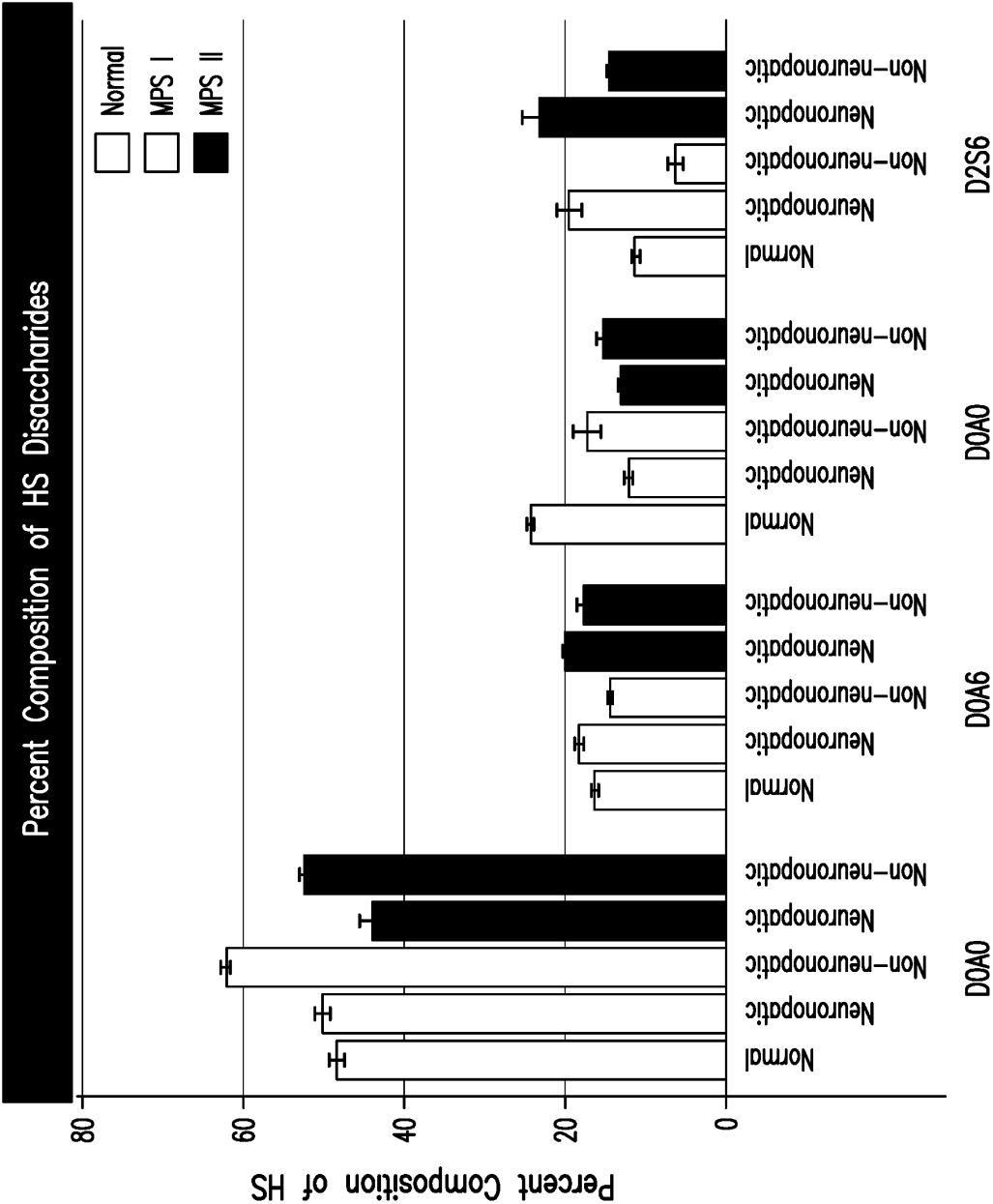


FIG. 21

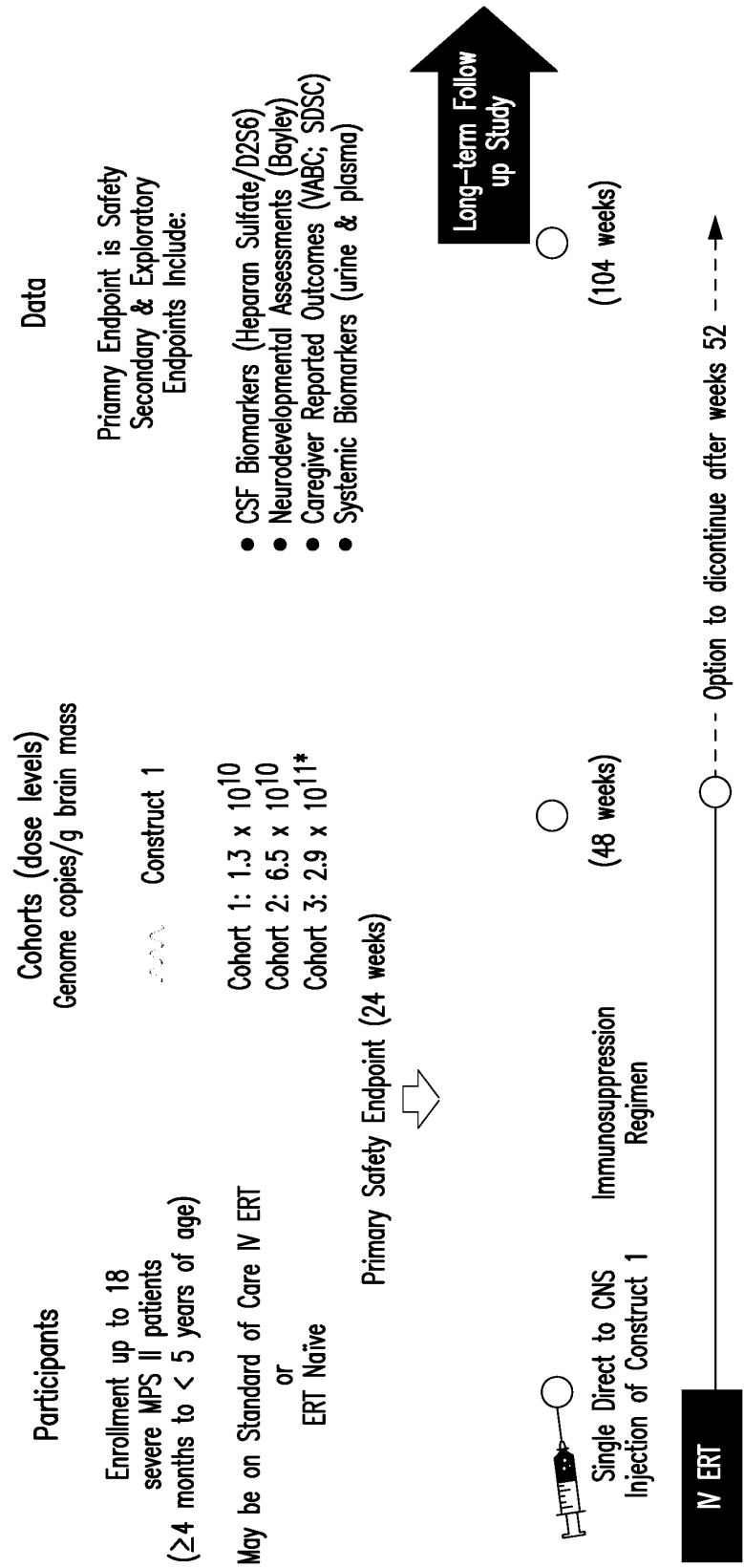


FIG. 22

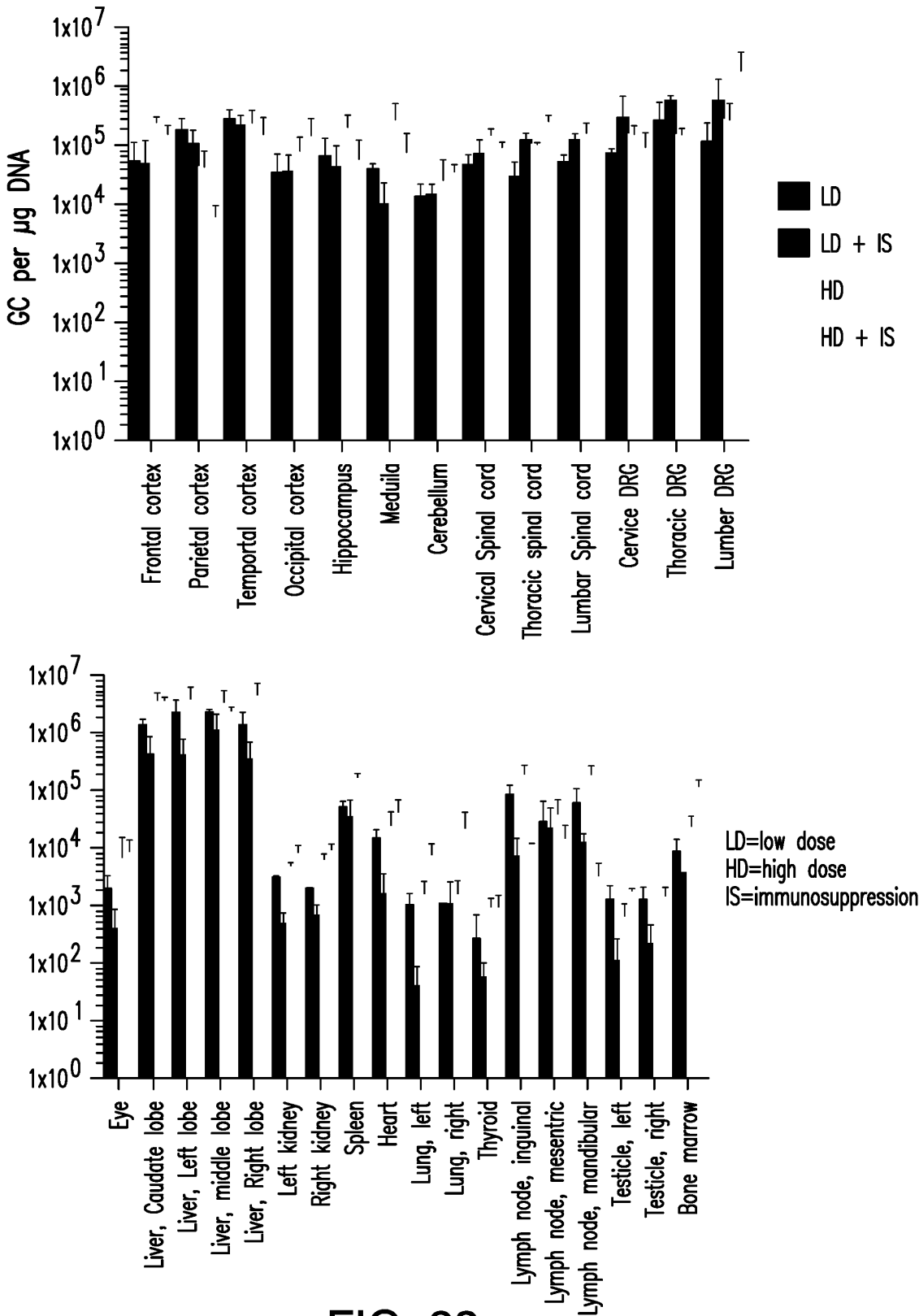


FIG. 23

Median Reductions

Cohort	Week 8	Week 24
1	-29.5% n=3	-20.6% n=2
2	-42.3% n=6	-36.4% n=5
3	-67.3% n=2	-63.9% n=1

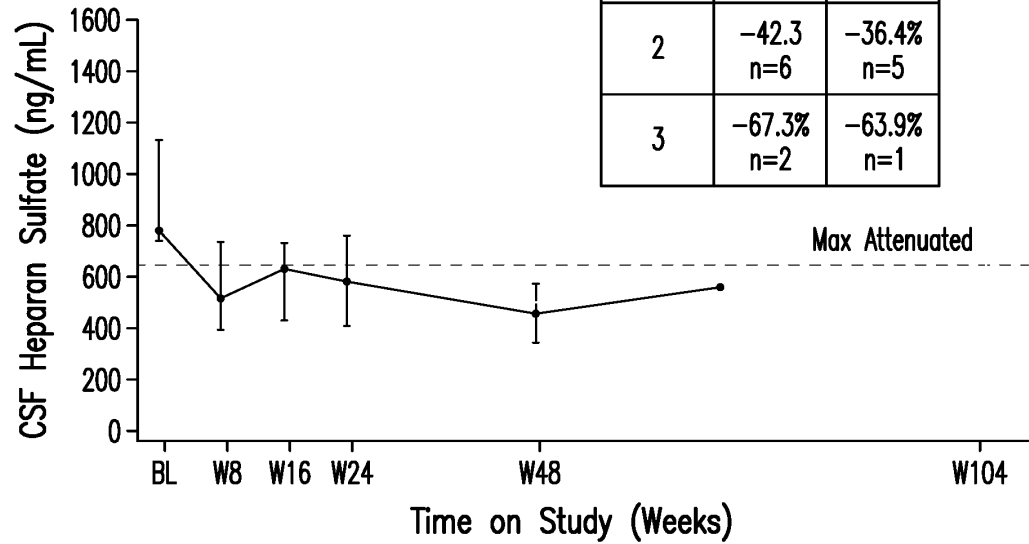


FIG. 24A

Individual Participants

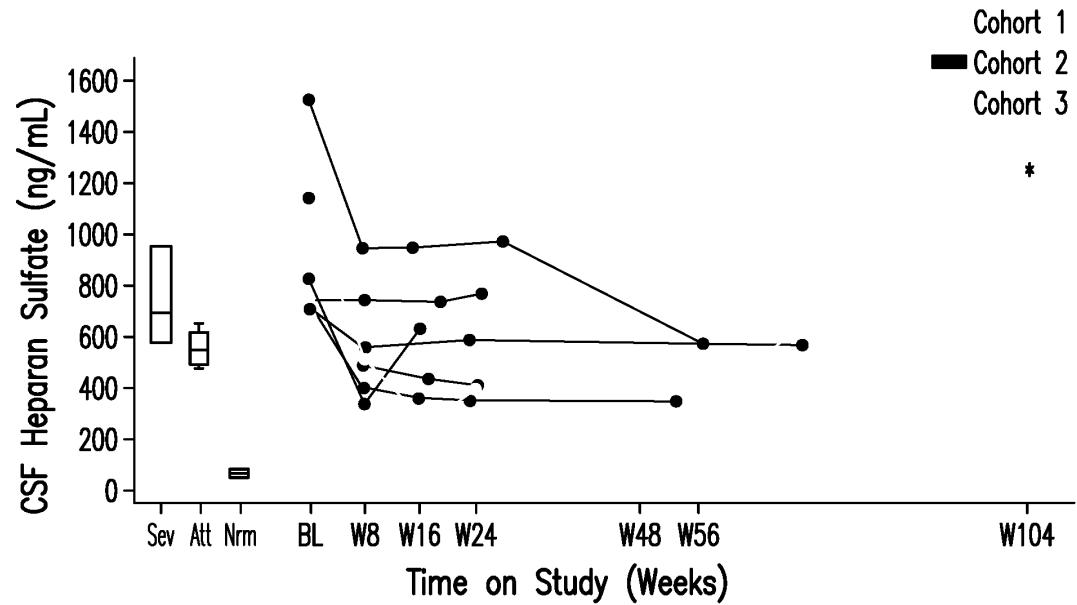


FIG. 24B

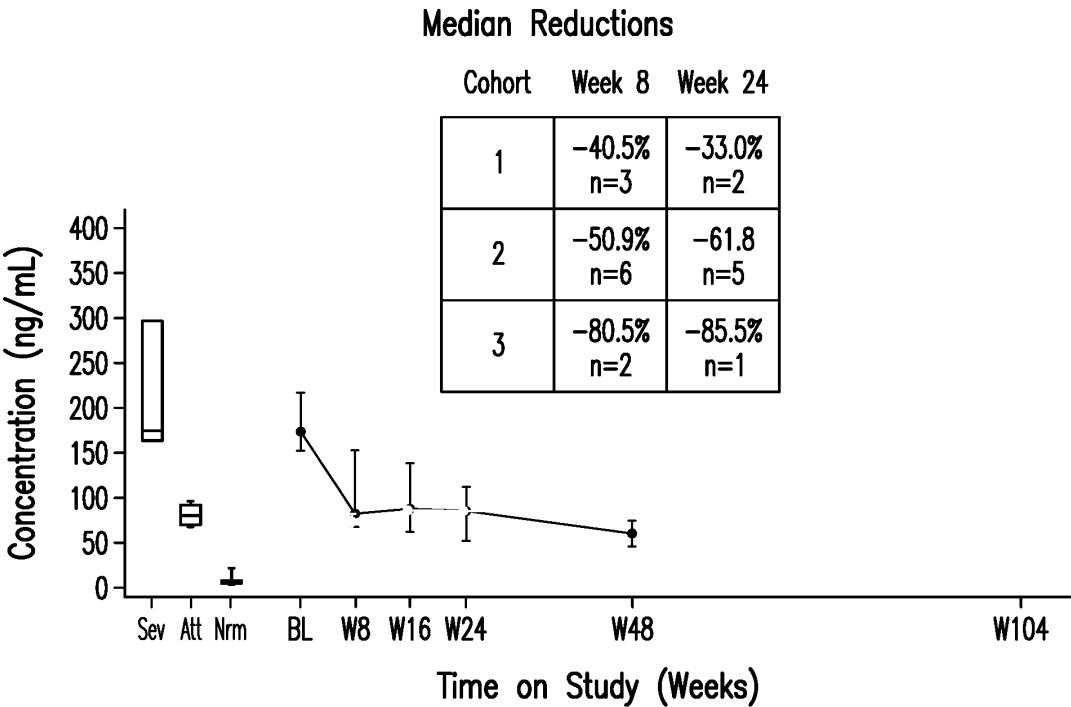


FIG. 25A

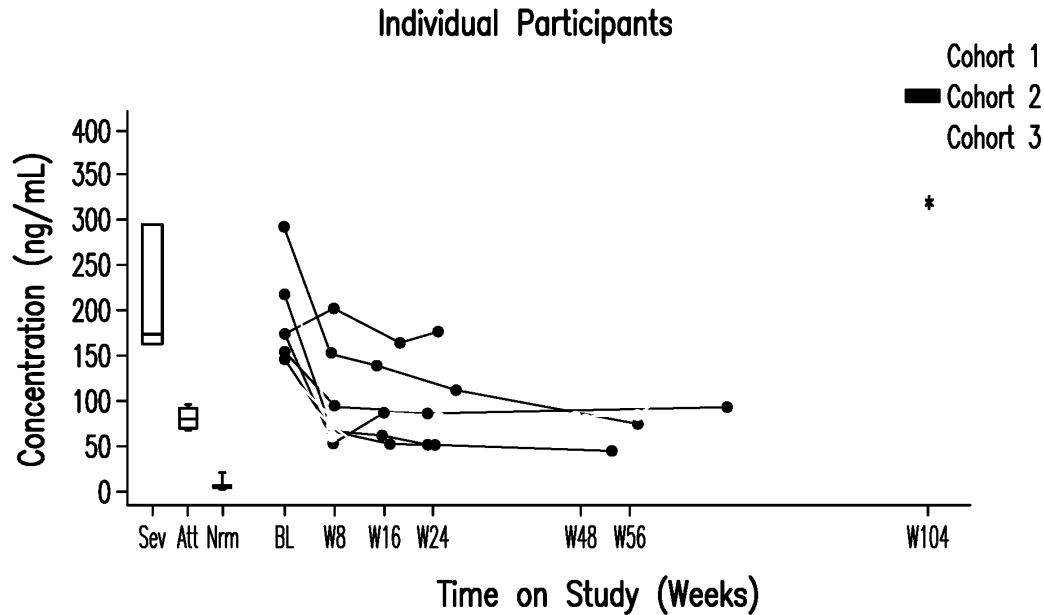
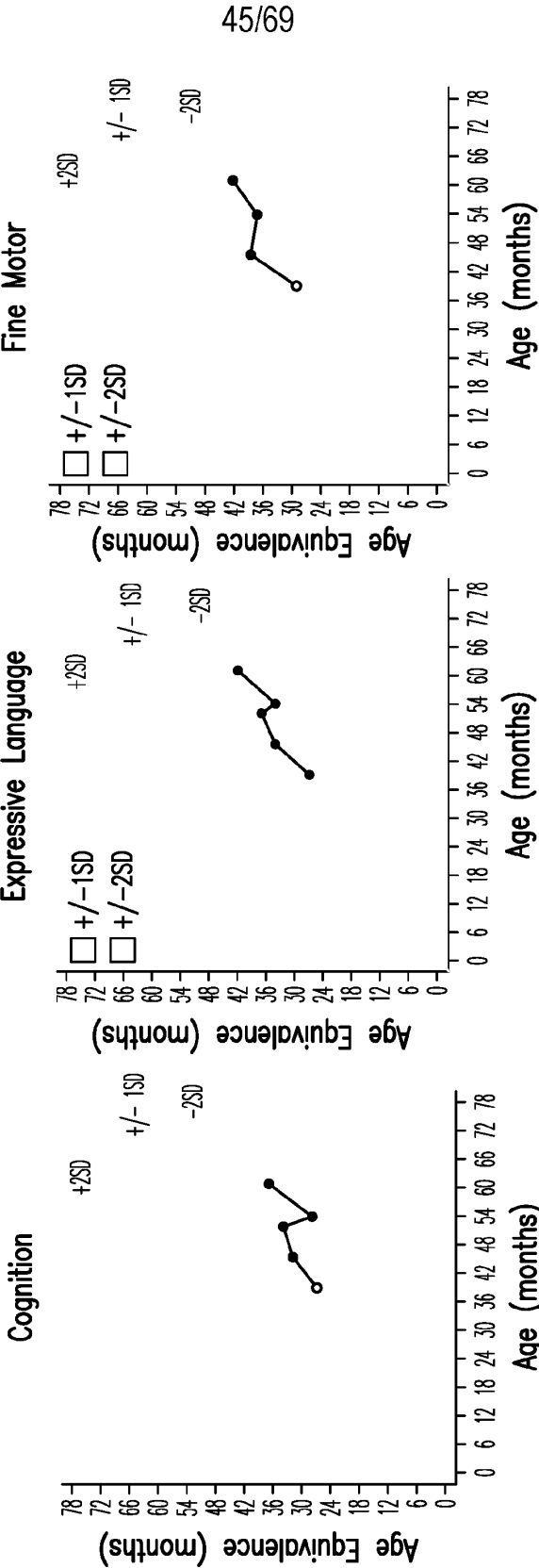


FIG. 25B

Cohort 1
— Cohort 2
○ Pre-dose



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FIG. 26C

FIG. 26B

FIG. 26A

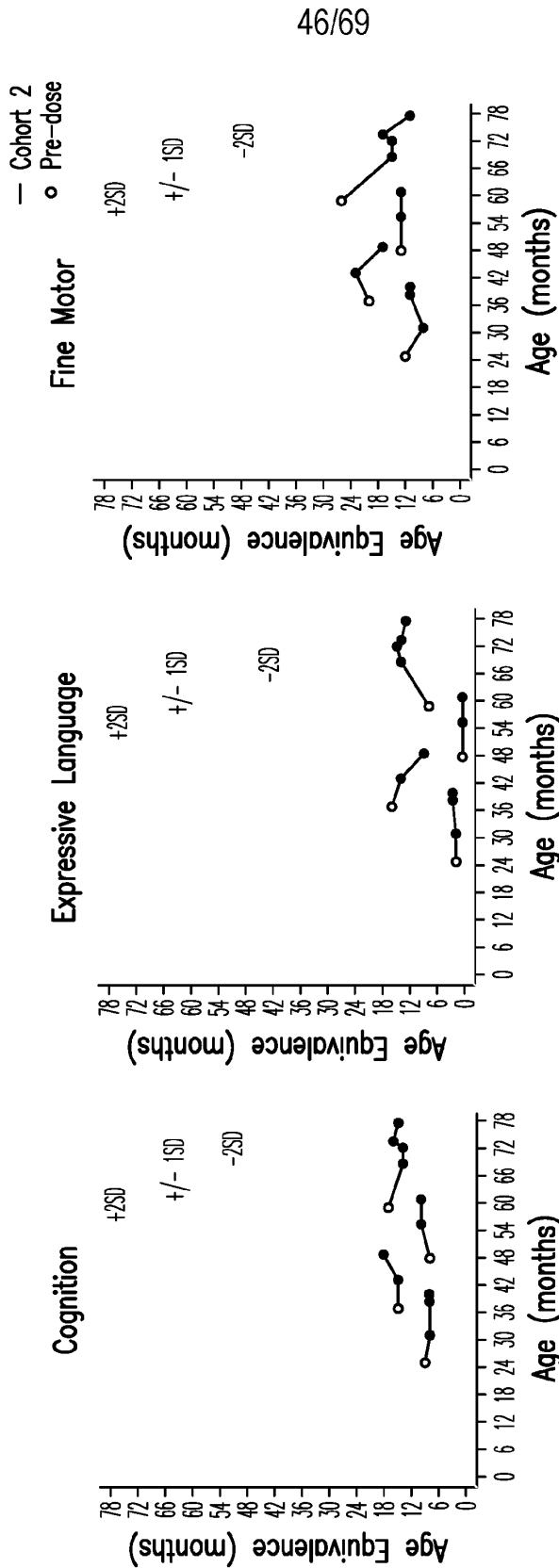


FIG. 27B

FIG. 27B

FIG. 27A

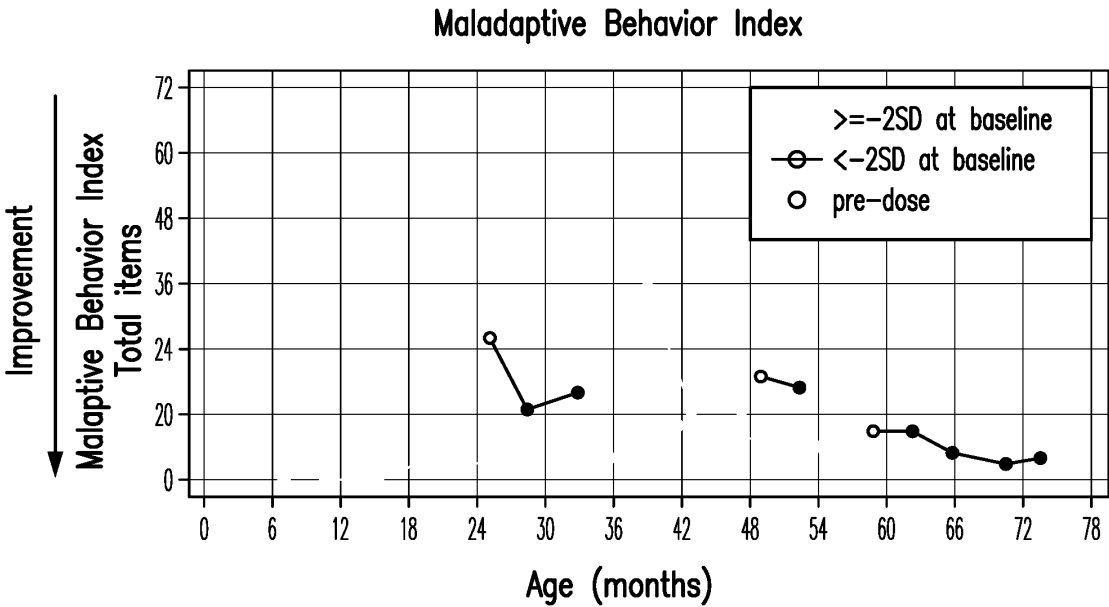


FIG. 28A

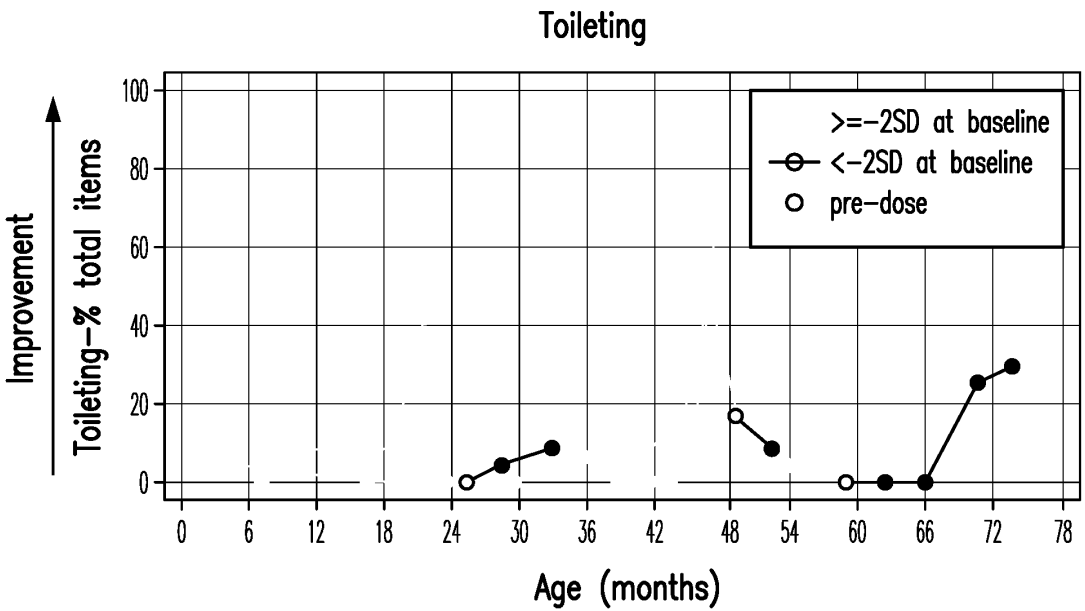


FIG. 28B

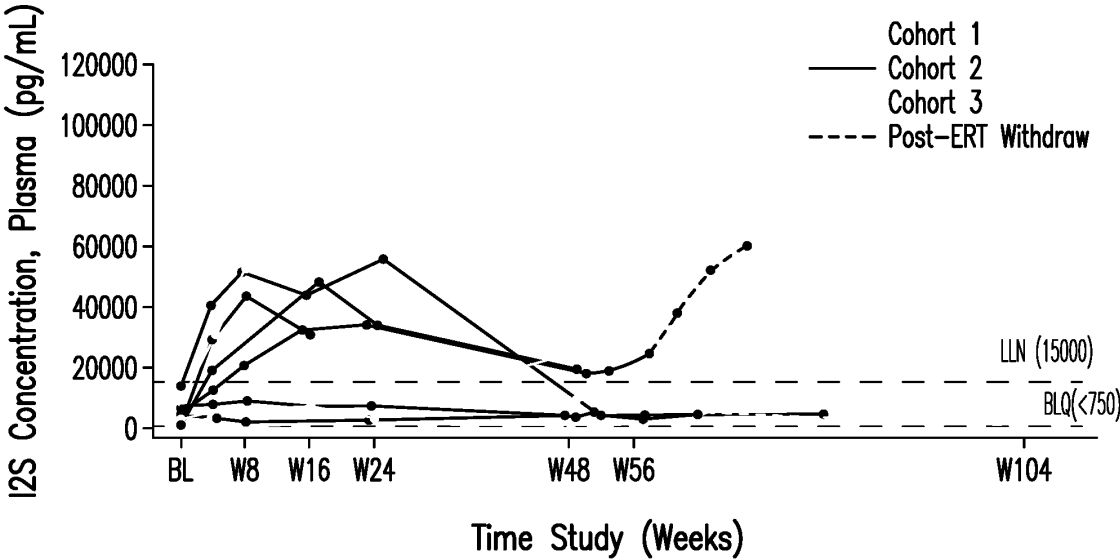


FIG. 29A

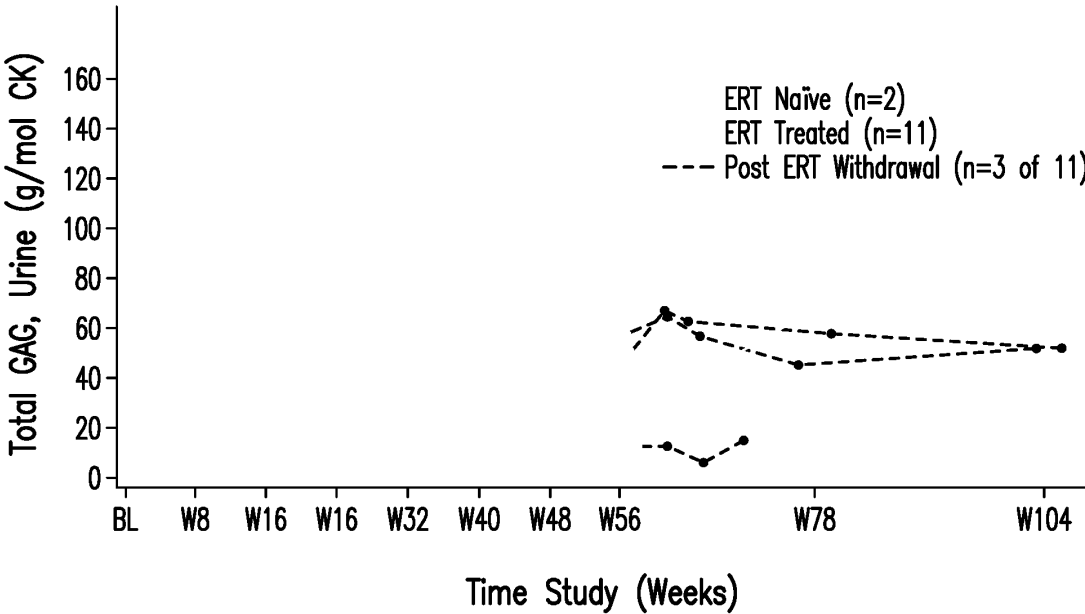


FIG. 29B

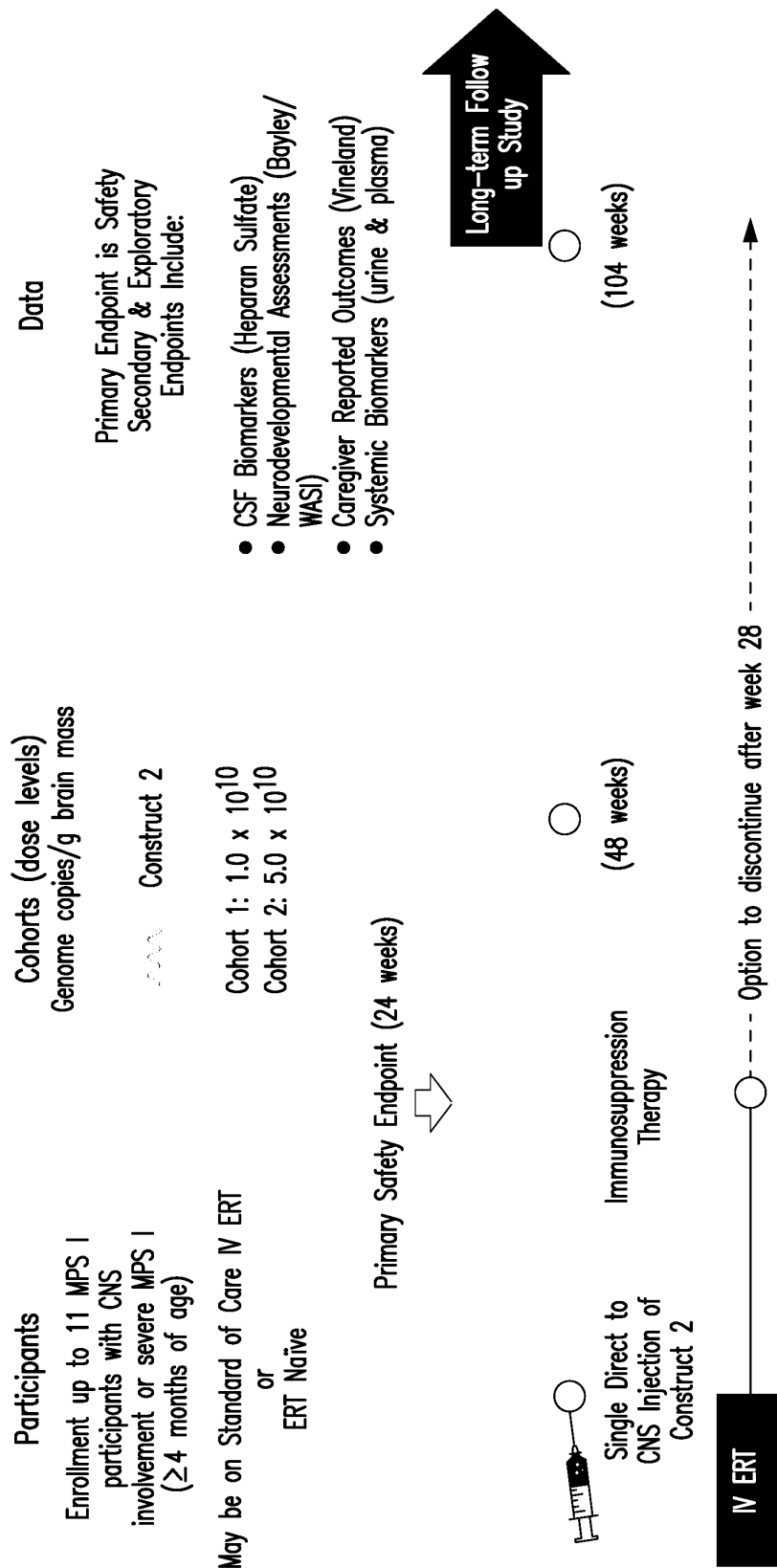


FIG. 30

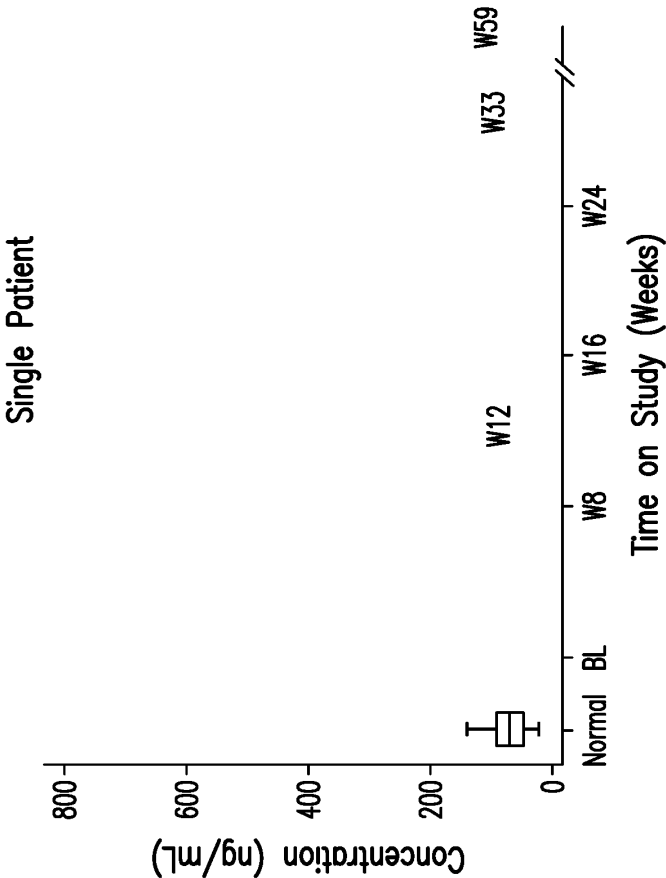


FIG. 31B

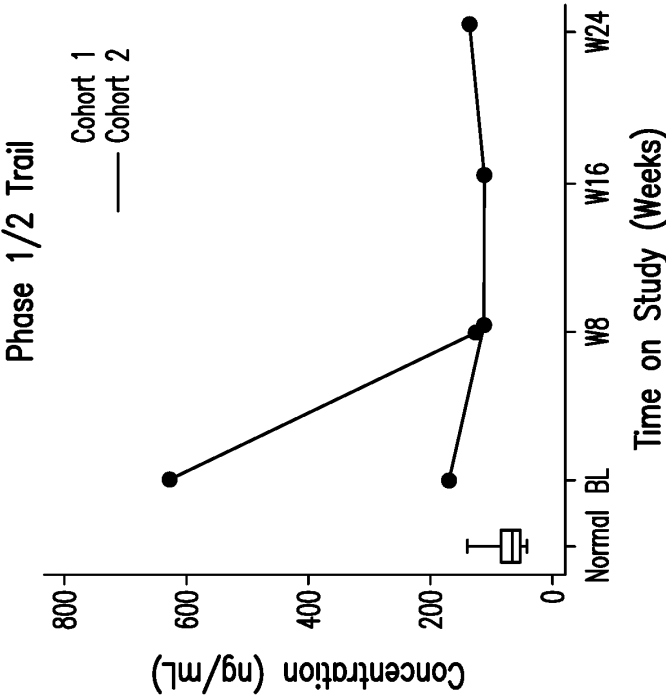


FIG. 31A

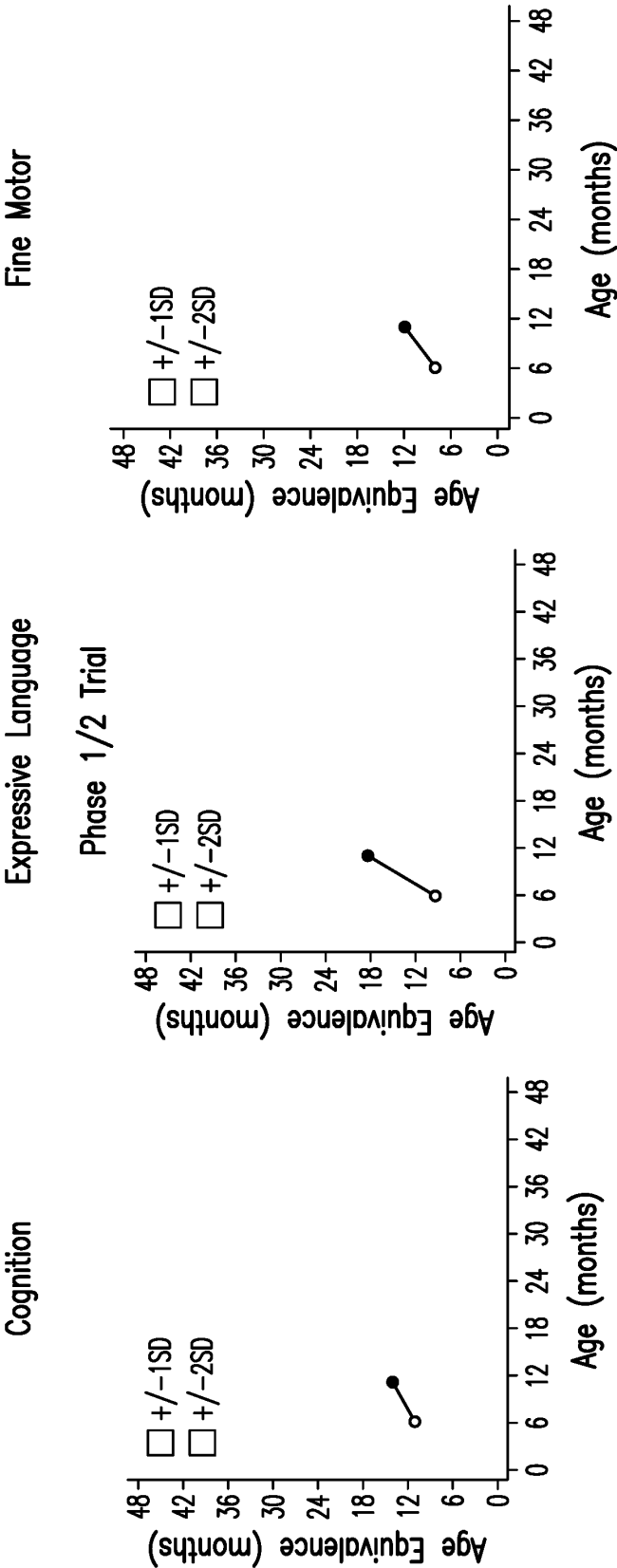


FIG. 32C

FIG. 32B

FIG. 32A

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Single Patient

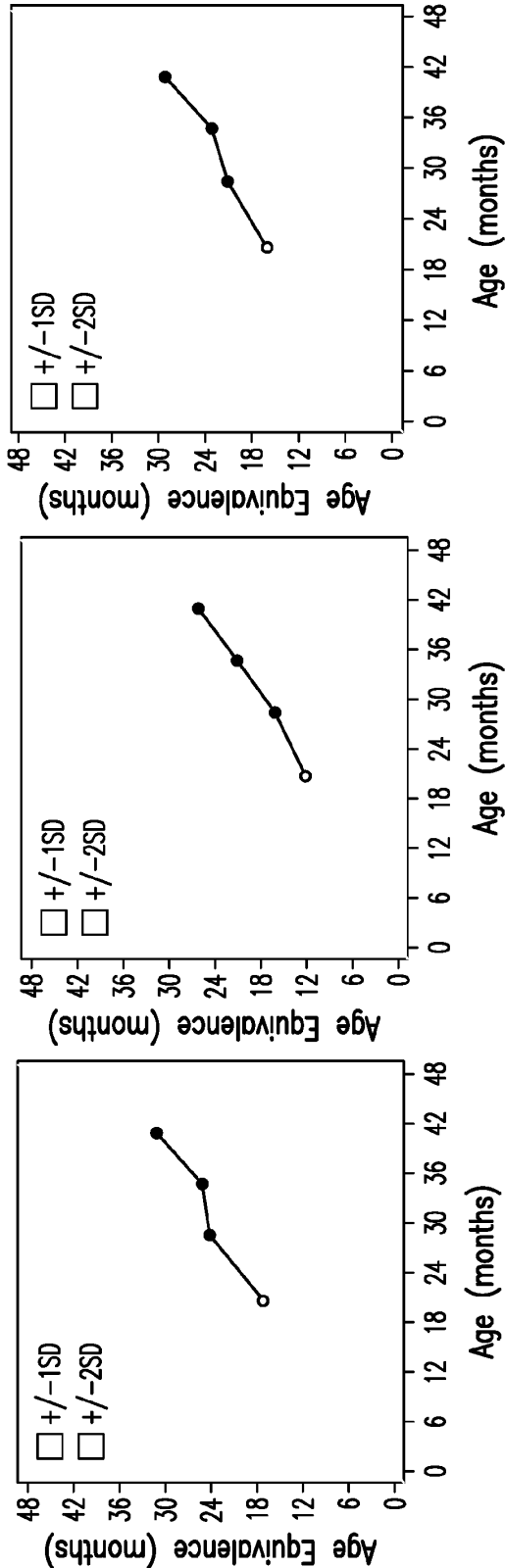


FIG. 32D

FIG. 32E

FIG. 32F

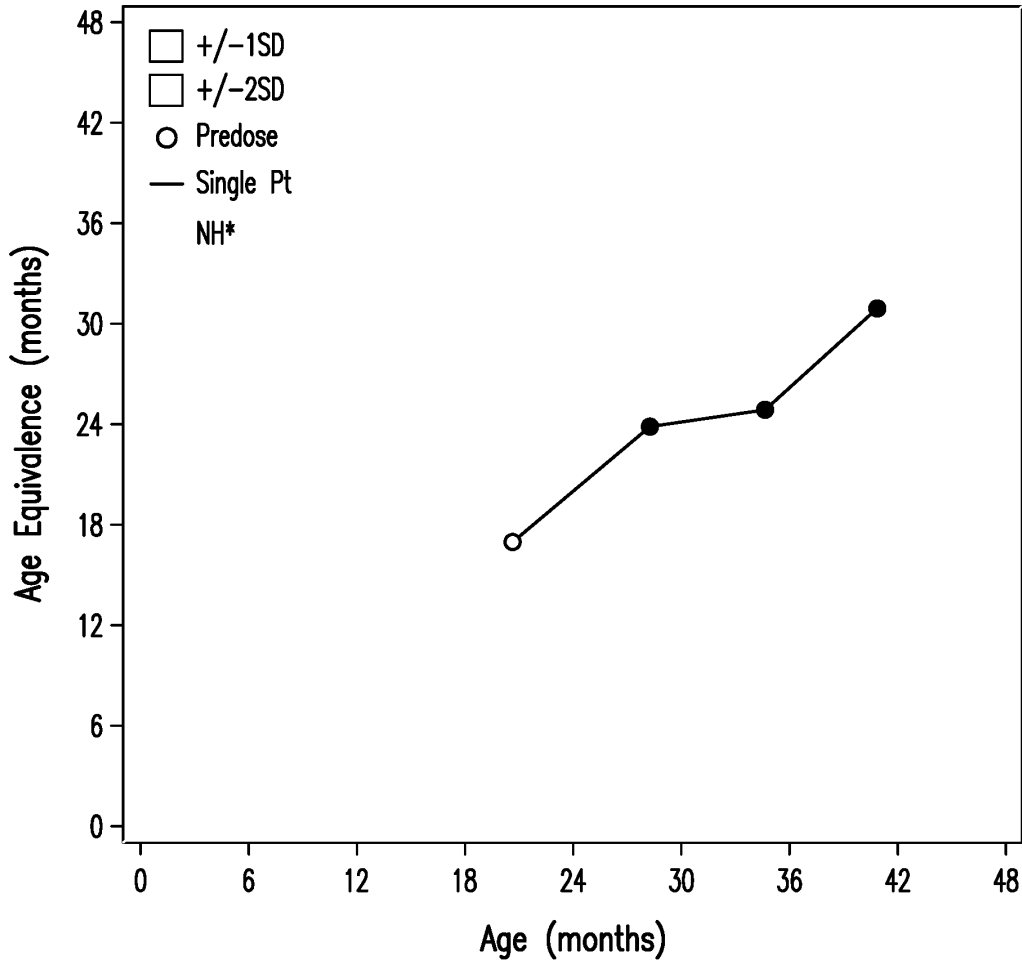


FIG. 33

VABS-III Age Equivalent Scores (year:month)		
	Baseline Chronological Age 13y	Week 52 Chronological Age 14y
Personal (dressing, feeding, toileting, and washing/hygiene)	4:1	7:10
Domestic	7:7	6:7
Community	7:4	6:10
Interpersonal Relationships	5:10	7:4
Play and Leisure	8:1	8:1
Coping Skill	3:4	9:10
Adaptive Behavior	6:3	7:10
Fine Motor	5:7	6:4
Gross Motor	4:0	4:6

WASI-II Full Scale Composite		
	Baseline Chronological Age 13y	Week 52 Chronological Age 14y
Mean 100 (SD 15)	43	47

FIG. 34

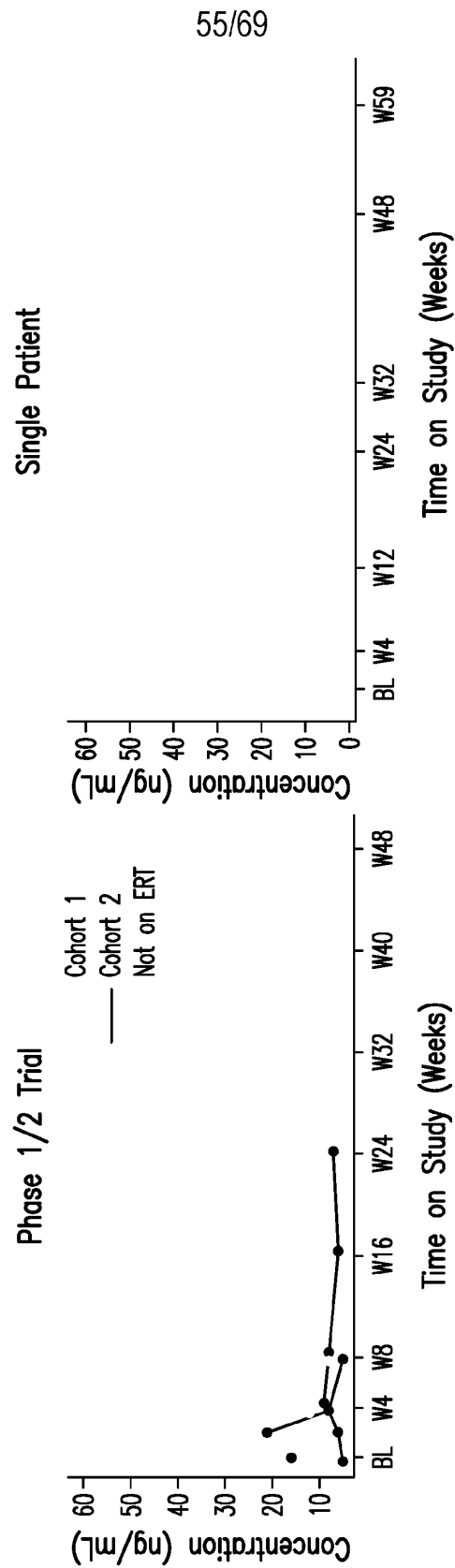
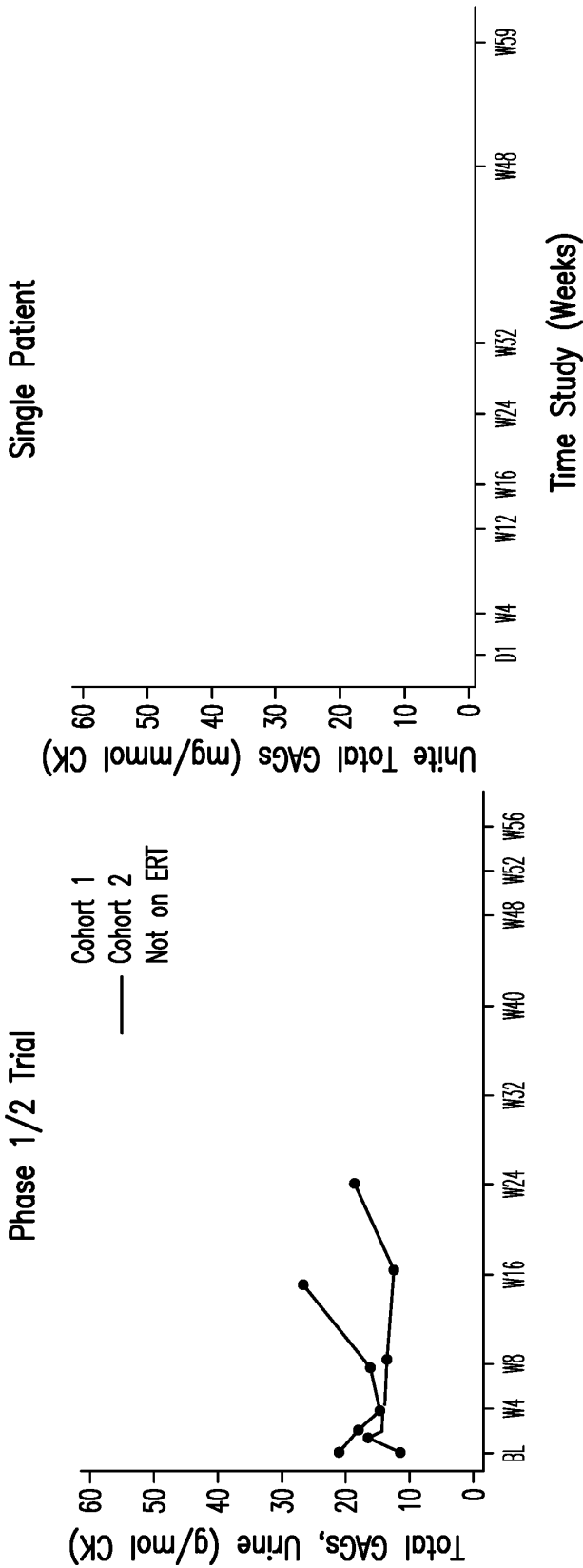


FIG. 35B

FIG. 35A



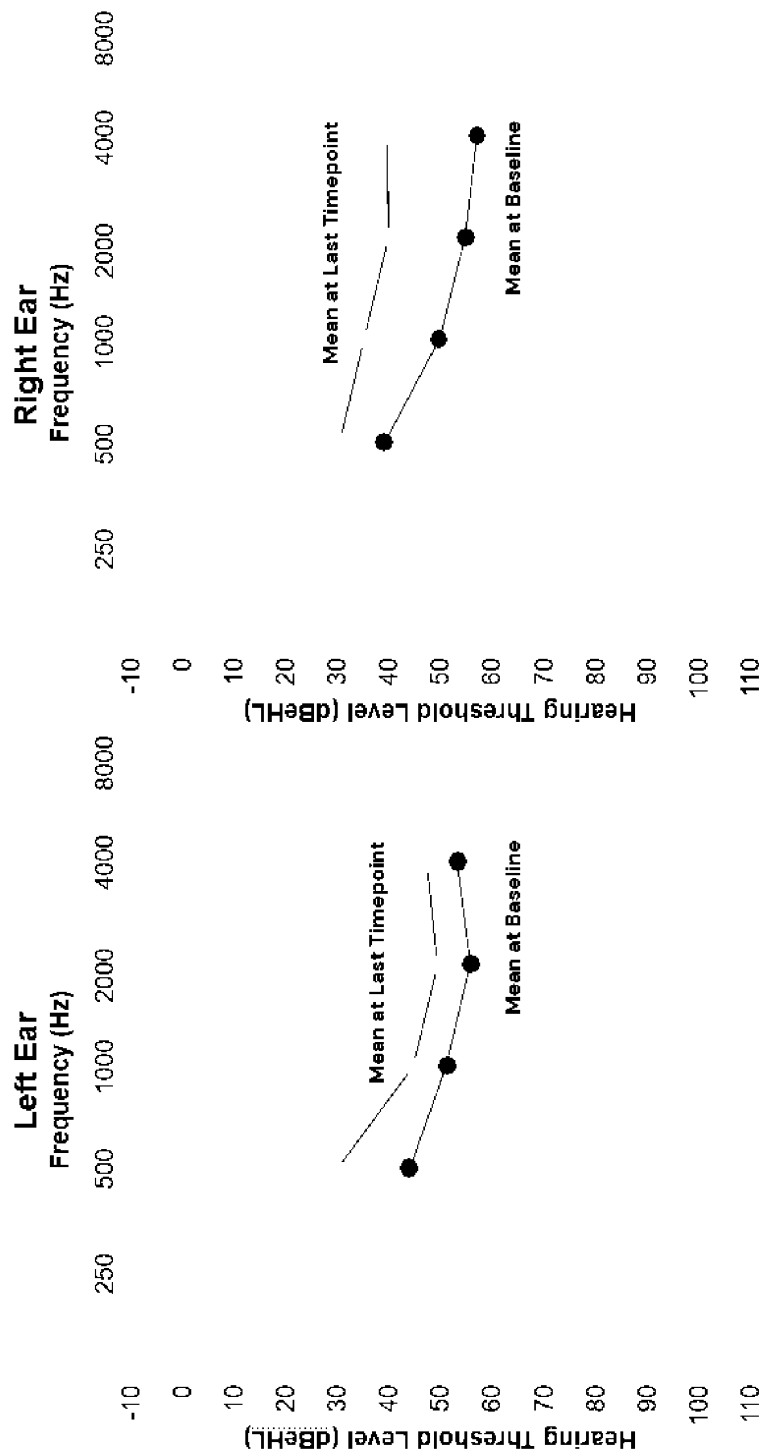


FIG. 37B

FIG. 37A

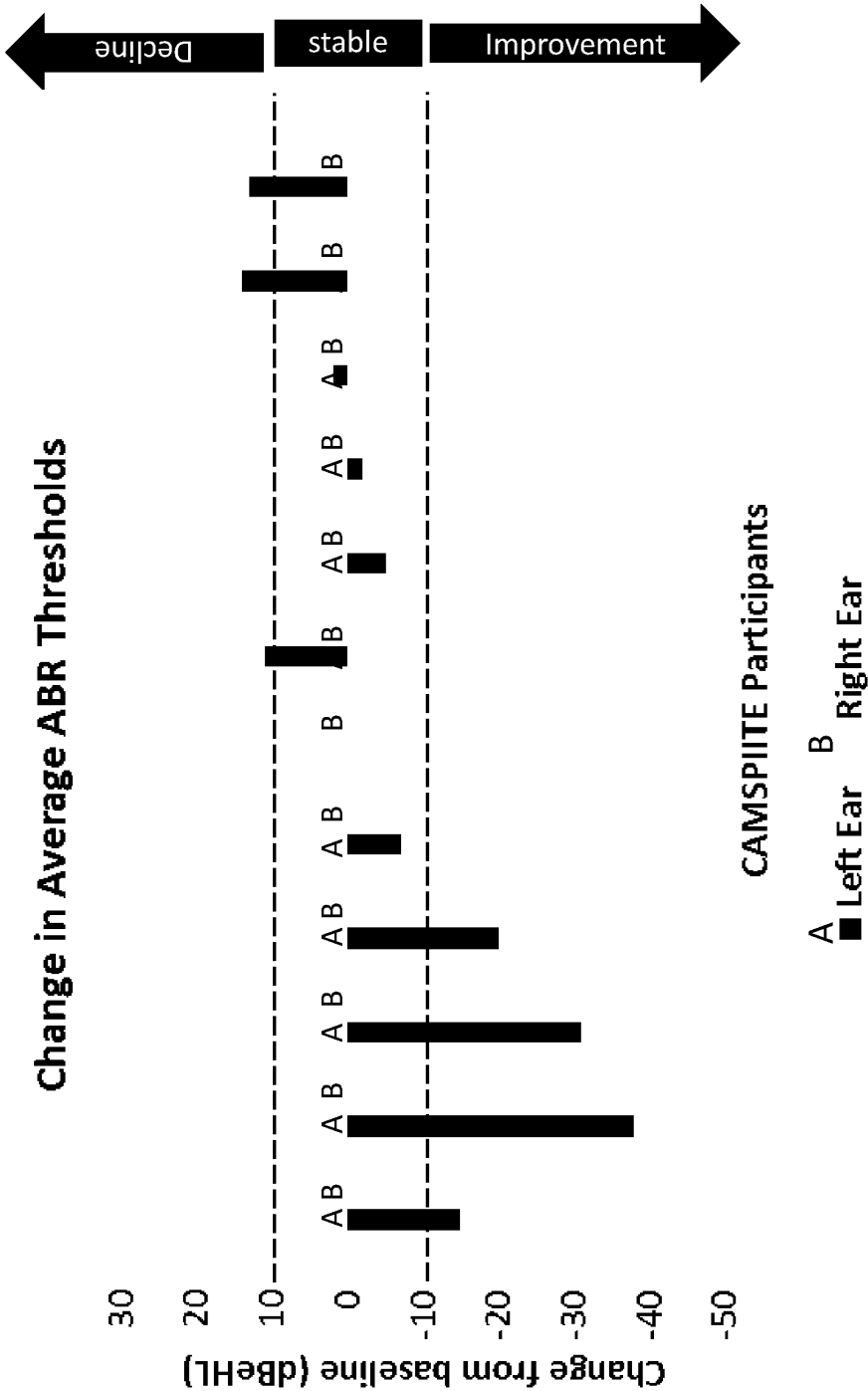


FIG. 38

Study Interval	Screening	Gene Therapy Inpatient Administration		Visits (Weeks)																					
Study Visit Number	1	2 ^a		3	4	5	6	7	8	9	10	11	12	13	15	16	17	18	19	20	21	EOS/ 22	ET ^b	Uns ^c	
Study Visit Window (Days)				±3	±3	±3	±3	±3	±3	±7	±7	±7	±7	±7	±7	±7	±14	±14	±14	±14	±14	±14			
Study Day or Week	D – 35 to –2	D – 2	D1 (Pre)	D1 (Post) ^d	D2 ^e																64 ^f	78	104		
General Procedures and Assessments																									
Informed Consent	X ^g																								
Confirm Eligibility		X	X																						
Medical History	X	X	X																						
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Physical Examination ^h	X		X	X			X					X						X				X			
Targeted Physical Examination ^h		X		X	X	X	X	X	X	X			X	X	X	X	X		X	X	X			X ⁱ	
Neurologic Assessment ^h			X	X	X	X	X	X		X		X						X			X	X			
Anesthesiologist Examination ^j	X		X																						
Somatosensory Evoked Potentials ^k			X					X				X				X							X		
Vital Signs	X	X	X	X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	X	X	X	
Height, Weight, and Head Circumference	X	X						X				X		X	X	X		X			X	X			
ECG	X																					X			
Renal Function ^{kl}	X																					X			
IC/ICV Administration Evaluation ^l	X	X																							
Head/Neck MRI ^{lm}	X											X				X							X		
Abdominal ultrasound ^p	X											X	X ^p				X			X ^p					

FIG. 39

Study Interval	Screening	Gene Therapy Inpatient Administration		Visits (Weeks)																					
Study Visit Number	1	2 ^a		3	4	5	6	7	8	9	10	11	12	13	15	16	17	18	19	20	21	EOS/22	ET ^b	Uns ^c	
Study Visit Window (Days)				±3	±3	±3	±3	±3	±3	±7	±7	±7	±7	±7	±7	±7	±14	±14	±14	±14	±14	±14			
Study Day or Week	D – 35 to –2	D1 (Pre)	D1 (Post) ^d	D2 ^e	1	2	3	4	8	12	16	20 ^g	24	28 ^g	32	40	48	52	60	64 ^f	78	104			
Viral testing ^z	X				X	X	X	X	X	X	X	X	X	X	X										
Vector Concentration (qPCR to Construct 1 DNA) in Serum and Urine		X					X	X		X		X													
Future Use Research Sample	X						X		X			X				X				X					
Construct 1 Administration (CT-Guided)																									
Construct 1 Administration ^s		X																							
Immunosuppression Therapy ^t																									
Dispense Prednisone (QD PO Day 2 to Week 12 Visits)				X			X																		
Methylprednisolone (IV Day 1 Visit) administration ^t		X																							
Dispense Tacrolimus (PO BID Day 2 to Week 24 Visits)				X			X	X		X		X													

FIG. 39 (Continued)

Study Interval	Screening	Gene Therapy Inpatient Administration		Visits (Weeks)																								
		1	D - 35 to -2	D -2	D1 (Pre)	D1 (Post) ^d	D2 ^e	3	4	5	6	7	8	9	10	11	12	13	15	16	17	18	19	20	21	EOS/22	ET ^b	Uns ^c
Study Visit Number																												
Study Visit Window (Days)																												
Study Day or Week																												
Dispense Sirolimus (Day -2 until Week 48 Visits)				X	X		X		X		X		X		X		X											
Dispense Sulfamethoxazole/Trimethoprim (Day -2 until Week 48 Visits)				X	X		X		X		X		X		X		X											
Immunosuppressant Drug Accountability													X		X		X			X								
Tacrolimus Whole Blood Levels												X	X		X		X											X ⁱ
Sirolimus Whole Blood Levels												X	X		X		X		X									X ⁱ
CSF Laboratory Assessments																												
Lumbar Puncture	X ^u								X ^u	X				X		X				X						X	X	
CSF Biomarkers ^r	X								X	X				X		X				X	X					X	X	
CSF Safety Laboratory ^w									X	X				X		X				X						X		
CSF Immune Response Monitoring ^q									X	X				X		X				X						X		
Vector Concentration (qPCR to Construct 1 DNA) in CSF									X	X				X		X												
Neurocognitive Assessments																												
Cognitive Testing ^x	X															X				X					X	X	X	X

Study Interval	Screening	Gene Therapy Inpatient Administration	Visits (Weeks)																			EOS/ 22	ET ^b	Uns ^c
			1	2 ^a	3	4	5	6	7	8	9	10	11	12	13	15	16	17	18	19	20	21		
Study Visit Number	1				±3	±3	±3	±3	±3	±3	±7	±7	±7	±7	±7	±7	±7	±14	±14	±14	±14	±14		
Study Visit Window (Days)																								
Study Day or Week	D - 35 to -2	D1 (Pre)	D1 (Post) ^d	D2 ^c	1	2	3	4	8	12	16	20 ^g	24	28 ^g	32	40	48	52	56	60	64 ^f	78	104	
Adaptive & Behavioral Function Testing ^x _{aa}	X									X		X			X		X		X			X	X	
Clinical Assessment of Disease ^{bb}	X	X							X	X	X		X		X	X	X	X	X	X	X	X	X	
Caregiver Assessment of Disease ^{aa}	X	X							X	X	X		X		X	X	X	X	X	X	X	X	X	
PedsQL ^{aa}	X									X			X				X					X	X	
Sleep Assessment ^{aa}	X									X			X				X		X			X	X	
Activities of Daily Living ^{aa}	X												X				X					X	X	
Burden of Illness Survey ^{aa}	X																X						X	

FIG. 39 (Continued)

Participant ID	Visit	Age (months)	ABR ¹ (dBeHL)		Tympanometry		Degree of Hearing Loss		Type of Hearing Loss		Tubes or TM Perf ²		Hearing Status	
			Right	Left	Right	Left	Right	Left	Right	Left	Yes	No	Right	Left
001*	Screening	5.1	8	10	A	A	Normal	Normal	-	-		X	Declined	Declined
	Year 5	65.4	28	23	A	A	Mild	Normal	-	Normal		X		
002*	Screening	35.5	65	68	N/A	N/A	Severe	Severe	-	-	X		Improved	Improved
	Year 3	71.3	45	30	B2	B2	Moderate	Mild	-	-	X			
003*	Screening	7.1	23	23	A	A	Normal	Normal	Normal	Normal		X	Stable	Stable
	Year 3	44	18	23	A	A	Normal	Normal	Normal	Normal		X		
004*	Screening	39.5	28	26	B2	B2	Mild	Mild	-	-	X		Improved	Improved
	Year 3	76	20	20	C	A	Normal	Normal	Normal	Normal		X		
005*	Screening	25.1	75	65	-	-	Severe	Severe	-	-	-	-	Improved	Improved
	Year 3	63.8	37	54	-	-	Mild	Moderate	-	-	-	-		
006	Screening ³	26.1	36	48	-	-	Mild	Moderate	-	-	-	-	Stable	Stable
	Week 104	49.9	15	41	-	-	Normal	Moderate	Normal	-	-	-		
007	Screening	58.6	53	55	N/A	N/A	Moderate	Moderate	-	-	X	-	Stable	Stable
	Week 72	75.9	50	53	B2	B2	Moderate	Moderate	MHL	MHL	X	-		
008*	Screening	37.1	43	40	B2	N/A	Moderate	Mild	-	-	X	-	Improved	Improved
	Week 136	68.9	20	23	B2	B2	Normal	Normal	Normal	Normal	-	-		
009	Screening	28.8	28	29	N/A	N/A	Mild	Mild	-	-	X		Declined	Declined
	Week 117	56	39	43	A	A	Mild	Moderate	SNHL	SNHL		X		
010	Screening	14.2	45	39	-	-	Moderate	Mild	-	-		X	Improved	Declined
	Week 104	38.8	23	50	A	B1	Normal	Moderate	Normal	-		X		
011	Screening	24.6	70	75	-	-	Severe	Severe	-	-	-	-	Improved	Improved
	Week 104	49.9	59	44	-	-	Moderate	Moderate	MHL	MHL	-	-		

FIG. 40

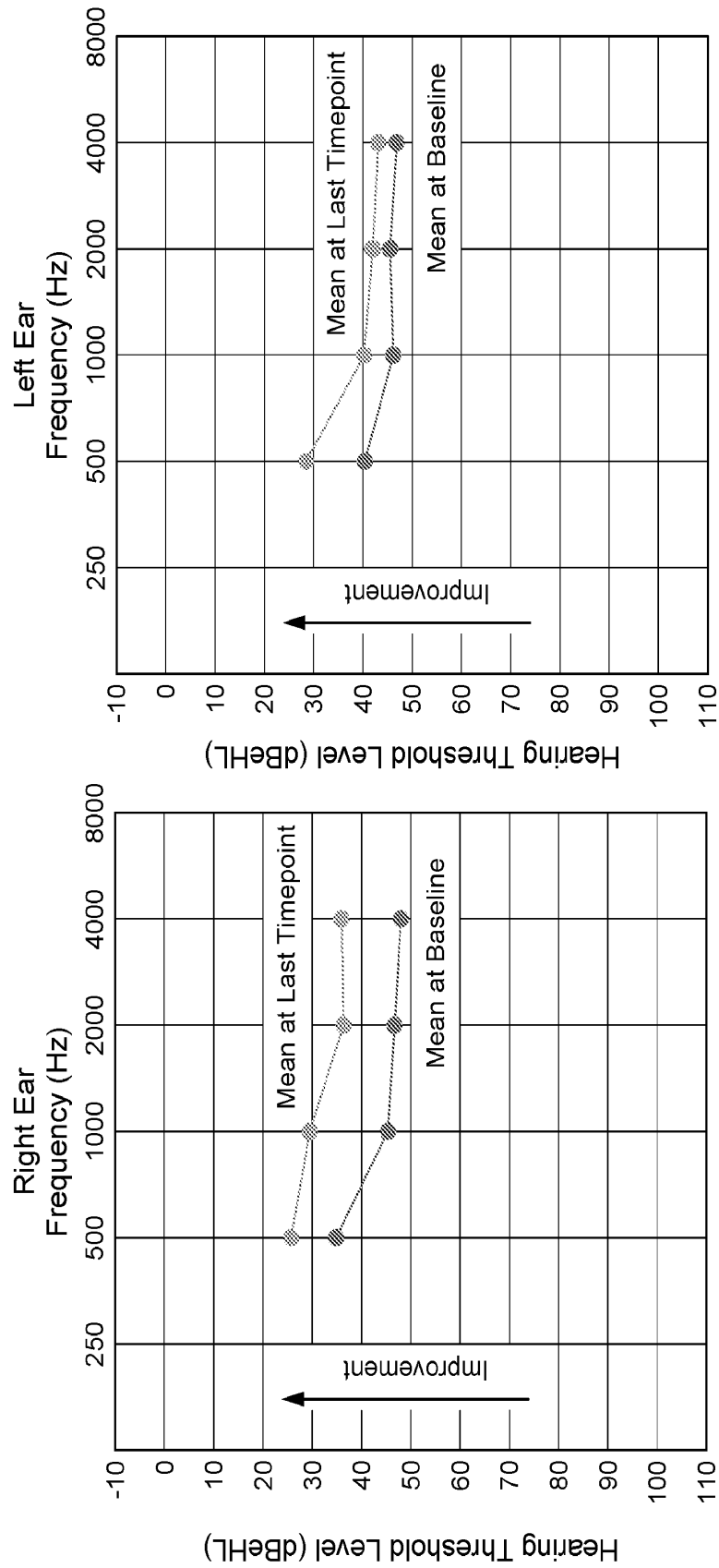


FIG. 41

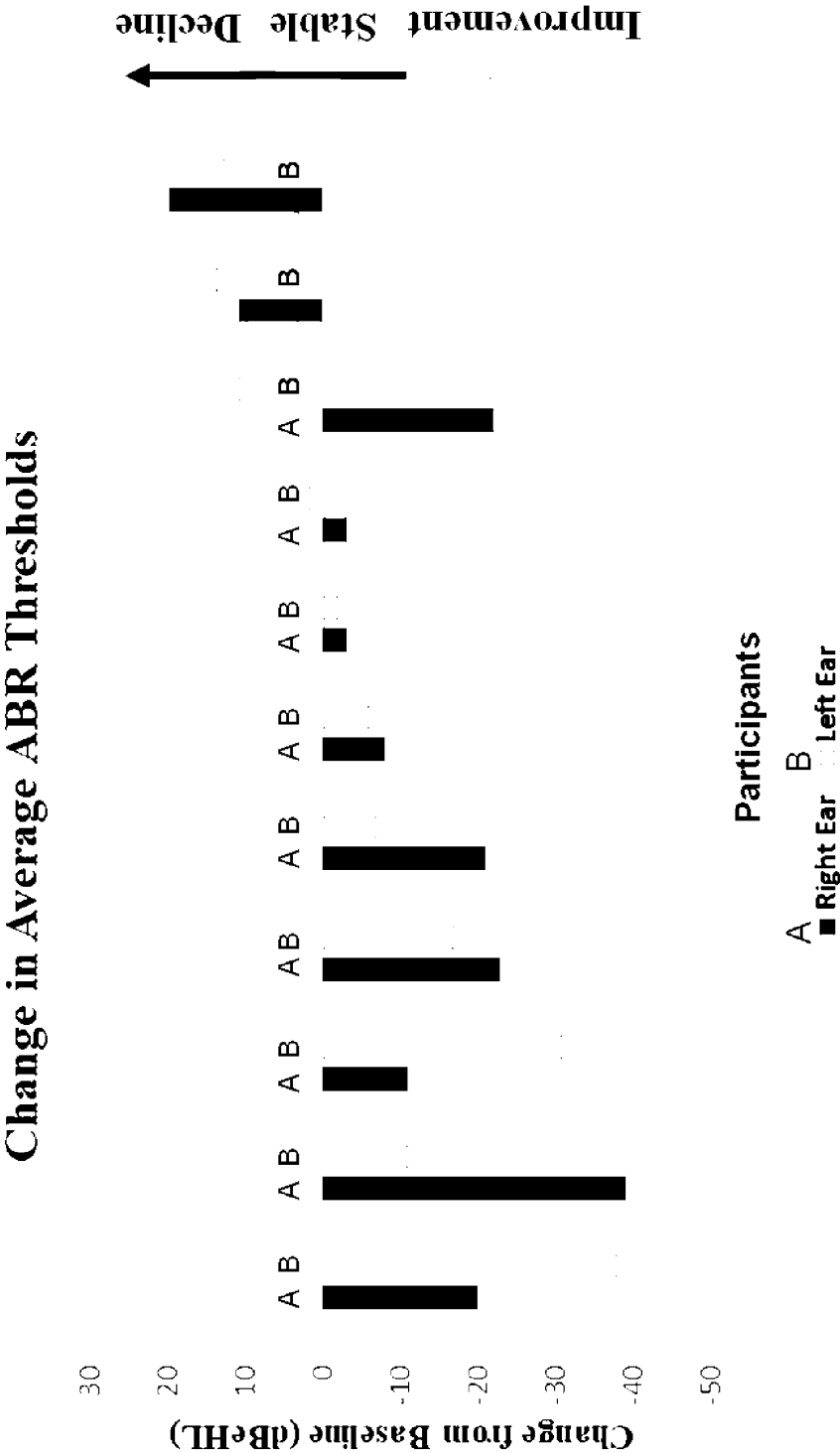


FIG. 42

Participant ID	Timepoint	Age (months)	ABR ¹ (dBeHL)		Tympanometry		Degree of Hearing Loss		Type of Hearing Loss		Tubes or TM Perf ²		Hearing Status	
			Right	Left	Right	Left	Right	Left	Right	Left	Yes	No	Right	Left
301	Screening	56.1	29	34	B2	B2	Mild	Mild	SNHL	SNHL	X		Stable	
	Week 24	62	39	39	B1	B1	Mild	Mild	MHL	MHL	X			Stable
302	Screening	38.3	25	26	B1	C	Normal	Mild	Normal	SNHL	-	X	Stable	Stable
	Week 24	44.6	20	33	B1	B1	Normal	Mild	Normal	-	-	X		
303	Screening	8	20	20	A	A	Normal	Normal	Normal	Normal	-	X	Stable	Stable
	Week 24	14	20	21	B1	B1	Normal	Normal	Normal	Normal	-	X		
304	Screening	47.4	36	48	A	B1	Mild	Moderate	CHL	MHL	-	X	Improved	Improved
	Week 24	53.6	24	20	A	A	Normal	Normal	Normal	Normal	-	X		
305	Screening	4.4	23	26	-	-	Normal	Mild	CHL ³	CHL	-	-	Declined	Declined
	Week 24	10.4	49	45	-	-	Moderate	Moderate	CHL	CHL	-	-		
306	Screening	50.5	70	60	B2	B2	Severe	Moderate	-	-	X	-	Improved	Stable
	Week 24	57.1	53	70	B2	B2	Moderate	Severe	MHL	MHL	X	-		
307	Screening	10.6	30	33	B2	B2	Mild	Mild	CHL	CHL	X	-	Improved	Improved
	Week 24	17.5	20	20	B2	B2	Normal	Normal	Normal	Normal	X	-	Stable	Stable
308	Screening	51.3	63	73	B1	B1	Severe	Severe	MHL	MHL	-	X	Improved	Improved
	Week 24	57.8	37	30	C	A	Mild	Mild	-	MHL	-	X		
309	Screening	42	33	25	B2	B2	Mild	Mild	CHL	CHL	X	-	Stable	Stable
	Week 24	48.7	28	18	B2	B2	Mild	Normal	CHL	Normal	X	-		
310	Screening	23.8	89	89	-	-	profound	profound	MHL	MHL	-	-	Improved	Stable
	Week 48	35.3	54	81	-	-	moderate	profound	MHL	MHL	-	-		
311	Screening	13.6	56	46	-	-	Moderate	Moderate	MHL	MHL	-	-	Stable	Stable
	Week 48	25.5	54	41	-	-	Moderate	Moderate	MHL	MHL	-	-		

FIG. 43

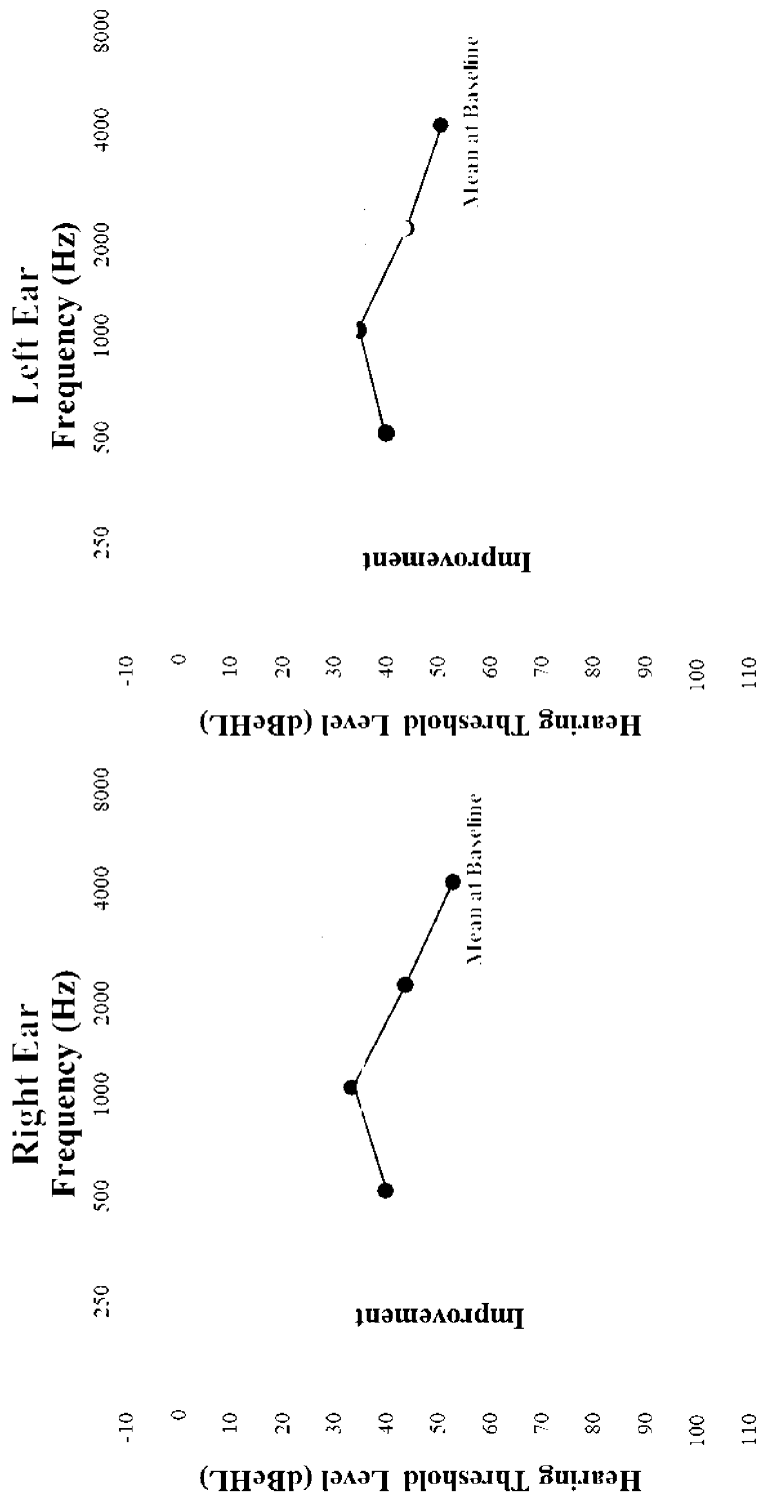


FIG. 44

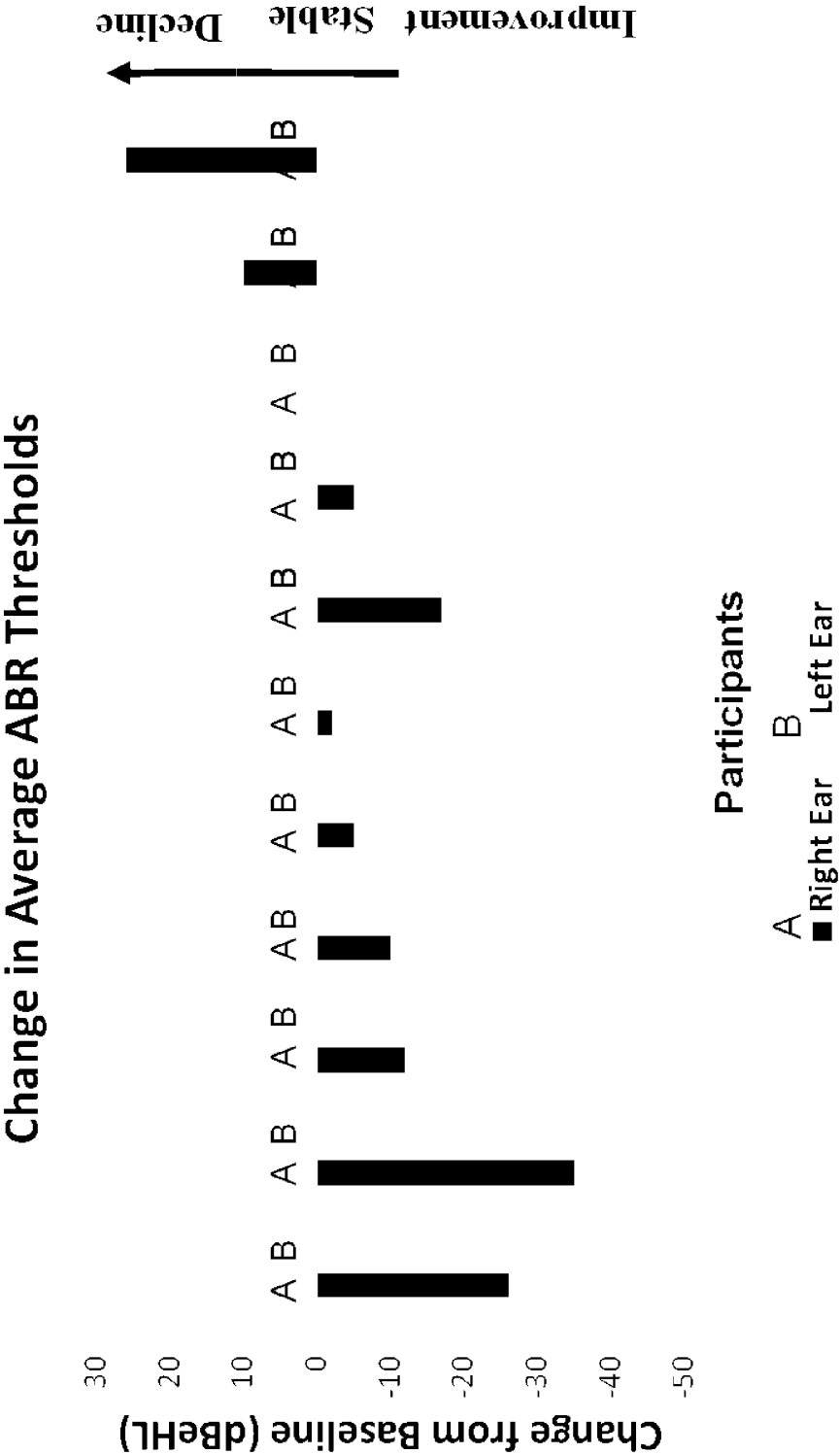


FIG. 45