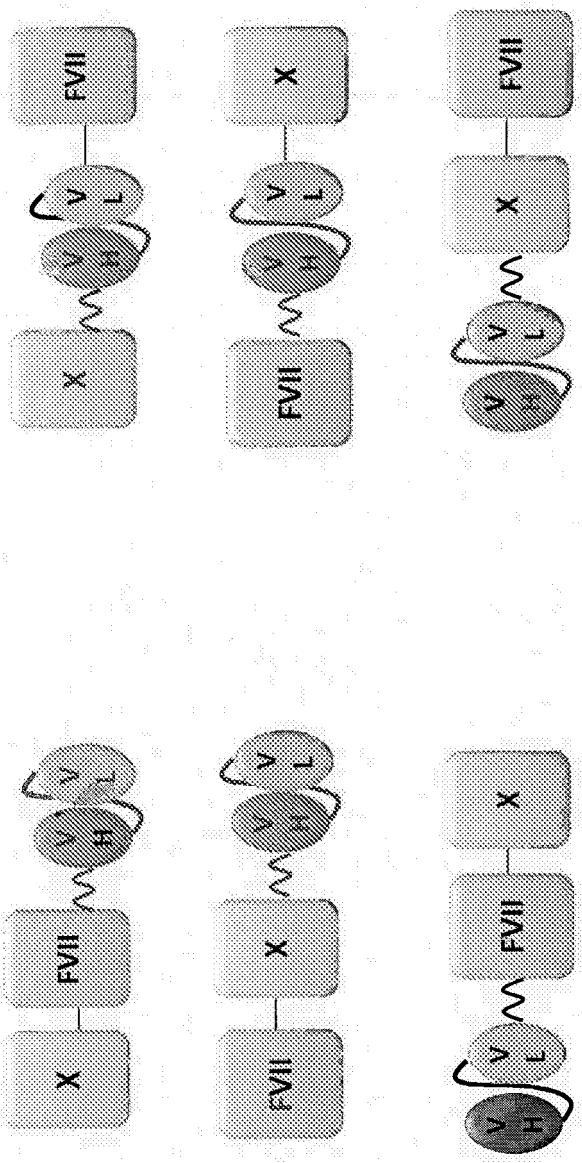
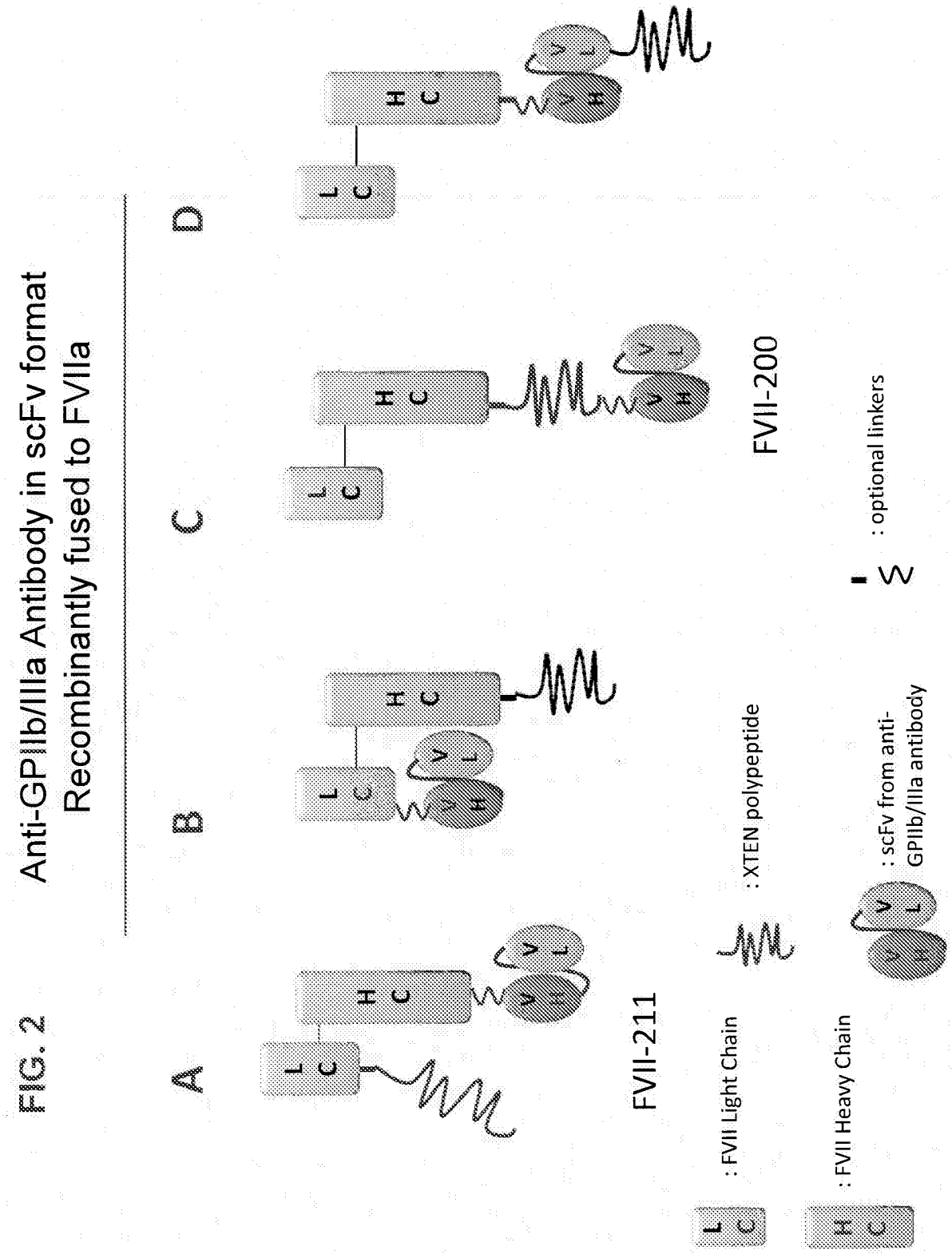


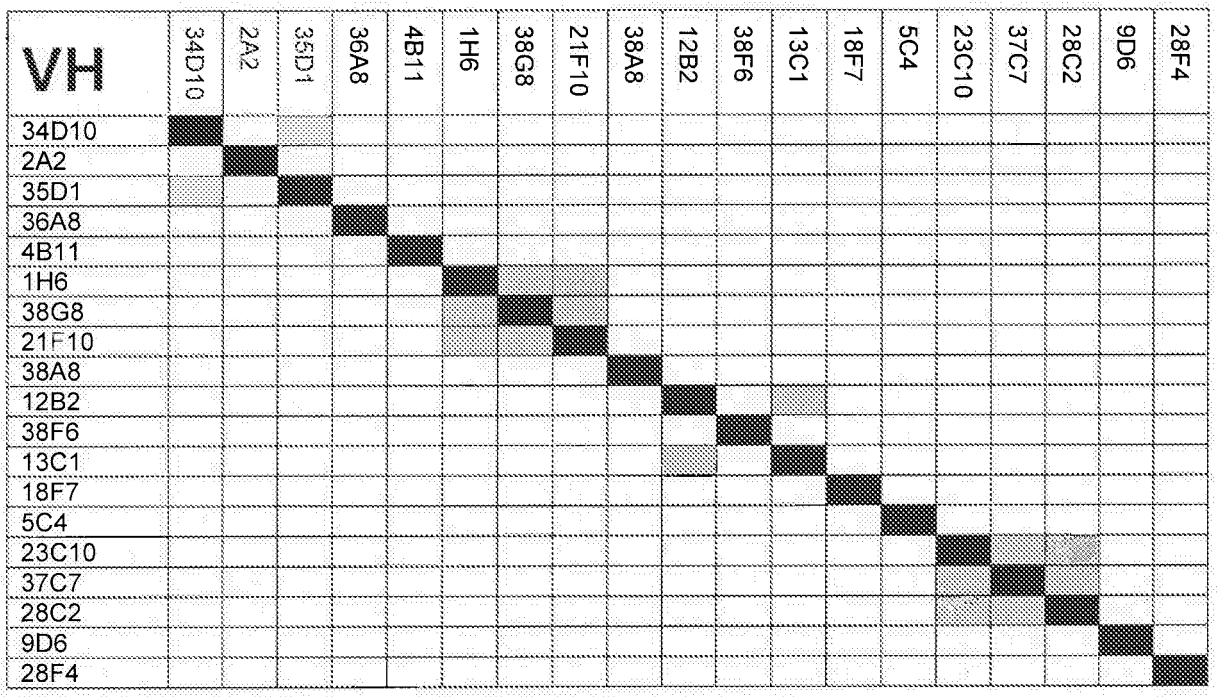
VH-VL: scFv derived from anti-GPIIb/IIIa Antibody, *e.g.*, from 34D10
X: XTEN polypeptide
FVII: FVII zymogen, activatable FVII, or activated FVII
∿ An optional linker

FIG. 1

FIG. 2


Anti-GPIIb/IIIa Antibody in scFv format
Recombinantly fused to FVIIa
A
B
C
D
FVII-211
FVII-200
: FVII Light Chain
: FVII Heavy Chain
: XTEN polypeptide
: scFv from anti-GPIIb/IIIa antibody
: optional linkers

A


VH
34D10
2A2
35D1
36A8
4B11
1H6
38G8
21F10
38A8
12B2
38F6
13C1
18F7
5C4
23C10
37C7
28C2
9D6
28F4

B

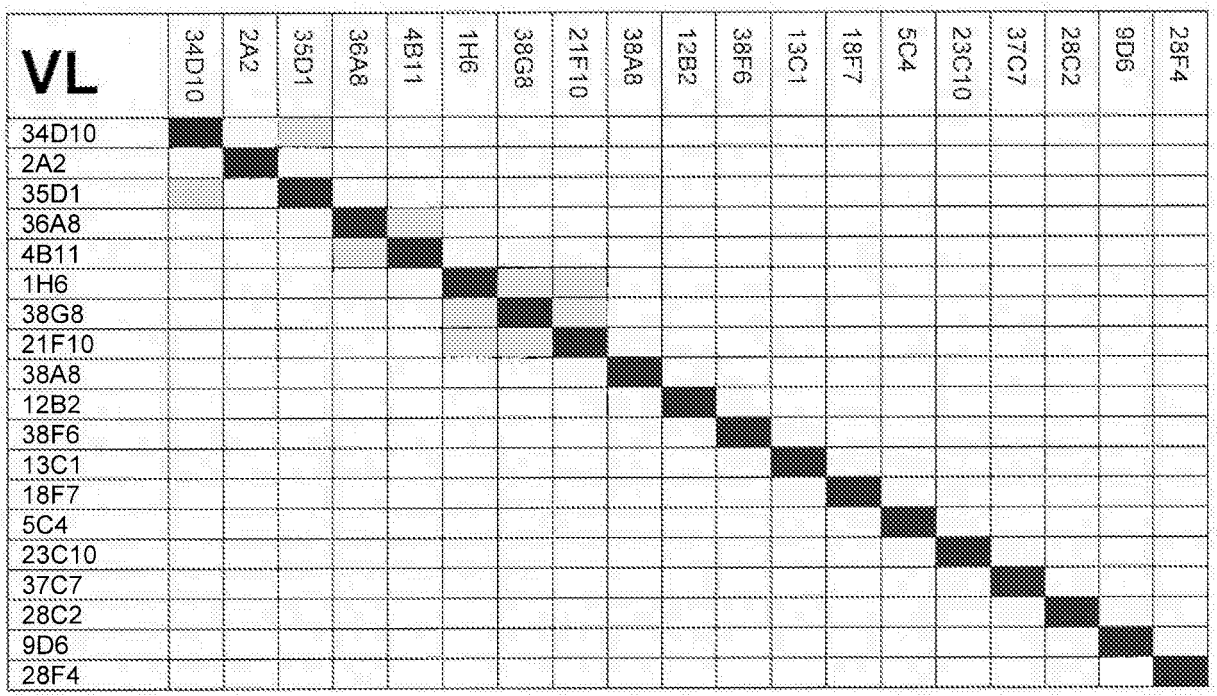
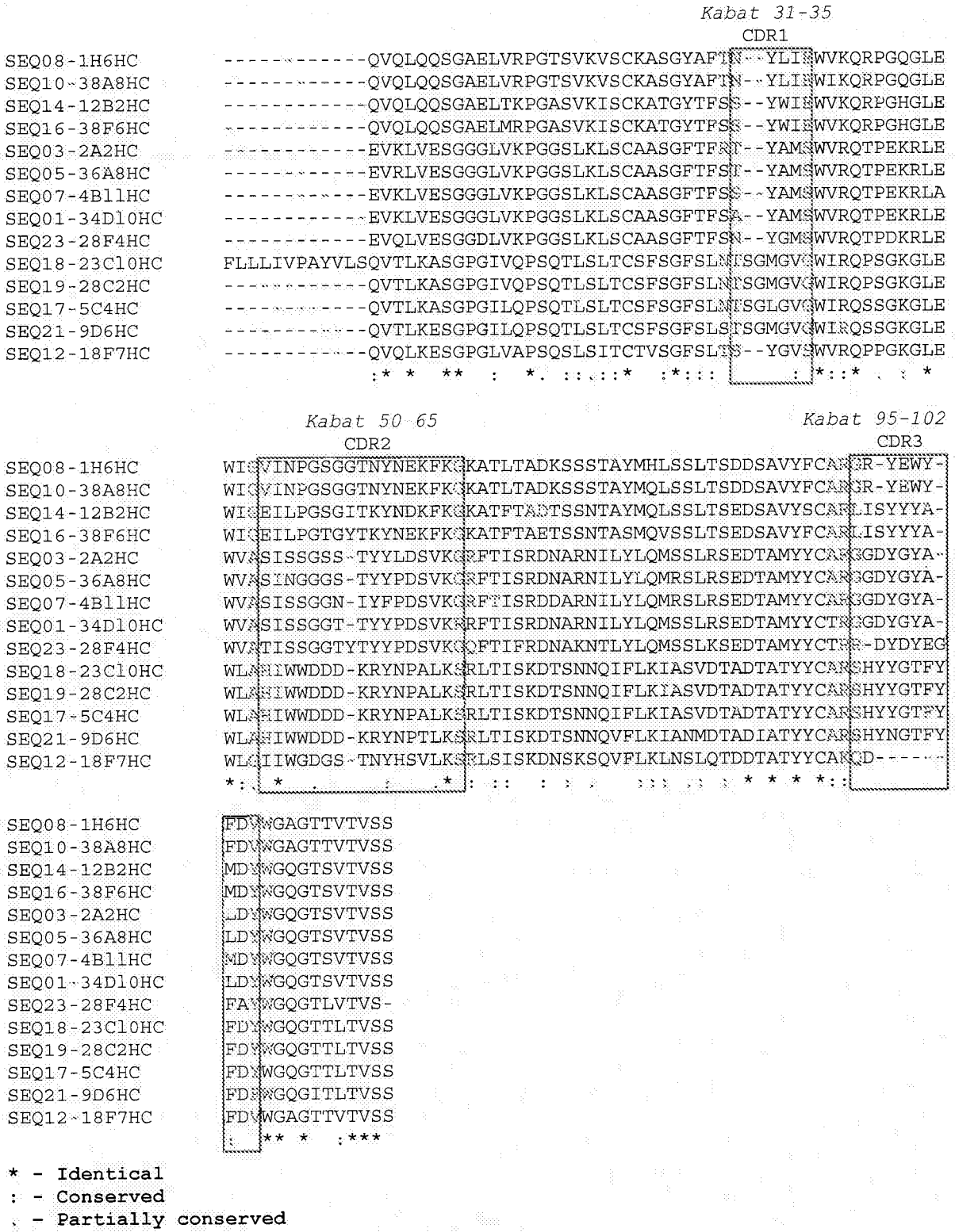

VL
34D10
2A2
35D1
36A8
4B11
1H6
38G8
21F10
38A8
12B2
38F6
13C1
18F7
5C4
23C10
37C7
28C2
9D6
28F4

FIG. 3

VH SEQUENCES - Full Alignment (All Sequenced VH and VL Included)

CLUSTAL 2.1 multiple sequence alignment



* - Identical
: - Conserved
. - Partially conserved

FIG. 4

VL SEQUENCES - Full Alignment (All Sequenced VH and VL Included)

CLUSTAL 2.1 multiple sequence alignment

```
                                          Kabat 24-34                    Kabat 50-56
                                              CDR1                           CDR2
SEQ20-28C2LC      DVQITQSPSYLAASPGETITINCRASKSISKYLAWYQEKPGTTYKLLIYSGSTLQSGIPS
SEQ22-9D6LC       DVQITQSPSYLAASPGETITINCRASKSISKYLAWYQEKPGKTNKLLIYSGSTLQSGIPS
SEQ09-1H6LC       DIQMTQTTSSLSASLGDRVTISCRASQDITNYLNWYQRKPDGTVKLLIYYTSRLHSGVPS
SEQ11-38A8LC      DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYLQKPDGTVKLLIYYTSRLHSGVPS
SEQ15-12B2LC      DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHSGVPS
SEQ13-18F7LC      DVQMIQSPFSLSASLGDIVTMTCQASQGTSINLNWFQQKPGKAPKLLIYGVSNLEDGVPS
SEQ24-28F4LC      DIVLTQSPATLSVTPGDSVSLSCRASQSISNNLHWYQQKSHESPRLLIKYASHSISGIPS
SEQ02-34D10LC     ENVLTQSPAIMSASLGEKVTMSCRASSSVN-YMYWYQQKSDASPKLWIYYTSNLAPGVPA
SEQ06-36A8LC      ENVLTQSPAIMSASLGEKVTMNCRASSSVN-YMYWYQQKSDASPKLWIFYTSNLAPGVPA
SEQ04-2A2LC       ENVLTQSPAIMSASLGEKVTMSCRASSSVN-YMYWYQQKSDASPKLWIYYTSNLAPGVPT
                  :  : *:.  ::.: *: ::::.*:**.. .  : *: .*.  : :* *   *    *:*:

                                                  Kabat 89-97
                                                      CDR3
SEQ20-28C2LC      RFSGSGSGTDFTLTISSLEPEDFAMYYCQQHIEYPWTFGGGTKLEIKR
SEQ22-9D6LC       RFSGSGSGTDFTLTISTLEPEDFAMYYCQQHIEYPWTFGGGTKLEIKR
SEQ09-1H6LC       RFSGSGSGTDYSLTISNLEQEDIATYFCQQGYTLPYTFGGGTKLEIKR
SEQ11-38A8LC      RFSGSGSGTDYSLSISNLEQEDIATYFCQQGYTLPYTFGGGTKLEIKR
SEQ15-12B2LC      RFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPPTFGGGTKLEIKR
SEQ13-18F7LC      RFSGSRYGTDFTLTIGSLEDEDMATYFCLQHSYLPYTFGGGTKLEIKR
SEQ24-28F4LC      RFSGSGSGTDFTLSINSVETEDFGMYFCQQSNNWPFTFGSGTKLEIKR
SEQ02-34D10LC     RFSGSGSGNSYSLTISSMEGEDAATYYCQQFSSSPWTFGGGTKLEIKR
SEQ06-36A8LC      RFSGSGSGNSYSLTISSMEGEDAATYYCQQFSSSPWTFGGGSKLEIKR
SEQ04-2A2LC       RFSGSGSGNSYSLTISSLEGEDAGTYYCQQFSSSPWTFGGGTKLEIKR
                  *****  *..::*:*..:* ** . *:*  *    * ***.*:******
```

* - Identical
: - Conserved
. - Partially conserved

FIG. 5

VL SEQUENCES - Percent Identity Matrix

	1	2	3	4	5	6	7	8	9	10
1: SEQ20-28C2LC	100	97	66	65	67	62	60	59	58	59
2: SEQ22-9D6LC	97	100	66	65	67	62	59	58	57	58
3: SEQ09-1H6LC	66	66	100	96	96	66	58	63	60	63
4: SEQ11-38A8LC	65	65	96	100	96	66	60	62	59	62
5: SEQ15-12B2LC	67	67	96	96	100	67	61	64	61	64
6: SEQ13-18F7LC	62	62	66	66	67	100	56	57	55	57
7: SEQ24-28F4LC	60	59	58	60	61	56	100	56	54	57
8: SEQ02-34D10LC	59	58	63	62	64	57	56	100	97	97
9: SEQ06-36A8LC	58	57	60	59	61	55	54	97	100	94
10: SEQ04-2A2LC	59	58	63	62	64	57	57	97	94	100

VH SEQUENCES - Percent Identity Matrix

Percent Identity Matrix

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1: SEQ08-1H6HC	100	98	75	74	48	47	44	45	47	37	37	36	33	50
2: SEQ10-38A8HC	98	100	75	74	48	47	44	45	47	38	38	37	34	49
3: SEQ14-12B2HC	75	75	100	92	54	53	53	53	52	36	36	36	34	42
4: SEQ16-38F6HC	74	74	92	100	50	50	49	49	50	36	36	36	33	41
5: SEQ03-2A2HC	48	48	54	50	100	94	91	94	81	46	46	45	42	50
6: SEQ05-36A8HC	47	47	53	50	94	100	92	93	81	46	46	45	42	51
7: SEQ07-4B11HC	44	44	53	49	91	92	100	92	79	43	43	42	40	47
8: SEQ01-34D10HC	45	45	53	49	94	93	92	100	84	44	44	43	41	49
9: SEQ23-28F4HC	47	47	52	50	81	81	79	84	100	41	41	40	38	49
10: SEQ18-23C10HC	37	38	36	36	46	46	43	44	41	100	100	98	90	65
11: SEQ19-28C2HC	37	38	36	36	46	46	43	44	41	100	100	98	90	65
12: SEQ17-5C4HC	36	37	36	36	45	45	42	43	40	98	98	100	90	64
13: SEQ21-9D6HC	33	34	34	33	42	42	40	41	38	90	90	90	100	62
14: SEQ12-18F7HC	50	49	42	41	50	51	47	49	49	65	65	64	62	100

FIG. 6

VH Sequences Clustered According to Alpha/Beta Specificity

Only sequences with both VH and VL sequenced included

CLUSTAL 2.1 multiple sequence alignment

ALPHA SUBUNIT SPECIFIC

```
                                                                                                  Kabat 31-35
                                                                                                       CDR1
SEQ08-1H6HC       ------------QVQLQQSGAELVRPGTSVKVSCKASGYAFTN--YLIEWVKQRPGQGLE
SEQ10-38A8HC      ------------QVQLQQSGAELVRPGTSVKVSCKASGYAFTN--YLIEWIKQRPGQGLE
SEQ03-2A2HC       ------------EVKLVESGGGLVKPGGSLKLSCAASGFTFRT--YAMSWVRQTPEKRLE
SEQ05-36A8HC      ------------EVRLVESGGGLVKPGGSLKLSCAASGFTFST--YAMSWVRQTPEKRLE
SEQ01-34D10HC     ------------EVKLVESGGGLVKPGGSLKLSCAASGFTFSA--YAMSWVRQTPEKRLE
SEQ12-18F7HC      ------------QVQLKESGPGLVAPSQSLSITCTVSGFSLTS--YGVSWVRQPPGKGLE

                                  Kabat 50-65                                                                  Kabat 95-102
                                       CDR2                                                                         CDR3
SEQ08-1H6HC       WIGVINPGSGGTNYNEKFKGKATLTADKSSSTAYMHLSSLTSDDSAVYFCARGR-YEWY-
SEQ10-38A8HC      WIGVINPGSGGTNYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCARGR-YEWY-
SEQ03-2A2HC       WVASISSGSS-TYYLDSVKGRFTISRDNARNILYLQMSSLRSEDTAMYYCARGGDYGYA-
SEQ05-36A8HC      WVASINGGGS-TYYPDSVKGRFTISRDNARNILYLQMRSLRSEDTAMYYCARGGDYGYA-
SEQ01-34D10HC     WVASISSGGT-TYYPDSVKGRFTISRDNARNILYLQMSSLRSEDTAMYYCTRGGDYGYA-
SEQ12-18F7HC      WLGLIWGDGS-TNYHSVLKSRLSISKDNSKSQVFLKLNSLQTDDTATYYCAKQD------

SEQ08-1H6HC       FDVWGAGTTVTVSS
SEQ10-38A8HC      FDVWGAGTTVTVSS
SEQ03-2A2HC       LDYWGQGTSVTVSS
SEQ05-36A8HC      LDYWGQGTSVTVSS
SEQ01-34D10HC     LDYWGQGTSVTVSS
SEQ12-18F7HC      FDVWGAGTTVTVSS
                  *
```

BETA SUBUNIT SPECIFIC

```
                                                                                                  Kabat 31-35
                                                                                                       CDR1
SEQ14-12B2HC      ------------QVQLQQSGAELTKPGASVKISCKATGYTFSS--YWIEWVKQRPGHGLE
SEQ23-28F4HC      ------------EVQLVESGGDLVKPGGSLKLSCAASGFTFSN--YGMSWVRQTPDKRLE
SEQ19-28C2HC      ------------QVTLKASGPGIVQPSQTLSLTCSFSGFSLNTSGMGVGWIRQPSGKGLE
SEQ21-9D6HC       ------------QVTLKESGPGILQPSQTLSLTCSFSGFSLSTSGMGVGWIRQSSGKGLE

                                  Kabat 50-65                                                                  Kabat 95-102
                                       CDR2                                                                         CDR3
SEQ14-12B2HC      WIGEILPGSGITKYNDKFKGKATFTADTSSNTAYMQLSSLTSEDSAVYSCARLISYYYA-
SEQ23-28F4HC      WVATISSGGTYTYYPDSVKGQFTIFRDNAKNTLYLQMSSLKSEDTAMYYCTRR-DYDYEG
SEQ19-28C2HC      WLANIWWDDD-KRYNPALKSRLTISKDTSNNQIFLKIASVDTADTATYYCARSHYYGTFY
SEQ21-9D6HC       WLANIWWDDD-KRYNPTLKSRLTISKDTSNNQVFLKIANMDTADIATYYCARSHYNGTFY

SEQ23-28F4HC      FAYWGQGTLVTVS-
SEQ19-28C2HC      FDYWGQGTTLTVSS
SEQ21-9D6HC       FDFWGQGITLTVSS
SEQ14-12B2HC      MDYWGQGTSVTVSS
```

FIG. 7

VL Sequences Clustered According to Alpha/Beta Specificity

Only sequences with both VH and VL sequenced included

CLUSTAL 2.1 multiple sequence alignment

ALPHA SUBUNIT SPECIFIC

```
                                                  Kabat 24-34                                  Kabat 50-56
                                                      CDR1                                         CDR2
SEQ09-1H6LC       DIQMTQTTSSLSASLGDRVTISCRASQDITNYLNWYQRKPDGTVKLLIYYTSRLHSGVPS
SEQ11-38A8LC      DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYLQKPDGTVKLLIYYTSRLHSGVPS
SEQ13-18F7LC      DVQMIQSPFSLSASLGDIVTMTCQASQGTSINLNWFQQKPGKAPKLLIYGVSNLEDGVPS
SEQ02-34D10LC     ENVLTQSPAIMSASLGEKVTMSCRASSSVN-YMYWYQQKSDASPKLWIYYTSNLAPGVPA
SEQ06-36A8LC      ENVLTQSPAIMSASLGEKVTMNCRASSSVN-YMYWYQQKSDASPKLWIFYTSNLAPGVPA
SEQ04-2A2LC       ENVLTQSPAIMSASLGEKVTMSCRASSSVN-YMYWYQQKSDASPKLWIYYTSNLAPGVPT

                                                  Kabat 89-97
                                                      CDR3
SEQ09-1H6LC       RFSGSGSGTDYSLTISNLEQEDIATYFCQQGYTLPYTFGGGTKLEIKR
SEQ11-38A8LC      RFSGSGSGTDYSLSISNLEQEDIATYFCQQGYTLPYTFGGGTKLEIKR
SEQ13-18F7LC      RFSGSRYGTDFTLTIGSLEDEDMATYFCLQHSYLPYTFGGGTKLEIKR
SEQ02-34D10LC     RFSGSGSGNSYSLTISSMEGEDAATYYCQQFSSSPWTFGGGTKLEIKR
SEQ06-36A8LC      RFSGSGSGNSYSLTISSMEGEDAATYYCQQFSSSPWTFGGGSKLEIKR
SEQ04-2A2LC       RFSGSGSGNSYSLTISSLEGEDAGTYYCQQFSSSPWTFGGGTKLEIKR
```

BETA SUBUNIT SPECIFIC

```
                                                  Kabat 24-34                                  Kabat 50-56
                                                      CDR1                                         CDR2
SEQ20-28C2LC      DVQITQSPSYLAASPGETITINCRASKSISKYLAWYQEKPGTTYKLLIYSGSTLQSGIPS
SEQ22-9D6LC       DVQITQSPSYLAASPGETITINCRASKSISKYLAWYQEKPGKTNKLLIYSGSTLQSGIPS
SEQ15-12B2LC      DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHSGVPS
SEQ24-28F4LC      DIVLTQSPATLSVTPGDSVSLSCRASQSISNNLHWYQQKSHESPRLLIKYASHSISGIPS
                                                  *** **  *                                    *  *

                                                  Kabat 89-97
                                                      CDR3
SEQ20-28C2LC      RFSGSGSGTDFTLTISSLEPEDFAMYYCQQHIEYPWTFGGGTKLEIKR
SEQ22-9D6LC       RFSGSGSGTDFTLTISTLEPEDFAMYYCQQHIEYPWTFGGGTKLEIKR
SEQ15-12B2LC      RFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPPTFGGGTKLEIKR
SEQ24-28F4LC      RFSGSGSGTDFTLSINSVETEDFGMYFCQQSNNWPFTFGSGTKLEIKR
                                                  **      *
```

FIG. 8

VH Sequence Clustered According to Competition with Fibrinogen

Only sequence with both VH and VL included

CLUSTAL 0(1.1.0) multiple sequence alignment

No Fibrinogen Competition

```
                                                    Kabat 31-35          Kabat 50-65
                                                        CDR1                 CDR2
SEQ04-2A2HC       EVKLVESGGGLVKPGGSLKLSCAASGFTFRTYAMSWVRQTPEKRLEWVASI-SSGSSTYY
SEQ01-34D10HC     EVKLVESGGGLVKPGGSLKLSCAASGFTFSAYAMSWVRQTPEKRLEWVASI-SSGGTTYY
SEQ05-36A8HC      EVRLVESGGGLVKPGGSLKLSCAASGFTFSTYAMSWVRQTPEKRLEWVASI-NGGGSTYY
SEQ14-12B2HC      QVQLQQSGAELTKPGASVKISCKATGYTFSSYWIEWVKQRPGHGLEWIGEILPGSGITKY
                                                    *                *      * *

                                                                  Kabat 95-102
                                                                      CDR3
SEQ04-2A2HC       LDSVKGRFTISRDNARNILYLQMSSLRSEDTAMYYCARGGDYGYALDYWGQGTSVTVSS
SEQ01-34D10HC     PDSVKRRFTISRDNARNILYLQMSSLRSEDTAMYYCTRGGDYGYALDYWGQGTSVTVSS
SEQ05-36A8HC      PDSVKGRFTISRDNARNILYLQMRSLRSEDTAMYYCARGGDYGYALDYWGQGTSVTVSS
SEQ14-12B2HC      NDKFKGKATFTADTSSNTAYMQLSSLTSEDSAVYSCARLISYYYAMDYWGQGTSVTVSS
                   * *                                    * ** **
```

Fibrinogen Competition

```
                                                    Kabat 31-35          Kabat 50-65
                                                        CDR1                 CDR2
SEQ08-1H6HC       QVQLQQSGAELVRPGTSVKVSCKASGYAFTN--YLIEWVKQRPGQGLEWIGVINPGSGGT
SEQ10-38A8HC      QVQLQQSGAELVRPGTSVKVSCKASGYAFTN--YLIEWIKQRPGQGLEWIGVINPGSGGT
SEQ12-18F7HC      QVQLKESGPGLVAPSQSLSITCTVSGFSLTS--YGVSWVRQPPGKGLEWLGIIW-GDGST
SEQ23-28F4HC      EVQLVESGGDLVKPGGSLKLSCAASGFTFSN--YGMSWVRQTPDKRLEWVATISSGGTYT
SEQ19-28C2HC      QVTLKASGPGIVQPSQTLSLTCSFSGFSLNTSGMGVGWIRQPSGKGLEWLAHIW-WDDDK
SEQ21-9D6HC       QVTLKESGPGILQPSQTLSLTCSFSGFSLSTSGMGVGWIRQSSGKGLEWLAHIW-WDDDK
                   * *  **     *       *  **          *  *     ***   *

                                                                  Kabat 95-102
                                                                      CDR3
SEQ08-1H6HC       NYNEKFKGKATLTADKSSSTAYMHLSSLTSDDSAVYFCARGRY--EWYFDVWGAGTTVTV
SEQ10-38A8HC      NYNEKFKGKATLTADKSSSTAYMQLSSLTSDDSAVYFCARGRY--EWYFDVWGAGTTVTV
SEQ12-18F7HC      NYHSVLKSRLSISKDNSKSQVFLKLNSLQTDDTATYYCAKQD------FDVWGAGTTVTV
SEQ23-28F4HC      YYPDSVKGQFTIFRDNAKNTLYLQMSSLKSEDTAMYYCTRRDYDY-EGFAYWGQGTLVTV
SEQ19-28C2HC      RYNPALKSRLTISKDTSNNQIFLKIASVDTADTATYYCARSHYYGTFYFDYWGQGTTLTV
SEQ21-9D6hC       RYNPTLKSRLTISKDTSNNQVFLKIANMDTADIATYYCARSHYNGTFYFDFWGQGITLTV
                   *    *       *                  * * * *           *  ** *   **

SEQ08-1H6HC       SS
SEQ1Q-38A8HC      SS
SEQ12-18F7HC      SS
SEQ23-28F4HC      S-
SSEQ19-28C2HC     SS
SEQ21-9D6HC       SS
                  *
```

FIG. 9

VH Sequences Clustered According to Competition with Fibrinogen

Only sequences with both VH and VL included

CLUSTAL 2.1 multiple sequence alignment

No Fibrinogen Competition

```
                                                 Kabat 24-34                    Kabat 50-56
                                                      CDR1                           CDR2
SEQ04-2A2LC       ENVLTQSPAIMSASLGEKVTMSCRASSSVN-YMYWYQQKSDASPKLWIYYTSNLAPGVPT
SEQ02-34D10LC     ENVLTQSPAIMSASLGEKVTMSCRASSSVN-YMYWYQQKSDASPKLWIYYTSNLAPGVPA
SEQ11-38A8LC      DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYLQKPDGTVKLLIYYTSRLHSGVPS
SEQ15-12B2LC      DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHSGVPS
                                          ***     *                 *** *

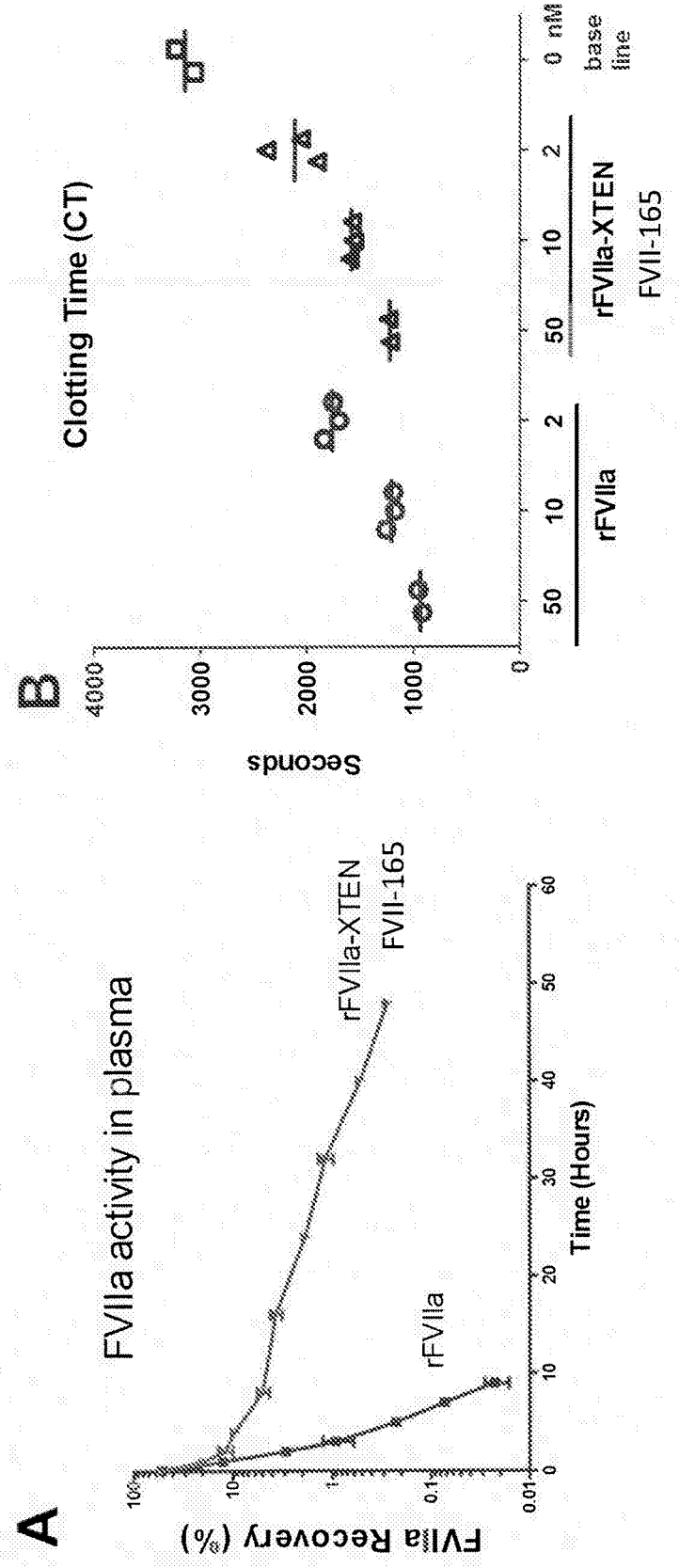
                                                 Kabat 89-97
                                                      CDR3
SEQ04-2A2LC       RFSGSGSGNSYSLTISSLEGEDAGTYYCQQFSSSPWTFGGGTKLEIKR
SEQ02-34D10LC     RFSGSGSGNSYSLTISSMEGEDAATYYCQQFSSSPWTFGGGTKLEIKR
SEQ11-38A8LC      RFSGSGSGTDYSLSISNLEQEDIATYFCQQGYTLPYTFGGGTKLEIKR
SEQ15-12B2LC      RFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPPTFGGGTKLEIKR

Fibrinogen Competition
                                                 Kabat 24-34                    Kabat 50-56
                                                      CDR1                           CDR2
SEQ09-1H6LC       DIQMTQTTSSLSASLGDRVTISCRASQDITNYLNWYQRKPDGTVKLLIYYTSRLHSGVPS
SEQ13-18F7LC      DVQMIQSPFSLSASLGDIVTMTCRASQGTSINLNWFQQKPGKAPKLLIYGVSNLEDGVPS
SEQ06-36A8LC      ENVLTQSPAIMSASLGEKVTMNCRASSSVN-YMYWYQQKSDASPKLWIHYTSNLAPGVPA
SEQ20-28C2LC      DVQITQSPSYLAASPGETITINCRASKSISKYLAWYQEKPGTTYKLLIYSGSTLQSGIPS
SEQ22-9D6LC       DVQITQSPSYLAASPGETITINCRASKSISKYLAWYQEKPGKTNKLLIYSGSTLQSGIPS
SEQ24-28F4LC      DIVLTQSPATLSVTPGDSVSLSCRASQSISNNLHWYQQKSHESPRLLIKYASHSISGIPS

                                                 Kabat 89-97
                                                      CDR3
SEQ09-1H6LC       RFSGSGSGTDYSLTISNLEQEDIATYFCQQGYTLPYTFGGGTKLEIKR
SEQ13-18F7LC      RFSGSRYGTDFTLTIGSLEDEDMATYFCLQHSYLPYTFGGGTKLEIKR
SEQ06-36A8LC      RFSGSGSGNSYSLTISSMEGEDAATYYCQQFSSSPWTFGGGSKLEIKR
SEQ20-28C2LC      RFSGSGSGTDFTLTISSLEPEDFAMYYCQQHIEYPWTFGGGTKLEIKR
SEQ22-9D6LC       RFSGSGSGTDFTLTISTLEPEDFAMYYCQQHIEYPWTFGGGTKLEIKR
SEQ24-28F4LC      RFSGSGSGTDFTLSINSVETEDFGMYFCQQSNNWPFTFGSGTKLEIKR
```

FIG. 10

FIG. 11. rFVIIa-XTEN PK and activity



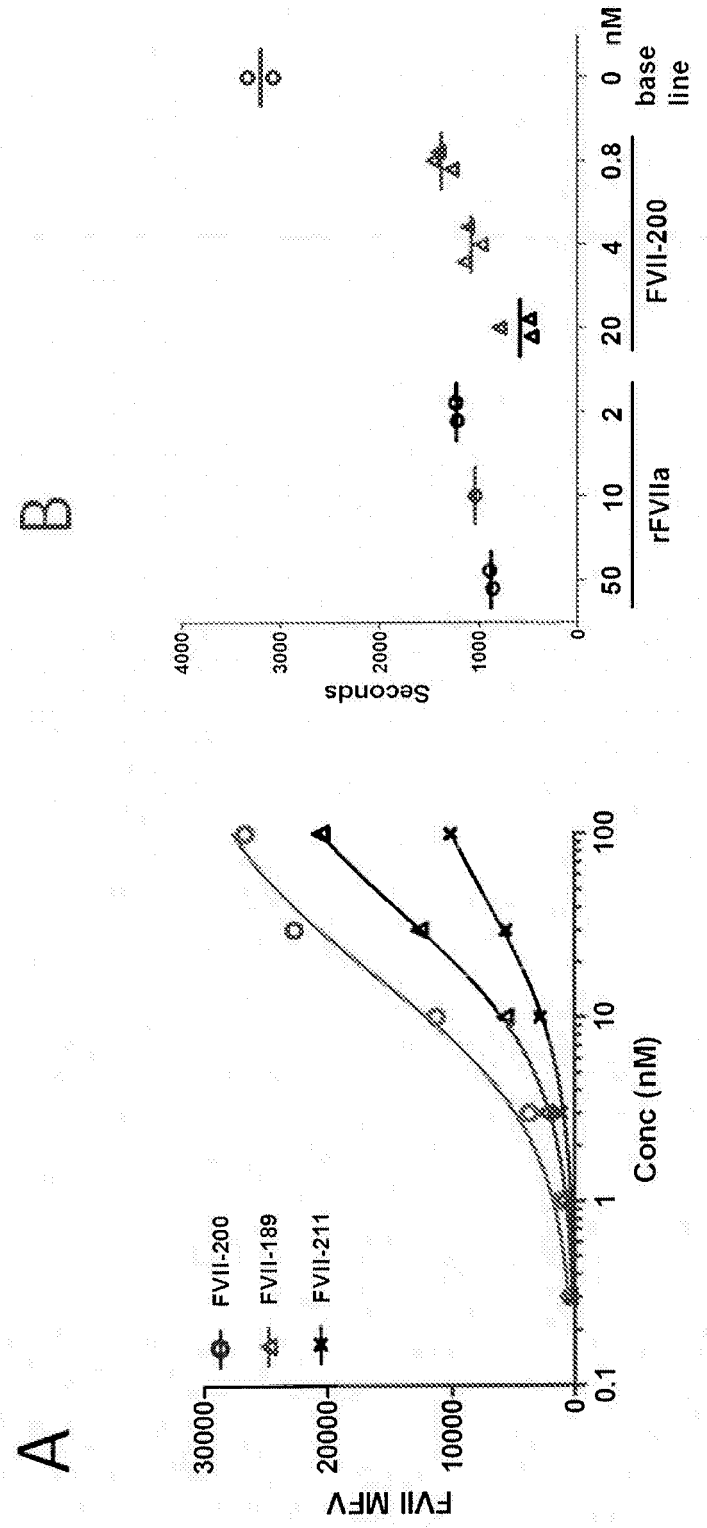

A
FVII MFV
30000
20000
10000
0
0.1
1
10
100
Conc (nM)
FVII-200
FVII-189
FVII-211
B
Seconds
4000
3000
2000
1000
0
50
10
2
rFVIIa
20
4
0.8
FVII-200
0 nM
base line

FIG. 12

PK analysis in human αIIb transgenic mice

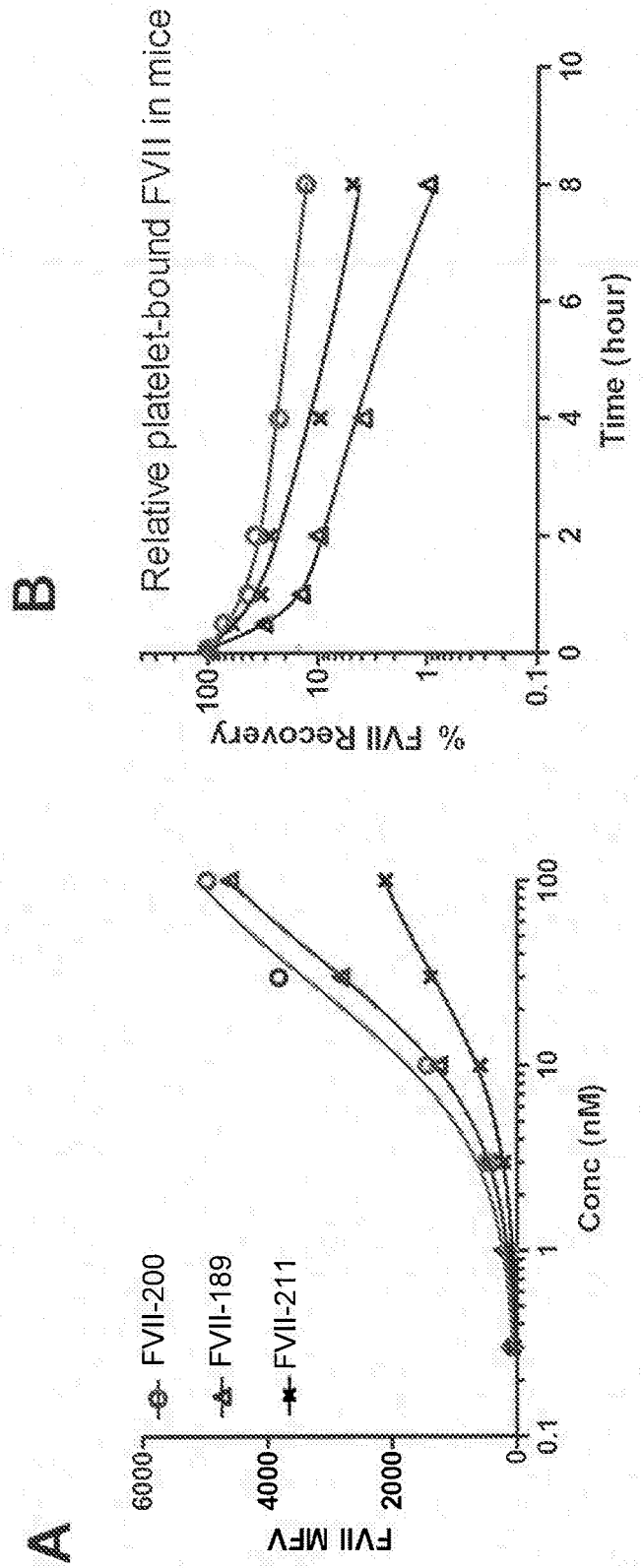


FIG. 13

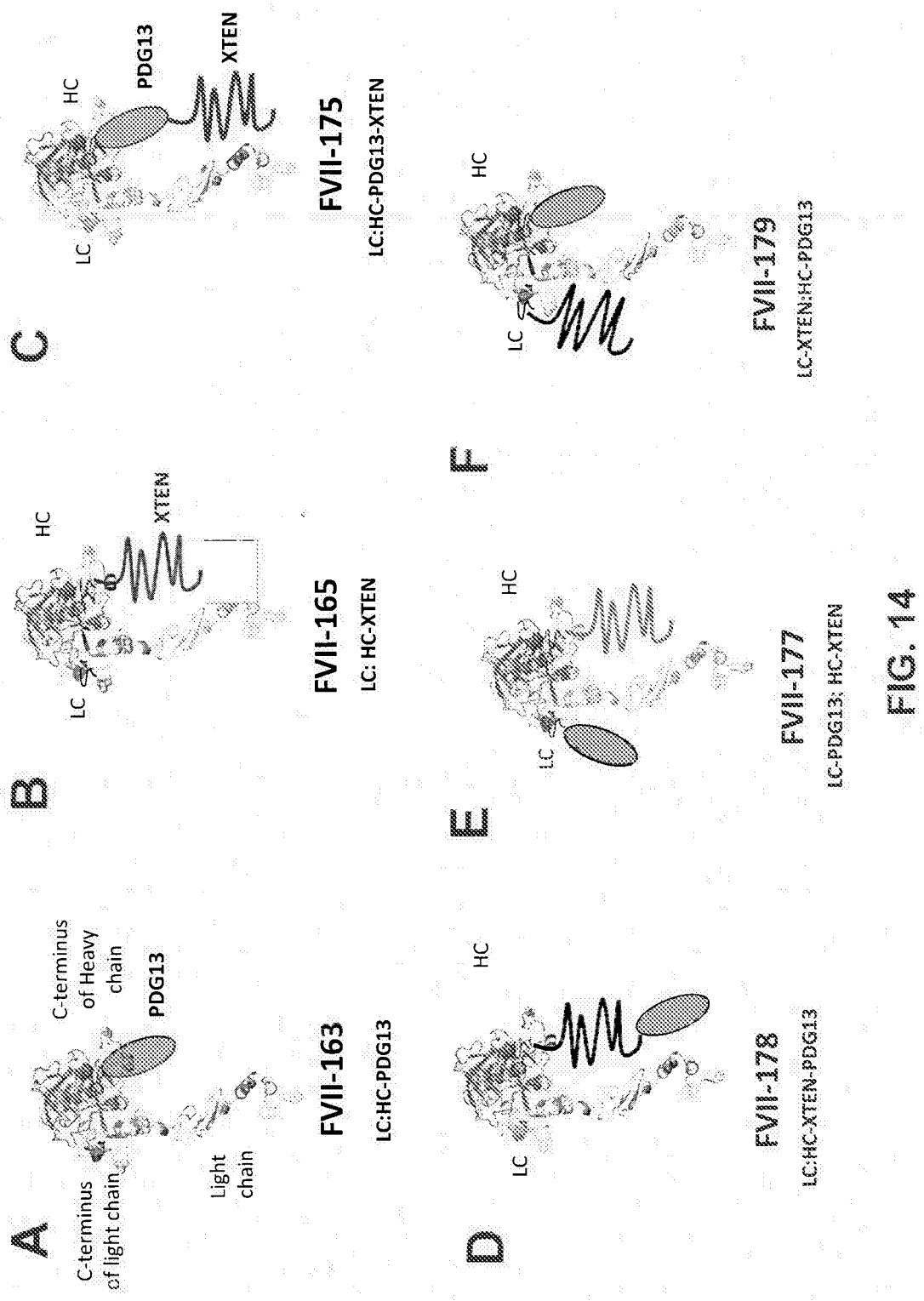

A
C-terminus of light chain
C-terminus of Heavy chain
PDG13
Light chain
FVII-163
LC:HC-PDG13
B
HC
XTEN
LC
FVII-165
LC: HC-XTEN
C
HC
PDG13
XTEN
LC
FVII-175
LC:HC-PDG13-XTEN
D
HC
LC
FVII-178
LC:HC-XTEN-PDG13
E
HC
LC
FVII-177
LC-PDG13; HC-XTEN
F
HC
LC
FVII-179
LC-XTEN:HC-PDG13

FIG. 14

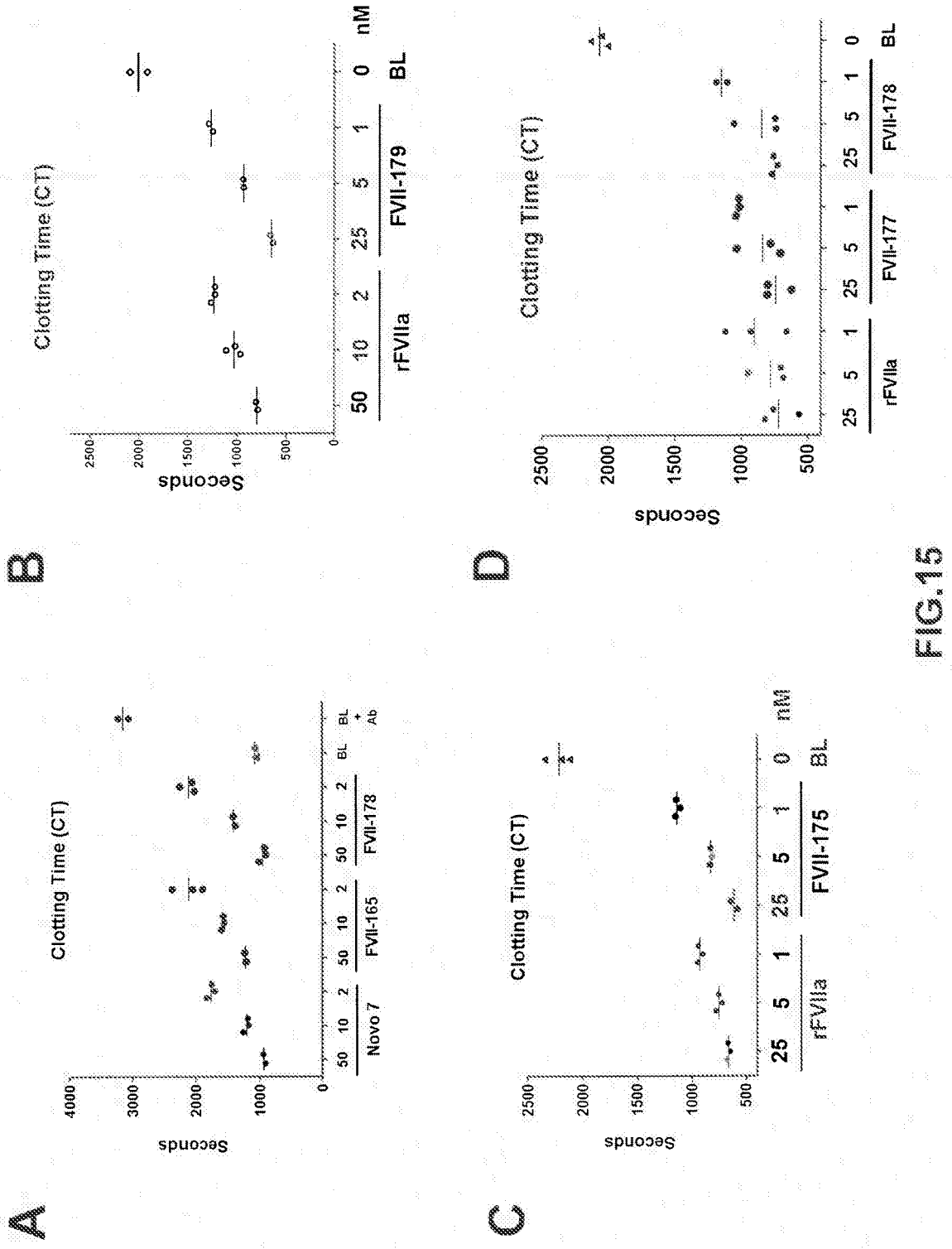

A
Clotting Time (CT)
Seconds
4000
3000
2000
1000
0
50 10 2 50 10 2 50 10 2 BL BL + Ab
Novo 7
FVII-165
FVII-178
B
Clotting Time (CT)
Seconds
2500
2000
1500
1000
500
0
50 10 2 25 5 1 0 nM BL
rFVIIa
FVII-179
C
Clotting Time (CT)
Seconds
2500
2000
1500
1000
500
25 5 1 25 5 1 0 nM BL
rFVIIa
FVII-175
D
Clotting Time (CT)
Seconds
2500
2000
1500
1000
500
25 5 1 25 5 1 25 5 1 0 BL
rFVIIa
FVII-177
FVII-178

FIG.15

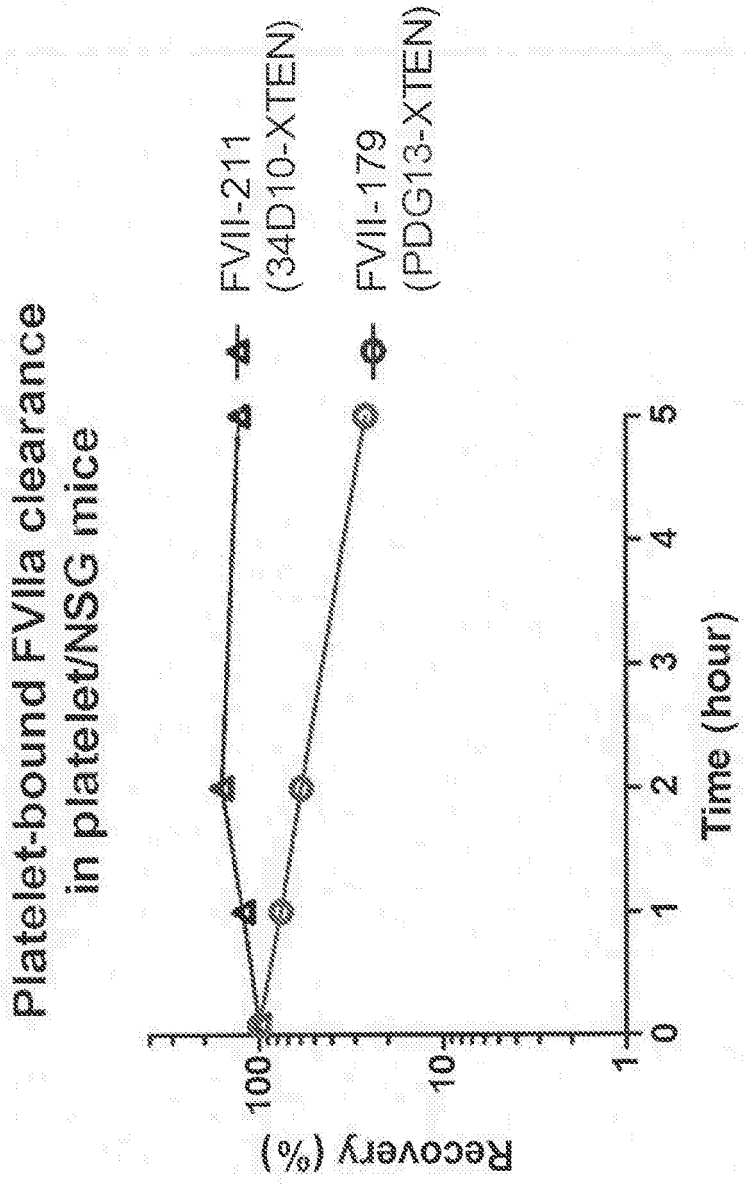

Platelet-bound FVIIa clearance
in platelet/NSG mice
FVII-211
(34D10-XTEN)
FVII-179
(PDG13-XTEN)
Recovery (%)
100
10
1
0
1
2
3
4
5
Time (hour)

FIG. 16

XTEN Technology
A.
XTEN AE 288
GTSESATPESGP GSEPATSGSETP GTSESATPESGP GSEPATSGSETP
GTSESATPESGP GTSTEPSEGSAP GSPAGSPTSTEE GTSESATPESGP
GSEPATSGSETP GTSESATPESGP GSPAGSPTSTEE GSPAGSPTSTEE
GTSTEPSEGSAP GTSESATPESGP GTSESATPESGP GTSESATPESGP
GSEPATSGSETP GSEPATSGSETP GSPAGSPTSTEE GTSTEPSEGSAP
GTSTEPSEGSAP GSEPATSGSETP GTSESATPESGP GTSTEPSEGSAP
B.
GFP-XTEN
Days: 0 1 7
Monkey plasma
Monkey in vivo
Rat kidney homogenate
Anti-GFP
rFVIIa
heavy chain
light chain
rFVIIa-XTEN

FIG. 17

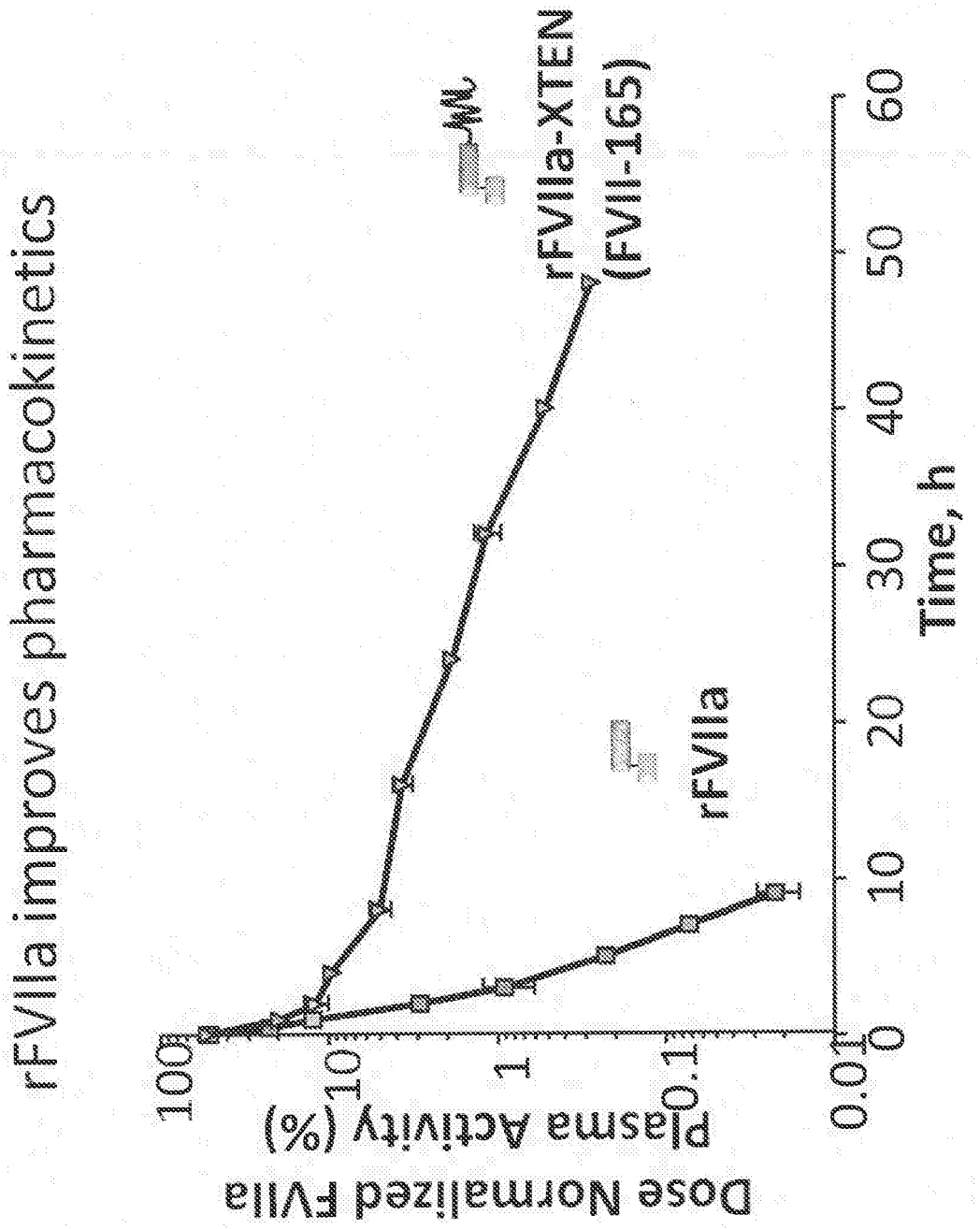

rFVIIa improves pharmacokinetics
rFVIIa-XTEN
(FVII-165)
rFVIIa
Dose Normalized FVIIa
Plasma Activity (%)
100
10
1
0.1
0.01
0
10
20
30
40
50
60
Time, h

FIG. 18

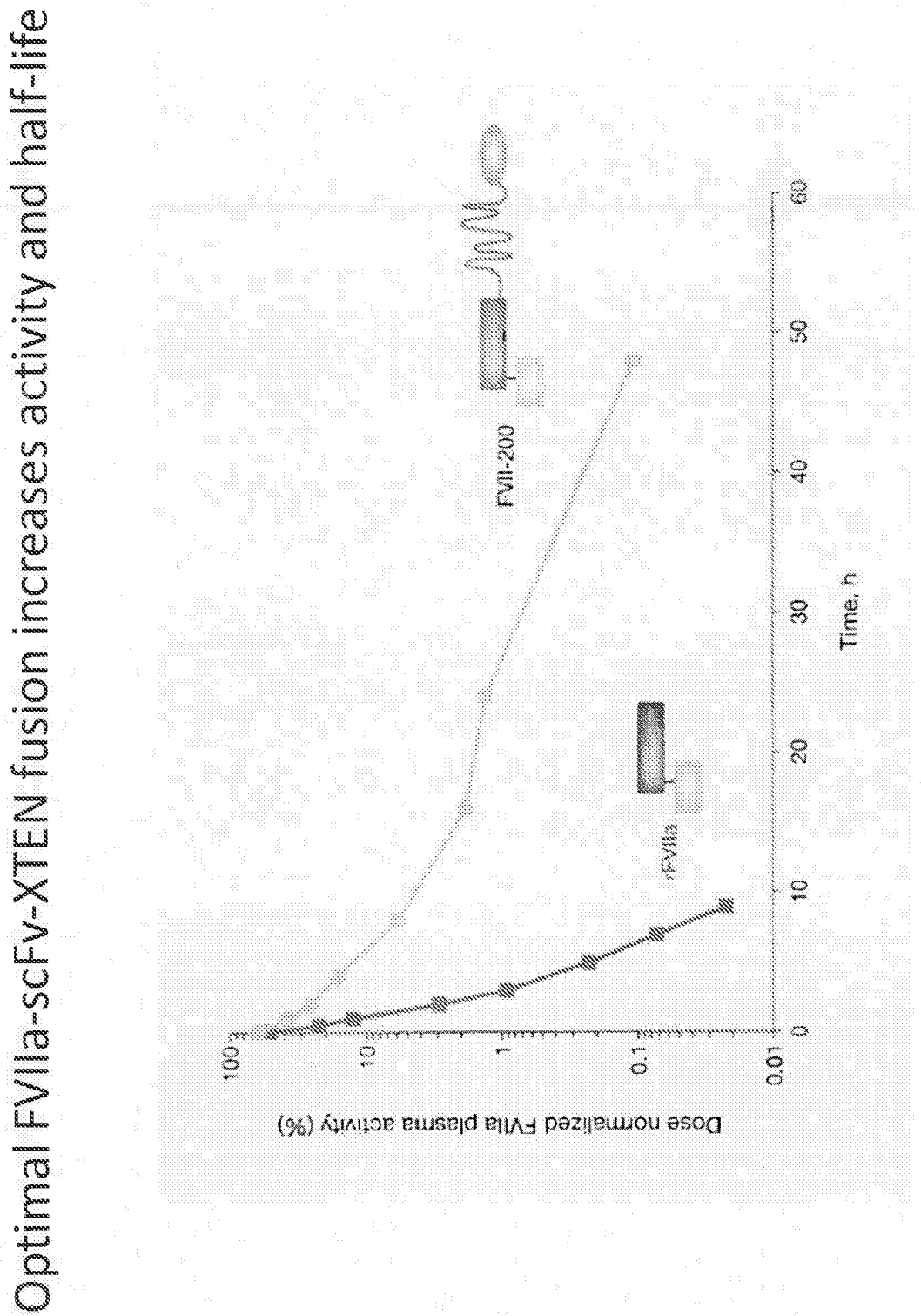

Optimal FVIIa-scFv-XTEN fusion increases activity and half-life
Dose normalized FVIIa plasma activity (%)
100
10
1
0.1
0.01
0
10
20
30
40
50
60
Time, h
rFVIIa
FVII-200

FIG. 19

Figure 20A-C. Activity of platelet targeted rFVIIa-XTEN variants determined by sTF-PT method

Configuration A

LC-XTEN	HC-XTEN	FVII-XXX
72	NA	FVII-227
144	NA	FVII-228
288	NA	FVII-211

Fig. 20A

Configuration B

LC-XTEN	HC-XTEN	FVII-XXX
NA	72	FVII-231
NA	144	FVII-232
NA	288	FVII-200

Fig. 20B

Configuration C

LC-XTEN	HC-XTEN	FVII-XXX
42	72	FVII-242
72	42	FVII-243
72	72	FVII-238

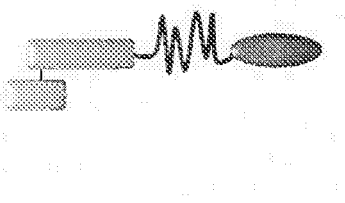
Fig. 20C

Figure 21A-D. Activity of platelet targeted rFVIIa-XTEN variants determined by ROTEM method



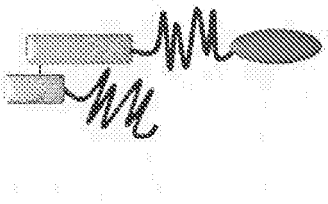
Configuration A

LC-XTEN	HC-XTEN	FVII-XXX
72	NA	FVII-227
144	NA	FVII-228
288	NA	FVII-211



Configuration B

LC-XTEN	HC-XTEN	FVII-XXX
NA	72	FVII-231
NA	144	FVII-232
NA	288	FVII-200



Configuration C

LC-XTEN	HC-XTEN	FVII-XXX
42	72	FVII-242
72	42	FVII-243
72	72	FVII-238

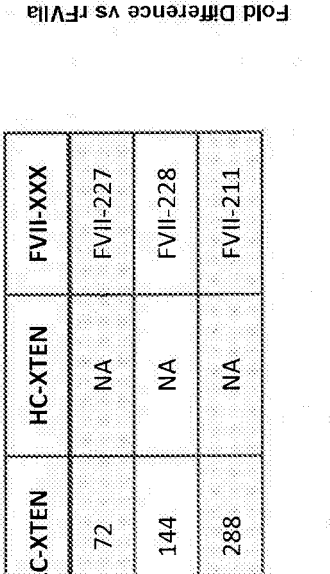


Fig. 21A

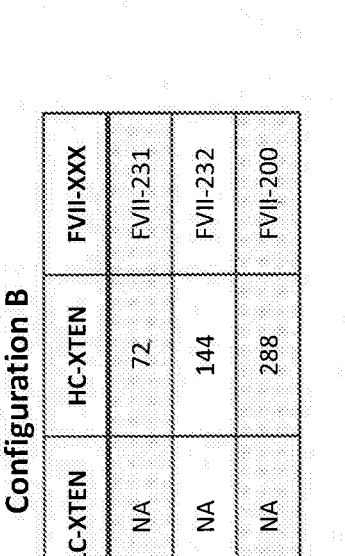


Fig. 21B

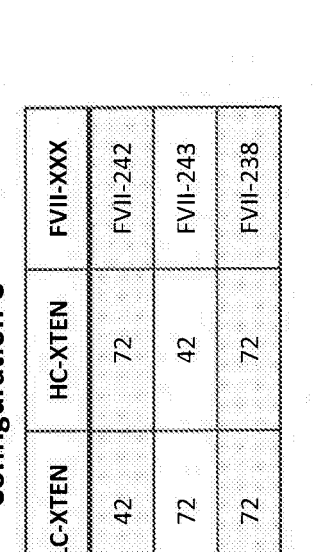


Fig. 21C

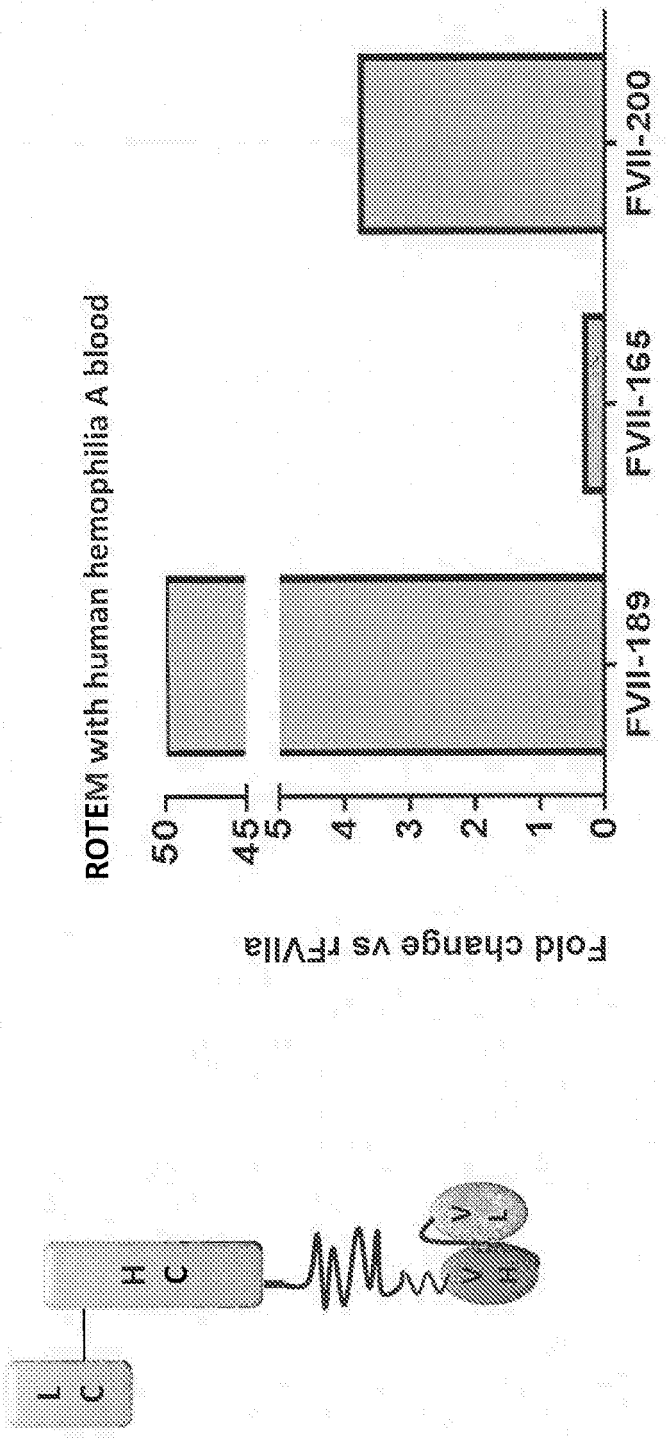
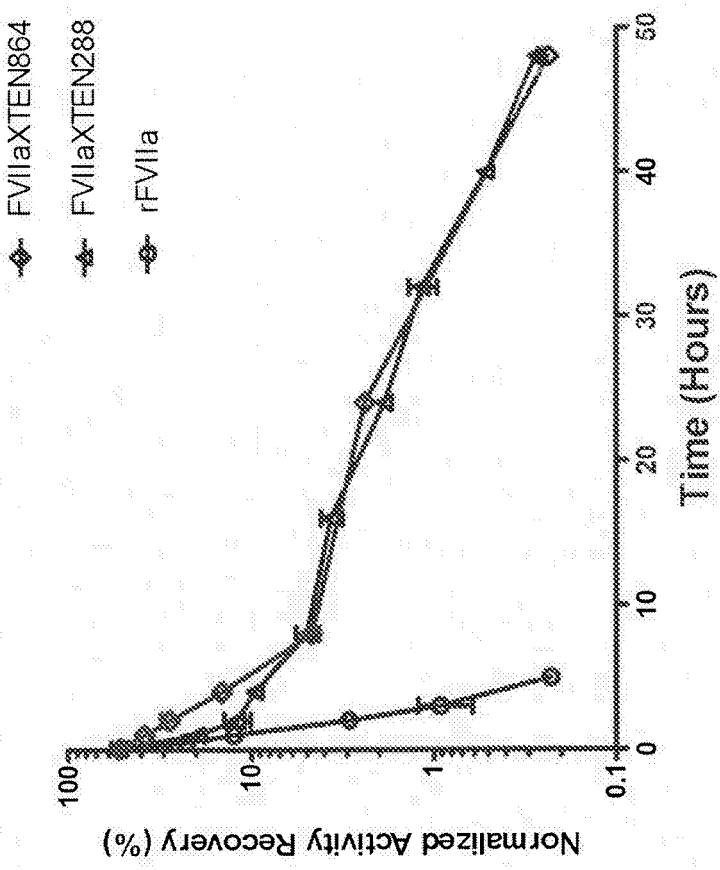

ROTEM with human hemophilia A blood
Fold change vs rFVIIa
50
45
5
4
3
2
1
0
FVII-189
FVII-165
FVII-200
L C
H C
FVII-200

Fig. 21D

A single XTEN with amino acid of 288 is sufficient for PK improvement



XTEN length longer than 288 did not provide additional PK benefit

FIG. 22

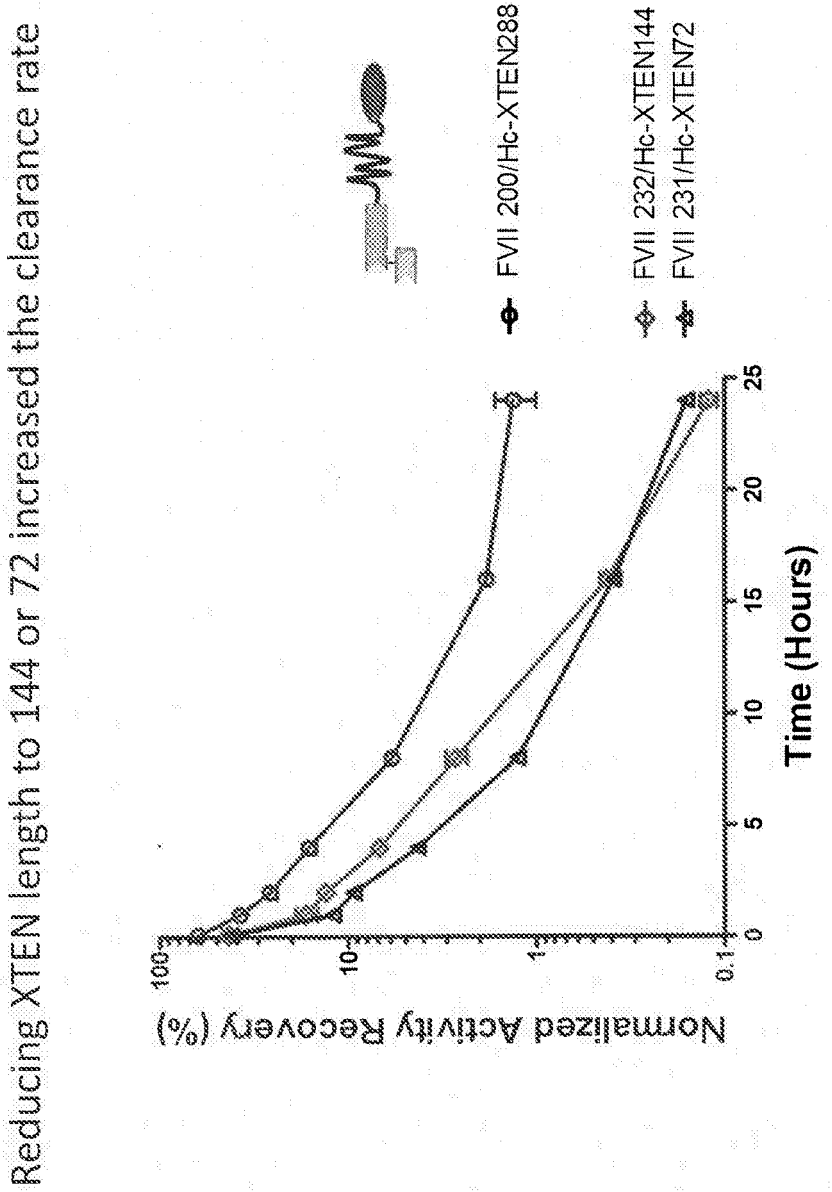
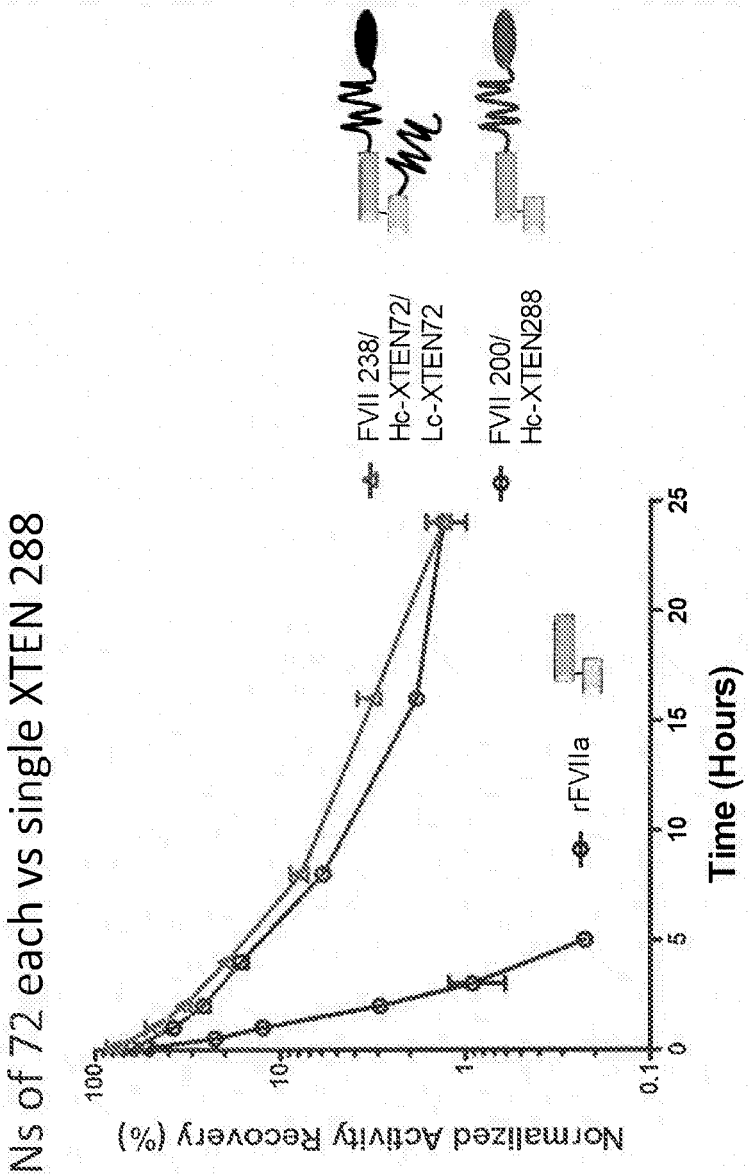

Reducing XTEN length to 144 or 72 increased the clearance rate
FVII 200/Hc-XTEN288
FVII 232/Hc-XTEN144
FVII 231/Hc-XTEN72
Normalized Activity Recovery (%)
100
10
1
0.1
0
5
10
15
20
25
Time (Hours)

FIG. 23



Treatment	CL (ml/hr/kg)	MRT (hr)	Vss (mL/kg)	AUC/D (hr*kg/L)	AUC ratio to rFVIIa
FVII-200	16.47	12.79	210.71	60.71	6.62
FVII-238	14.63	6.28	91.8	68.36	7.46
rFVIIa	109.1	0.82	89.54	9.17	1.00

FIG. 24

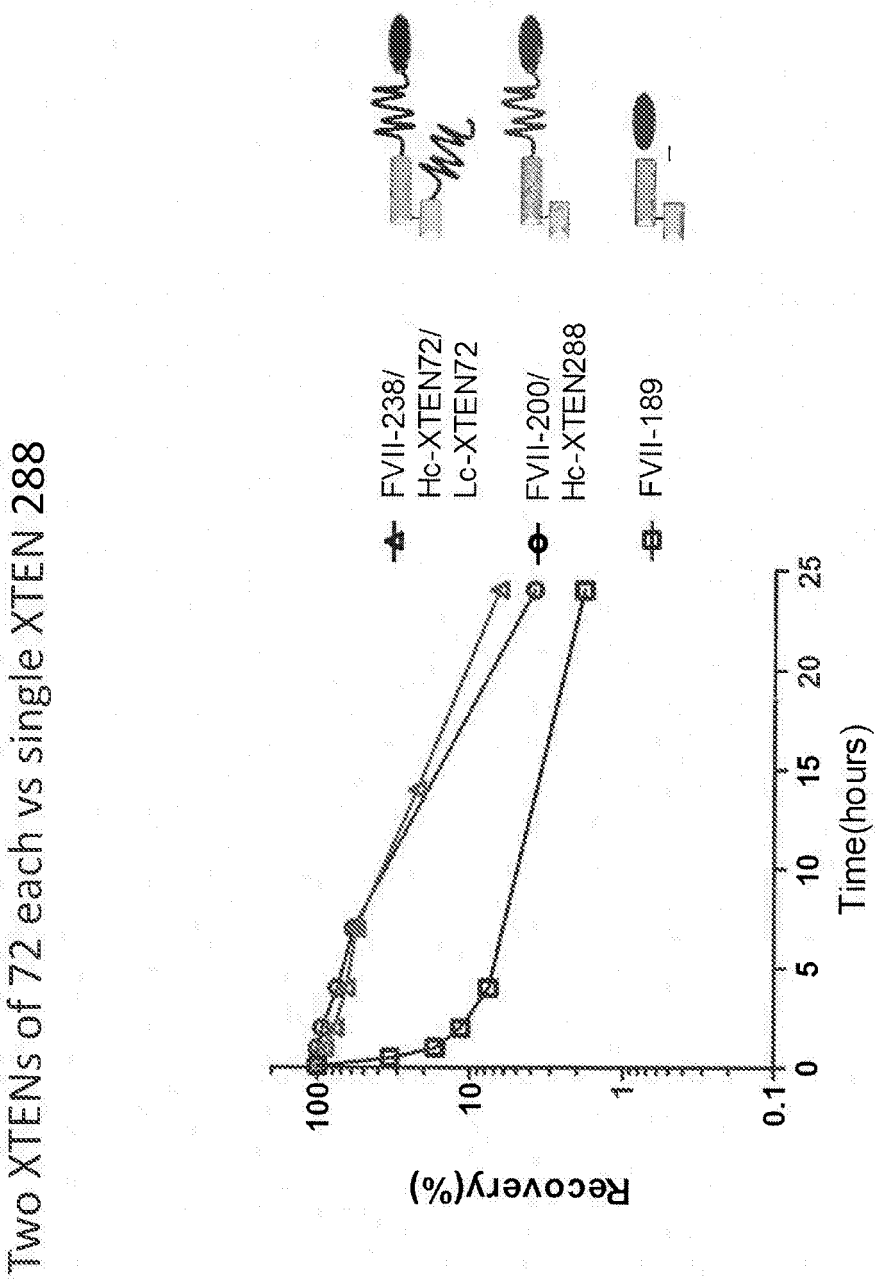

Two XTENs of 72 each vs single XTEN 288
FVII-238/
Hc-XTEN72/
Lc-XTEN72
FVII-200/
Hc-XTEN288
FVII-189
Recovery(%)
100
10
1
0.1
0
5
10
15
20
25
Time(hours)

FIG. 25

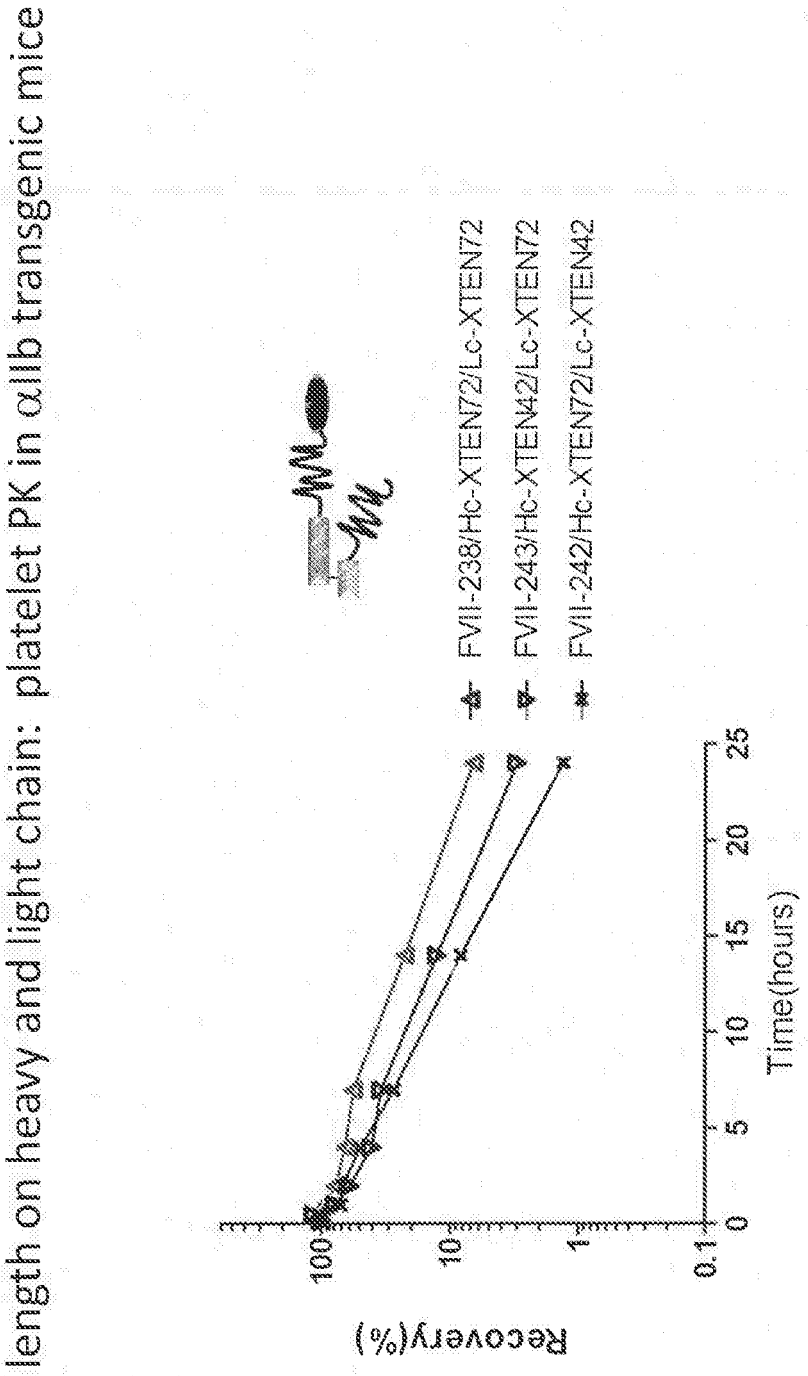

XTEN length on heavy and light chain: platelet PK in αIIb transgenic mice
FVII-238/Hc-XTEN72/Lc-XTEN72
FVII-243/Hc-XTEN42/Lc-XTEN72
FVII-242/Hc-XTEN72/Lc-XTEN42
Recovery(%)
100
10
1
0.1
0
5
10
15
20
25
Time(hours)

FIG. 26