

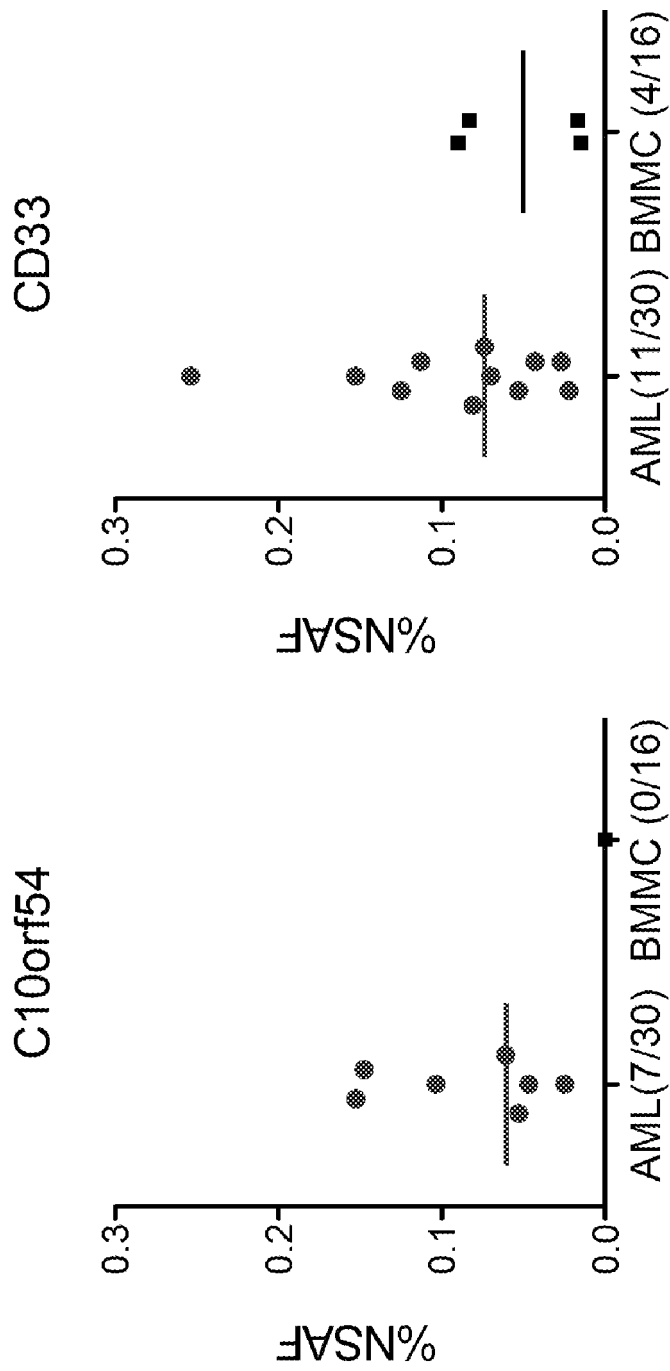


FIG. 1A

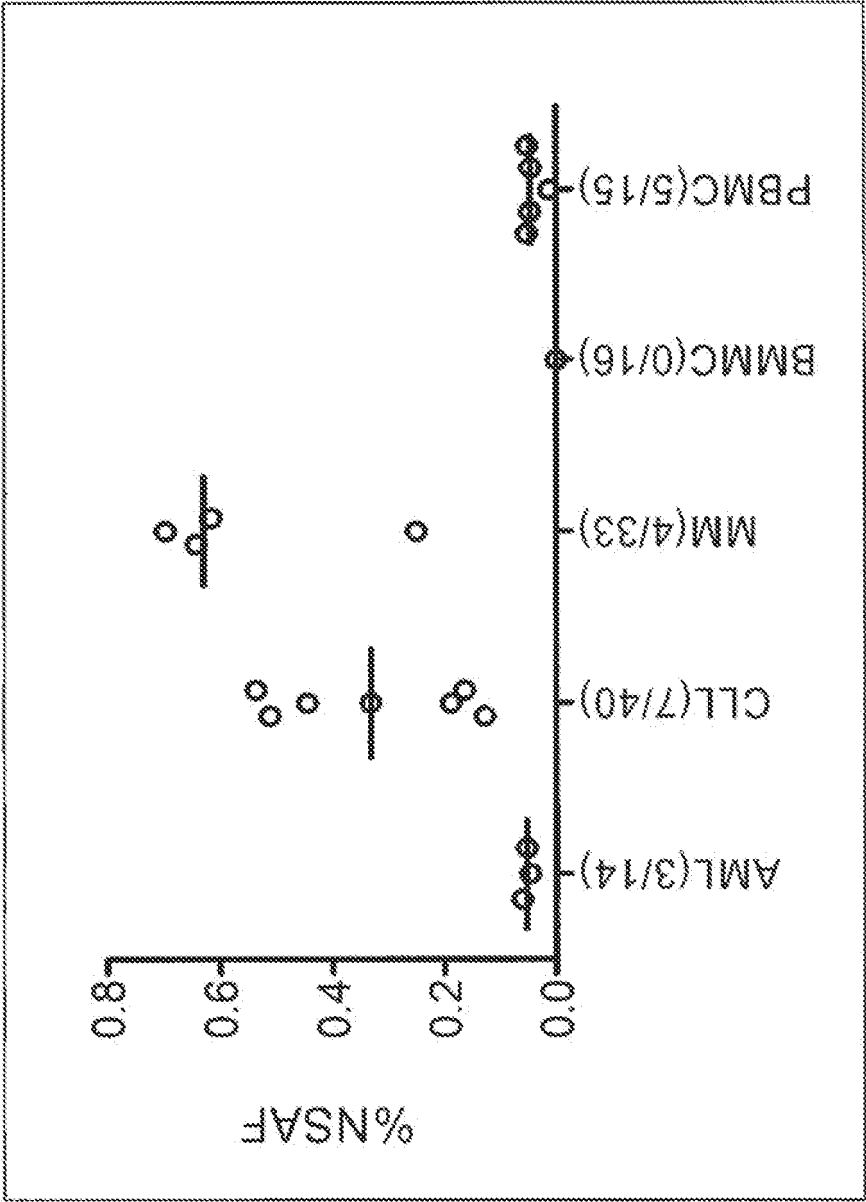


FIG. 1B

|          | CD13 <sup>+</sup> /CD33 <sup>+</sup> |          |          |  | CD34 <sup>+</sup> /CD33 <sup>+</sup> |          |          |  | CD34 <sup>+</sup> /CD33 <sup>-</sup> |          |          |  |
|----------|--------------------------------------|----------|----------|--|--------------------------------------|----------|----------|--|--------------------------------------|----------|----------|--|
|          | Incidence <sup>*</sup>               | Pos, [%] | Fold MFI |  | Incidence <sup>*</sup>               | Pos, [%] | Fold MFI |  | Incidence <sup>*</sup>               | Pos, [%] | Fold MFI |  |
| C10ORF54 |                                      |          |          |  |                                      |          |          |  |                                      |          |          |  |
| AML      | 18/23<br>(3 relapses)                | 31       | 48.6     |  | 10/21<br>(3 relapses)                | 41       | 50.9     |  | 9/21<br>(3 relapses)                 | 25       | 8.5      |  |
| BMNC     | 3/3                                  | 75       | 28.1     |  | 1/3                                  | 31       | 0.9      |  | 0/3                                  | 1.5      | 0.5      |  |

FIG. 2



huVH3  
Potential humanized sequence based on IMGT IGHV3-48 acceptor framework (method 2)  
EVQLVESGGGLVQPGGSLRLSCAAS **GFTFSSYS****MIN** WVRQAPGKGLEWVS **YISSSSTIYADSVK**G RFTISRDNAKNSLYQMNSLRAEDTAVYYCAR

Joining region  
IMGT J00256|IGHJ4\*01|YFDYWGQTLVTVSS

| seq    | 10               | 20                   | 30                  | 40             | 50                      | 60      | 70                     | 80                      | 90                               |
|--------|------------------|----------------------|---------------------|----------------|-------------------------|---------|------------------------|-------------------------|----------------------------------|
| 76E1   | b b b            | b b b                | b b b               | b i i          | i i b b                 | b b     | i b                    | b b b                   | b b b                            |
|        | EVQL             | LSGPELEKPGASVKISCKAS | <b>GYSFTGYN</b> MIN | WVKQSN         | KGSL                    | EWIG    | <b>NIDPYDY</b> TSYNLKF | KD                      | KATLTVDKSSSTAYMQLKSLTSEDSAVYYCAT |
|        | ** ** *          | ** ** *              | ** ** *             | ** ** *        | ** ** *                 | ** ** * | ** ** *                | ** ** *                 | ** ** *                          |
| huVH3a | EVQL             | VESGGLVQPGGSLRLSCAAS | <b>GYSFTGYN</b> MIN | WVRQAPGKGLEWVS | <b>NIDPYDY</b> TSYNLKF  | KD      | RFTISRDN               | AKNSLYQMNSLRAEDTAVYYCAR | I                                |
|        | Q                | V I                  | Q                   | S              | <u>IG</u>               | E       | Q                      | A L <u>Y K</u>          | S A M L                          |
|        |                  |                      | S                   | S              | S                       |         | S                      |                         |                                  |
|        |                  |                      | D                   | A              | A                       |         | D                      |                         |                                  |
|        |                  |                      | A                   | A              | A                       |         | A                      |                         |                                  |
| AbM    | 10               | 20                   | 30                  | 40             | 50                      | a       | 60                     | 70                      | abc                              |
| huVH3b | EVQL             | VESGGLVQPGGSLRLSCAAS | <b>GYSFTGYN</b> MIN | WVRQAPGKGLEWVS | <b>NIDPYDY</b> TSYADSVK | G       | RFTISRDN               | AKNSLYQMNSLRAEDTAVYYCAR | I                                |
|        | Q                | V I                  | Q                   | S              | <u>IG</u>               | E       | F                      | A L <u>Y K</u>          | S A M L                          |
|        |                  |                      | S                   | S              | S                       |         | S                      |                         |                                  |
|        |                  |                      | D                   | A              | A                       |         | D                      |                         |                                  |
|        |                  |                      | A                   | A              | A                       |         | A                      |                         |                                  |
| seq    | 100              | 110                  |                     |                |                         |         |                        |                         |                                  |
| 76E1   | ib               | i b b b              |                     |                |                         |         |                        |                         |                                  |
|        | <b>STMITPFDY</b> | <b>WGQGT</b> TLTVSS  |                     |                |                         |         |                        |                         |                                  |
|        |                  | **                   |                     |                |                         |         |                        |                         |                                  |
| huVH3a | <b>STMITPFDY</b> | <b>WGQGT</b> TLTVSS  |                     |                |                         |         |                        |                         |                                  |
|        | L                | L                    |                     |                |                         |         |                        |                         |                                  |
| AbM    | 100a             | 110                  |                     |                |                         |         |                        |                         |                                  |
| huVH3b | <b>STMITPFDY</b> | <b>WGQGT</b> TLTVSS  |                     |                |                         |         |                        |                         |                                  |
|        | L                | L                    |                     |                |                         |         |                        |                         |                                  |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international ImMuNoGeNeTics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
- (3) Residue numbering shown as sequential (seq) or according to website [www.bioinf.org.uk/abs/](http://www.bioinf.org.uk/abs/) (AbM).
- (4) "b" notes buried sidechain; "i" notes sidechain at interface between VH and VL domains.
- (5) Sequence differences between each humanized sequence and murine sequence noted by asterick (\*).
- (6) Potential humanized framework mutations from human sequence to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.
- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isoaspartate formation or Asp-Pro (DP) bond cleavage.

FIG. 3B

huVH1

Potential humanized sequence based on IMGT IGHV1-18 acceptor framework (method 1)

QVQLVQSGAEVKKPGASVKCKAS **GYTFTSYGIS** WVRQAPGQGLEWMG **WISAYNGNTNYAQLQG** RVTMTTDTSTSTAYMELSLRSDDTAVYYCAR

FIG. 4A

Joining region  
IMGT 00256|IGHJ4\*01|YFDYWGQGLVTVSS

|        |                           |                   |                |                          |                                  |     |       |       |       |
|--------|---------------------------|-------------------|----------------|--------------------------|----------------------------------|-----|-------|-------|-------|
| seq    | 10                        | 20                | 30             | 40                       | 50                               | 60  | 70    | 80    | 90    |
|        | b b b                     | b b b             | b b b          | b i i                    | i i b b                          | i b | b b b | b b b | b b b |
| 141A   | QVQLQQSGAELMKPGASVKISCKAT | <b>GYTFSRYWIE</b> | WKQRPCHGLEWIG  | <b>EILPGSGSTNYNEKFKG</b> | KATFTADTSSNTAYMQLSSLTSEDSAVYYCAG |     |       |       |       |
|        | *                         | **                | *              | *                        | *                                | *   | *     | *     | *     |
| huVH1a | QVQLVQSGAEVKKPGASVKVCKAS  | <b>GYTFSRYWIE</b> | WVRQAPGQGLEWMG | <b>EILPGSGSTNYNEKFKG</b> | RVTMTTDTSTSTAYMELSLRSDDTAVYYCAR  |     |       |       |       |
|        | M                         | I                 |                | I                        |                                  | Q Q | A F A | N     | G     |
|        |                           |                   |                |                          |                                  | S S |       |       |       |
|        |                           |                   |                |                          |                                  | D D |       |       |       |
|        |                           |                   |                |                          |                                  | A A |       |       |       |

|        |                          |                   |                |                         |                                 |     |       |    |    |
|--------|--------------------------|-------------------|----------------|-------------------------|---------------------------------|-----|-------|----|----|
| AbM    | 10                       | 20                | 30             | 40                      | 50                              | 60  | 70    | 80 | 90 |
| huVH1b | QVQLVQSGAEVKKPGASVKVCKAS | <b>GYTFSRYWIE</b> | WVRQAPGQGLEWMG | <b>EILPGSGSTNYAQLQG</b> | RVTMTTDTSTSTAYMELSLRSDDTAVYYCAR |     |       |    |    |
|        | M                        | I                 |                | I                       |                                 | Q F | A F A | N  | G  |
|        |                          |                   |                |                         |                                 | S   |       |    |    |
|        |                          |                   |                |                         |                                 | D   |       |    |    |
|        |                          |                   |                |                         |                                 | A   |       |    |    |

|      |            |            |       |
|------|------------|------------|-------|
| seq  | 100        | 110        | 120   |
|      | ib         | i          | b b b |
| 141A | EEVDGYPWFY | WGQGLVTVSA | *     |

|        |            |            |
|--------|------------|------------|
| huVH1a | EEVDGYPWFY | WGQGLVTVSS |
|        | E          |            |
|        | S          |            |
|        | A          |            |

|        |            |            |
|--------|------------|------------|
| AbM    | 100abcd    | 110        |
| huVH1b | EEVDGYPWFY | WGQGLVTVSS |
|        | E          |            |
|        | S          |            |
|        | A          |            |

- (1) CDR sequences noted in bold.
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- (5) Sequence differences between each humanized sequence and murine sequence noted by asterick (\*).
- (6) Potential humanized framework mutations from human sequence to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.
- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isoaspartate formation or Asp-Pro (DP) bond cleavage.



huVH1  
Potential humanized sequence based on IMGT IGHV1-18 acceptor framework (method 1)  
QVQLVQSGAEVKKPGASVKCKAS **GYTFTSYGIS** WVRQAPGQGLEWMG **WISAYNGNTNYAQLQG** RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR  
Joining region  
IMGT J00256|IGHJ4\*01|YFDYWGQTLVTVSS

|        |                           |                    |                |                          |                                  |          |       |       |       |
|--------|---------------------------|--------------------|----------------|--------------------------|----------------------------------|----------|-------|-------|-------|
| seq    | 10                        | 20                 | 30             | 40                       | 50                               | 60       | 70    | 80    | 90    |
|        | b b b                     | b b b              | b b b          | b b i                    | i i b b                          | b b i    | b b b | b b b | b b b |
| 175A   | QVQLQQSGAELMKPGASVKISCKAT | <b>GYTFTSTHWIE</b> | WVKQRPCHGLEWIG | <b>EILPCSGSTSYNEKFKG</b> | KATFTADTSSNTAYMQLSSLTSEDS        | SAVYYCAR |       |       |       |
|        | *                         | **                 | *              | *                        | *                                | *        | *     | *     | *     |
| huVH1a | QVQLVQSGAEVKKPGASVKVCKAS  | <b>GYTFTSTHWIE</b> | WVRQAPGQGLEWMG | <b>EILPCSGSTSYNEKFKG</b> | RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR |          |       |       |       |
|        | I                         |                    | I              |                          |                                  |          | A F A | N     |       |

|        |                          |                    |                |                         |                                  |    |    |       |    |
|--------|--------------------------|--------------------|----------------|-------------------------|----------------------------------|----|----|-------|----|
| AbM    | 10                       | 20                 | 30             | 40                      | 50                               | 60 | 70 | 80    | 90 |
| huVH1b | QVQLVQSGAEVKKPGASVKVCKAS | <b>GYTFTSTHWIE</b> | WVRQAPGQGLEWMG | <b>EILPCSGSTSYAQLQG</b> | RVTMTTDTSTSTAYMELRSLRSDDTAVYYCAR |    |    |       |    |
|        | I                        |                    | I              |                         |                                  |    | F  | A F A |    |

|        |                   |             |
|--------|-------------------|-------------|
| seq    | 100               | 110         |
|        | ib i b b b        |             |
| 175A   | <b>WLLYYYANDY</b> | WGQGTSVTVSS |
|        | *                 |             |
| huVH1a | <b>WLLYYYANDY</b> | WGQGTLVTVSS |
| AbM    | 100ab             | 110         |
| huVH1b | <b>WLLYYYANDY</b> | WGQGTLVTVSS |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international ImMuNoGeneTics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
- (3) Residue numbering shown as sequential (seq) or according to website [www.bioinf.org.uk/abs/](http://www.bioinf.org.uk/abs/) (AbM).
- (4) "b" notes buried sidechain; "i" notes sidechain at interface between VH and VL domains.
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- (6) Potential humanized framework mutations from human sequence to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.
- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isoaspartate formation or Asp-Pro (DP) bond cleavage.

FIG. 5A

huVH3

Potential humanized sequence based on IMGT IGHV3-48 acceptor framework (method 2)  
EVQLVESGGGLVQPGGSLRLSCAAS **GYTFSSYS**IN WVRQAPGKGLEWVS **YISSSSTI**YADSVKG RFTISRDNAKNSLYQMNSLRAEDTAVYYCAR

Joining region  
IMGT J00256|IGHJ4\*01|YFDYWGQTLVTVSS

|        |                           |                    |                |                           |                                  |     |         |       |       |
|--------|---------------------------|--------------------|----------------|---------------------------|----------------------------------|-----|---------|-------|-------|
| seq    | 10                        | 20                 | 30             | 40                        | 50                               | 60  | 70      | 80    | 90    |
|        | b b b                     | b b b              | b b b          | b b i                     | i i b b                          | b b | b b b   | b b b | b b b |
| 175A   | QVQLQQSGAELMKPGASVKISCKAT | <b>GYTFSTH</b> WIE | WVKQRPGHGLEWIG | <b>EILPCG</b> SGTSYNEKFKG | KATFTADTSSNTAYMQLSSLTSEDSAVYYCAR |     |         |       |       |
|        | * * * * *                 | * * * * *          | * * *          |                           |                                  |     |         |       |       |
| huVH3a | EVQLVESGGGLVQPGGSLRLSCAAS | <b>GYTFSTH</b> WIE | WVRQAPGKGLEWVS | <b>EILPCG</b> SGTSYNEKFKG | RFTISRDNAKNSLYQMNSLRAEDTAVYYCAR  |     |         |       |       |
|        | Q                         | V I                |                | <u>IG</u>                 |                                  | Q   | A F A I | A M L |       |
|        |                           |                    |                |                           |                                  | S   |         |       |       |
|        |                           |                    |                |                           |                                  | D   |         |       |       |
|        |                           |                    |                |                           |                                  | A   |         |       |       |

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|        |                           |                    |                |                           |                                 |    |         |       |    |
|--------|---------------------------|--------------------|----------------|---------------------------|---------------------------------|----|---------|-------|----|
| AbM    | 10                        | 20                 | 30             | 40                        | 50                              | 60 | 70      | 80    | 90 |
| huVH3b | EVQLVESGGGLVQPGGSLRLSCAAS | <b>GYTFSTH</b> WIE | WVRQAPGKGLEWVS | <b>EILPCG</b> SGTSYADSVKG | RFTISRDNAKNSLYQMNSLRAEDTAVYYCAR |    |         |       |    |
|        | Q                         | V I                |                | <u>IG</u>                 |                                 | F  | A F A I | A M L |    |

|        |                   |             |
|--------|-------------------|-------------|
| seq    | 100               | 110         |
|        | ib                | i b b b     |
| 175A   | <b>WLLYYYANDY</b> | WGQGTSVTVSS |
|        |                   | *           |
| huVH3a | <b>WLLYYYANDY</b> | WGQGTLVTVSS |
|        |                   |             |
| AbM    | 100ab             | 110         |
| huVH3b | <b>WLLYYYANDY</b> | WGQGTLVTVSS |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international ImMuNoGeNeTiCs information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
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FIG. 5B

huVK2  
Potential humanized sequence based on IMGT IGKV2-28 acceptor framework (method 1)  
DIVMTQSP<sup>LS</sup>LPVTPGEPASISC **RSSQSLHSNGVNYLD** WYLQKPGQSPQLLIY **LGSNRAS** GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC **MQALQTP**

Joining region  
IMGT J00242|IGKJ2\*01|YTFGQGTKLEIK

|       |          |                 |               |                   |                 |                                                 |                   |                 |                                             |
|-------|----------|-----------------|---------------|-------------------|-----------------|-------------------------------------------------|-------------------|-----------------|---------------------------------------------|
| seq   | 10       | 20              | 30            | 40                | 50              | 60                                              | 70                | 80              | 90                                          |
| AbM   | 10       | 20              | 30abcde       | 40                | 50              | 60                                              | 70                | 80              |                                             |
|       | b b b    | b b b           | b b b         | b i b i           | i i i b b i     | i b b                                           | b b b             | b b b           | b b b                                       |
| 76E1  | DVLM     | QTPLSLP         | VS            | LG                | DQASISC         | <b>RSSQSI</b>                                   | <b>VHSNGNTYLE</b> | WYLQKPGQSPKLLIY | <b>KVSNRFS</b> GVPDRFSGSGSGTDFTLKINRVEAEDLG |
|       | **       | *               | **            | **                | *               | *                                               | *                 | *               | *                                           |
| huVK2 | DIVMTQSP | LSLPVTPGEPASISC | <b>RSSQSI</b> | <b>VHSNGNTYLE</b> | WYLQKPGQSPQLLIY | <b>KVSNRFS</b> GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC |                   |                 |                                             |
|       | V        |                 | Q             | Q                 | Q               | S                                               | S                 | D               | A                                           |

|       |                  |            |
|-------|------------------|------------|
| seq   | 100              | 110        |
| AbM   | 90               | 100        |
|       | i b i            | i b b      |
| 76E1  | <b>FGGSHVPWT</b> | FGGGTKLEIK |
|       | *                |            |
| huVK2 | <b>FGGSHVPWT</b> | FGGGTKLEIK |

- (1) CDR sequences noted in bold.  
(2) Human germline and joining sequences from IMGT® the international Immunogenetics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).  
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(5) Sequence differences between each humanized sequence and murine sequence noted by asterick (\*).  
(6) Potential humanized framework mutations from human sequences to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.  
(7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isooaspartate formation or Asp-Pro (DP) bond cleavage.

FIG. 6A

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huVK1

Potential humanized sequence based on IMGT IGV1-39 acceptor framework (method 2)

DIQMTQSPSSLSASVGDRVTITC **RASQSISSYLN** WYQKPGKAPKLLIY **AASSLQS** GVPSRFSGSGGTDFTLTISSLQPEDFATYYC **QQSYSTP**

Joining region

IMGT J00242|IGKJ2\*01|YTFGQGTKLEIK

|       |       |         |         |         |             |        |        |         |         |
|-------|-------|---------|---------|---------|-------------|--------|--------|---------|---------|
| seq   | 10    | 20      | 30      | 40      | 50          | 60     | 70     | 80      | 90      |
| AbM   | 10    | 20      | 30abcde | 40      | 50          | 60     | 70     | 80      |         |
|       | b b b | b b b   | b b b   | b i b i | i i i b b i | i b b  | b b b  | b b b   | b b b   |
| 76E1  | DVLM  | QTPLSLP | VS      | LG      | QASIS       | C      | RSSQSI | VH      | SN      |
|       | ***   | ***     | ***     | ***     | ***         | ***    | ***    | ***     | ***     |
| huVK1 | DIQMT | QSPSS   | LSASV   | GDRVT   | ITC         | RSSQSI | VH     | SN      | NTYLE   |
|       | V     | V       | A       |         |             | WYQK   | PGKAPK | LLIY    | KVSNRFS |
|       |       |         |         |         |             | GVPSR  | FSGSGG | TDFTLT  | IS      |
|       |       |         |         |         |             | SLQ    | PE     | DFATYYC |         |
|       |       |         |         |         |             |        |        |         | V LG    |

|       |          |            |
|-------|----------|------------|
| seq   | 100      | 110        |
| AbM   | 90       | 100        |
|       | i b i    | i b b b    |
| 76E1  | FQGSHPWT | FCGGTKLEIK |
|       | *        |            |
| huVK1 | FQGSHPWT | FCGGTKLEIK |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international Immunogenetics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
- (3) Residue numbering shown as sequential (seq) or according to website [www.bioinf.org.uk/abs/](http://www.bioinf.org.uk/abs/) (AbM).
- (4) "b" notes buried sidechain; "i" notes sidechain at interface between VH and VL domains.
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- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isopartate formation or Asp-Pro (DP) bond cleavage.

FIG. 6B

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huVK3  
Potential humanized sequence based on IMGT IGV3-20 acceptor framework (method 1)  
EIVLTQSPGTLSPGERATLSC **RASQSVSSSYLA** WYQKPGQAPRLLIY **GASSRAT** GIPDRFSGSGGTFTLTISRLEPEDFAVYYC **QQYGSSP**

Joining region  
IMGT J00242|IGKJ2\*01|YTFGQGTKLEIK

|       |                       |           |                |         |                                |       |       |       |
|-------|-----------------------|-----------|----------------|---------|--------------------------------|-------|-------|-------|
| seq   | 10                    | 20        | 30             | 40      | 50                             | 60    | 70    | 80    |
| AbM   | 10                    | 20        | 34             | 40      | 50                             | 60    | 70    | 80    |
| 141A  | b b b                 | b b b     | b b b          | i i i   | i i i                          | b b b | b b b | b b b |
| huVK3 | QIVLSQSPAILSASPEKVTMT | RASSLSYMH | WYQKPGSSPKWY   | ATSNLAS | GVPARFSGSGTSLTISRVEADAATYYC    |       |       |       |
|       | * * *                 | * * *     | ** **          | ** **   | * * *                          | * * * | * * * | * * * |
|       | EIVLTQSPGTLSPGERATLSC | RASSLSYMH | WYQKPGQAPRLLIY | ATSNLAS | GIPDRFSGSGGTFTLTISRLEPEDFAVYYC |       |       |       |
|       | A                     | V M       | S P W          | Q V     | Y V                            |       |       |       |

|       |           |            |
|-------|-----------|------------|
| seq   | 90        | 100        |
| AbM   | 90        | 100        |
| 141A  | ibi iib i | b b b      |
| huVK3 | QQWSSNPYT | FCGGTKLEIK |
|       | *         |            |
|       | QQWSSNPYT | FCGGTKLEIK |
|       | Q         | S          |
|       |           | A          |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international Immunogenetics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
- (3) Residue numbering shown as sequential (seq) or according to website [\(AbM\)](http://www.bioinf.org.uk/abs/).
- (4) "b" notes buried sidechain; "i" notes sidechain at interface between VH and VL domains.
- (5) Sequence differences between each humanized sequence and murine sequence noted by asterick (\*).
- (6) Potential humanized framework mutations from human sequence to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.
- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isopartate formation or Asp-Pro (DP) bond cleavage.

FIG. 7A

Joining region  
IMGT J00242 | ICKJ2\*01 | YTFGQGTKLEIK

| seq   | 90        | 100         |
|-------|-----------|-------------|
| AbM   | 90        | 100         |
|       | ibi       | iib i b b b |
| 141A  | QQWSSNPYT | FGGCTKLEIK  |
|       |           | *           |
| huVK1 | QQWSSNPYT | FGGCTKLEIK  |
|       |           | Q S A       |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international ImmunoGenetics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
- (3) Residue numbering shown as sequential (seq) or according to website [www.bioinf.org.uk/abs/](http://www.bioinf.org.uk/abs/) (AbM).
- (4) "b" notes buried sidechain; "i" notes sidechain at interface between VH and VL domains.
- (5) Sequence differences between each humanized sequence and murine sequence noted by asterick (\*).
- (6) Potential humanized framework mutations from human sequence to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.
- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isoaspartate formation or Asp-Pro (DP) bond

FIG. 7B

huVK2  
Potential humanized sequence based on IMGT IGKV2-28 acceptor framework (method 1)  
DIVMTQSP<sup>LS</sup>LPVTPGEPASIS**C RSSQSLHSNGVNYLD** WYLQPGQSPQLLIY **LGSNRAS** GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC **MQALQTP**

Joining region  
IMGT J00242|IGKJ2\*01|YTFGQGTKLEIK

|       |          |                |          |                          |                 |                          |                                  |                |                              |
|-------|----------|----------------|----------|--------------------------|-----------------|--------------------------|----------------------------------|----------------|------------------------------|
| seq   | 10       | 20             | 30       | 40                       | 50              | 60                       | 70                               | 80             | 90                           |
| AbM   | 10       | 20             | 30abcde  | 40                       | 50              | 60                       | 70                               | 80             | 90                           |
|       | b b b    | b b b          | b b b    | b i b i                  | i i i b b i     | i b b                    | b b b                            | b b b          | b b b                        |
| 175A  | DVLM     | QTPLSLP        | VS       | LG                       | DQASIS <b>C</b> | <b>RSSQSI</b> VHSNGNTYLE | WYLQPGQSPKLLIY                   | <b>KLSNRFS</b> | GVPDRFSGSGSGTDFTLKISRVEAEDLG |
|       | **       | *              | **       | **                       | **              | *                        | *                                | *              | *                            |
| huVK2 | DIVMTQSP | LSLPVTPGEPASIS | <b>C</b> | <b>RSSQSI</b> VHSNGNTYLE | WYLQPGQSPQLLIY  | <b>KLSNRFS</b>           | GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC |                |                              |
|       | V        |                |          | Q Q                      | Q               | S                        | D                                | A              | L                            |
|       |          |                |          | S S                      | S               | D                        | A                                |                |                              |
|       |          |                |          | A A                      | D               | A                        |                                  |                |                              |

|       |                  |            |
|-------|------------------|------------|
| seq   | 100              | 110        |
| AbM   | 90               | 100        |
|       | i b i            | i i b i    |
| 175A  | <b>FCGSHFPYT</b> | FCGGTKLEIK |
|       | *                | *          |
| huVK2 | <b>FCGSHFPYT</b> | FCGGTKLEIK |

- (1) CDR sequences noted in bold.
- (2) Human germline and joining sequences from IMGT® the international Immunogenetics information system® [www.imgt.org](http://www.imgt.org) (founder and director: Marie-Paule Lefranc, Montpellier, France).
- (3) Residue numbering shown as sequential (seq) or according to website [www.bioinf.org.uk/abs/](http://www.bioinf.org.uk/abs/) (AbM).
- (4) "b" notes buried sidechain; "i" notes sidechain at interface between VH and VL domains.
- (5) Sequence differences between each humanized sequence and murine sequence noted by asterick (\*).
- (6) Potential humanized framework mutations from human sequence to parental mouse sequence are noted below sequence in red; underlined residues are positions to alter first.
- (7) Potential changes in CDR sequence noted below each CDR sequence. These may prevent asparagines (N) deamidation (N), methionine (M) oxidation, Asp-Gly (DG) isopartate formation or Asp-Pro (DP) bond cleavage.

FIG. 8A

Joining region  
IMGT J00242 | ICKJ2\*01 | YTFGQGTKLEIK

| seq   | 100             | 110              |
|-------|-----------------|------------------|
| AbM   | 90              | 100              |
|       | ibi iib i       | b b b            |
| 175A  | <b>FQGSHPYT</b> | <b>FGGKTLEIK</b> |
|       |                 | *                |
| huVK1 | <b>FQGSHPYT</b> | <b>FGGKTLEIK</b> |

**FIG. 8B**

76E1 VH  
EVQLLQSGPELEKPGASVKISCKAS**GYSF****FAAAAAA**WVKQSNKGKSL**EWIGAI****IAAAAAAAAAAAAAAAAA**KATLTVDKSSSTAYMQLKSLTSEDSAVYYC  
AT**AAAAAFDY**WGQGTTLTVSS (SEQ ID NO:1143)  
human subgroup I

141A VH  
QVQLQSGAELMKPGASVKISCKAT**GYTF****FAAAAAA**WVKQRPFGHGLEW**IGAI****IAAAAAAAAAAAAAAAAA**KATFTADTSSNTAYMQLSSLTSEDSAVYYC  
AG**AAAAA****AAAAA**AWGQGTTLTVSA (SEQ ID NO:1144)  
human subgroup I

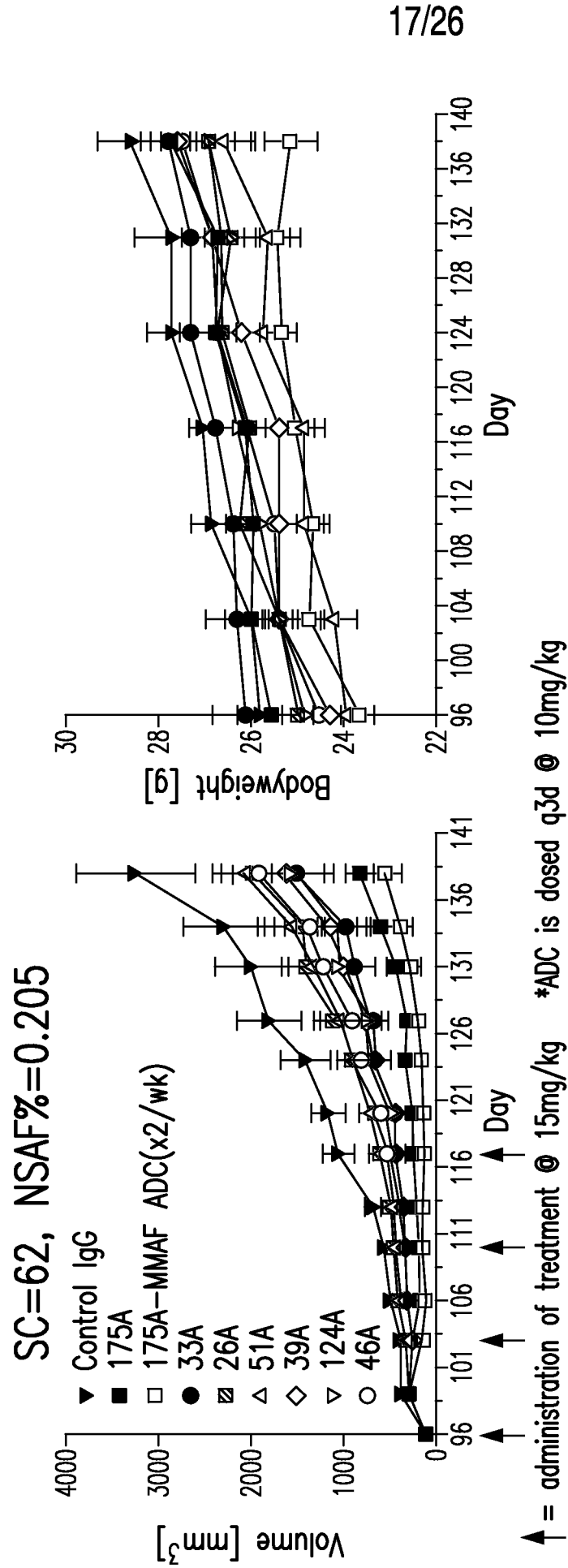
175A VH  
QVQLQSGAELMKPGASVKISCKAT**GYTF****FAAAAAA**WVKQRPFGHGLEW**IGAI****IAAAAAAAAAAAAAAAAA**KATFTADTSSNTAYMQLSSLTSEDSAVYYC  
AR**AAAAAY**AMDYWGQGTSTVTVSS (SEQ ID NO:1145)  
human subgroup I

76E1 VL  
DVLMTQTPLSLPVSLGDQASISCR**SSQ****SA****AAAAAAAAA**WYLQKPGQSPKLLIY**AAAAAA**GVDPDRFSGSGGTDFTLKINRVEAEDLGVIYCA**QA**  
**AAAPAT**FGGGTKLEIK (SEQ ID NO:1146)  
human kappa II

141A VL  
QIVLSQSPAILSASPGKEKVTMT**CR****AS****AAAAA**WYQKPGSSPKPIY**AAANLAS**GVPARFSGSGGTSYSLTISRVEAEDAATYYC**QQ****AAAAAPAT**  
FGGGTKLEIK (SEQ ID NO:1147)  
human kappa III

175A VL  
DVLMTQTPLSLPVSLGDQASISCR**SSQ****SA****AAAAAAAAA**WYLQKPGQSPKLLIY**AAAAAA**GVDPDRFSGSGGTDFTLKISRVEAEDLGVIYCA**QA**  
**AAAPAT**FGGGTKLEIK (SEQ ID NO:1148)  
human kappa II

FIG. 9



|                 |                              |         |           |           |          |          |           |          |          |
|-----------------|------------------------------|---------|-----------|-----------|----------|----------|-----------|----------|----------|
| Kasumi-3<br>NOD | Control<br>IgG <sub>2a</sub> | 175A    | 175A-MMAF | 33A       | 26A      | 51A      | 39A       | 124A     | 46A      |
| Volume±SD       | 3255±1704                    | 833±429 | 555±511   | 1514±1156 | 1982±997 | 1668±638 | 2039±1102 | 1305±674 | 1925±791 |
| TGI             | -                            | -77     | -86       | -55       | -41      | -51      | -39       | -62      | -42      |
| p-Value         | -                            | 0.0088  | 0.0050    | 0.0447    | 0.1154   | 0.0507   | 0.1370    | 0.0363   | 0.0937   |

FIG. 10

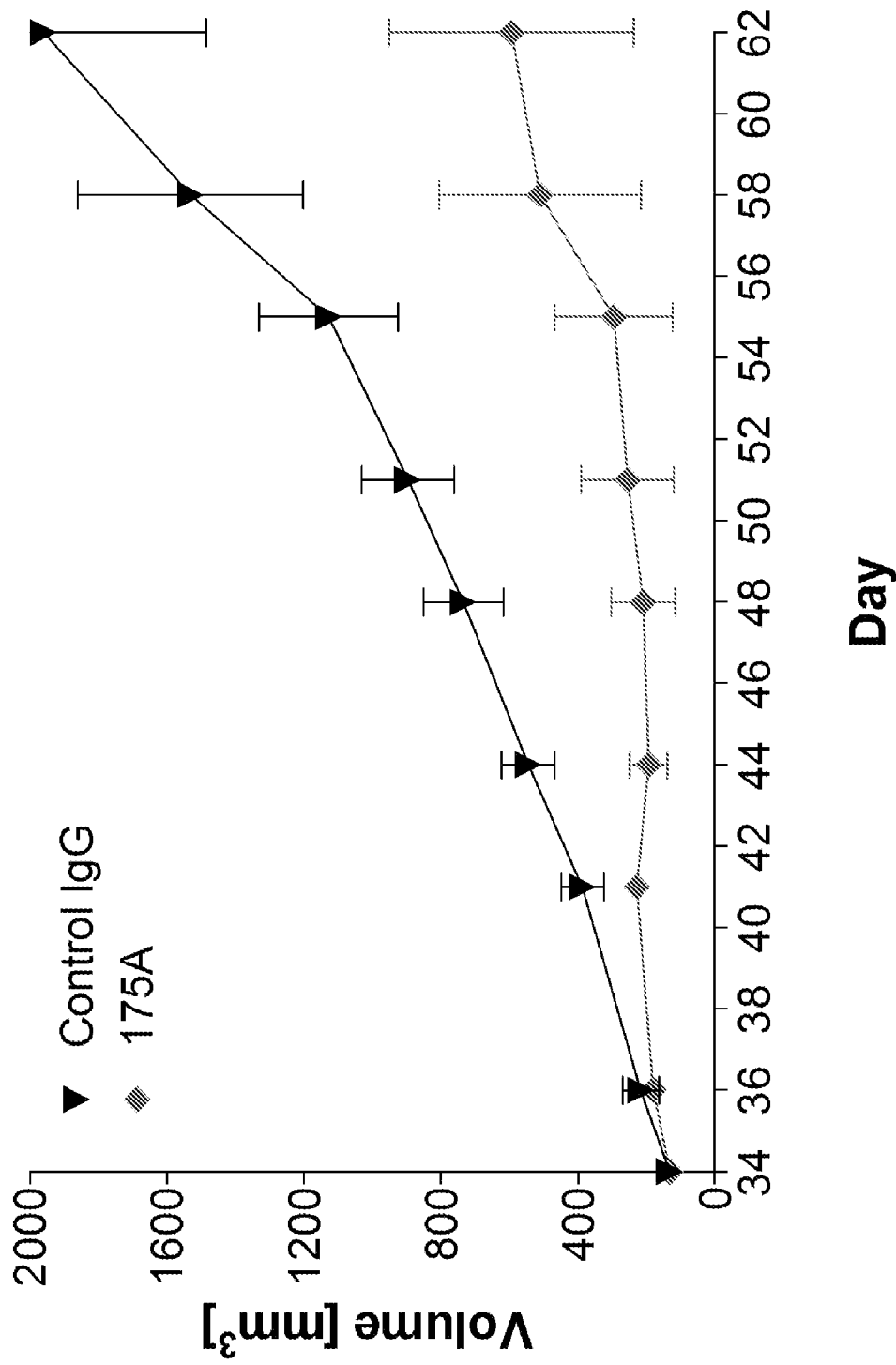


FIG. 11

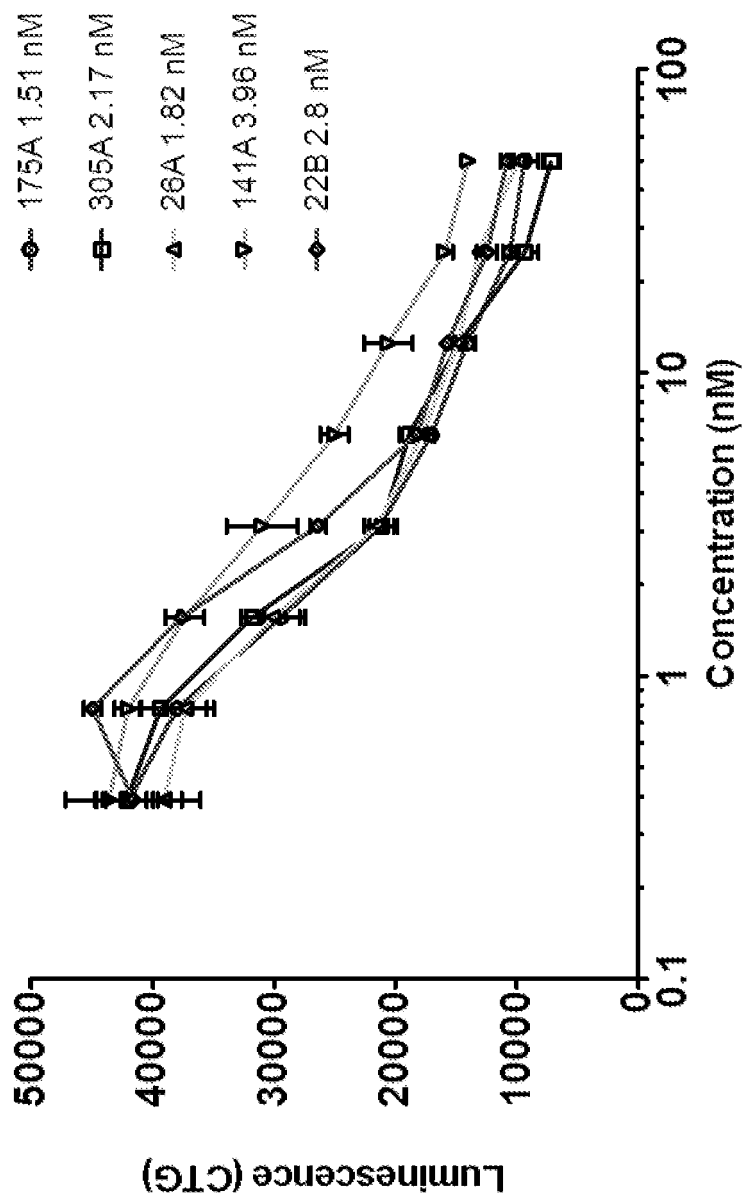
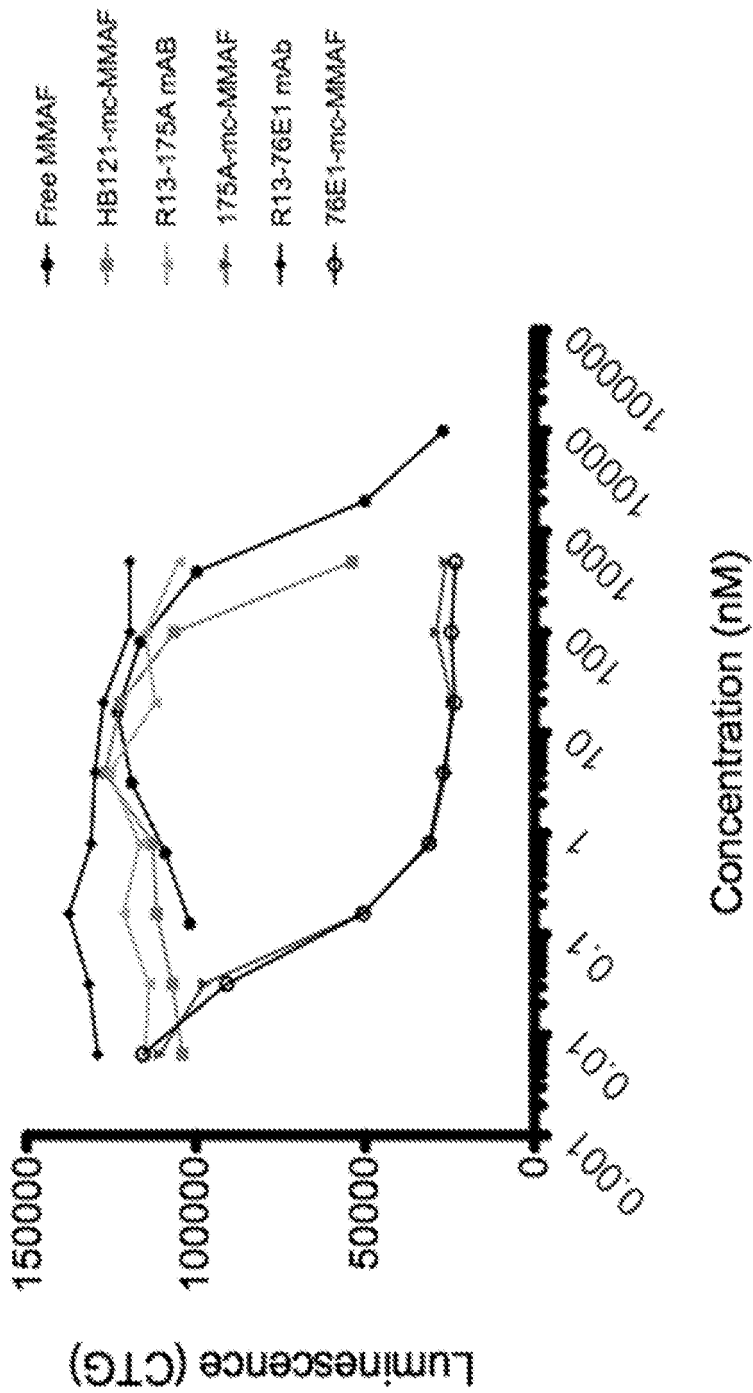
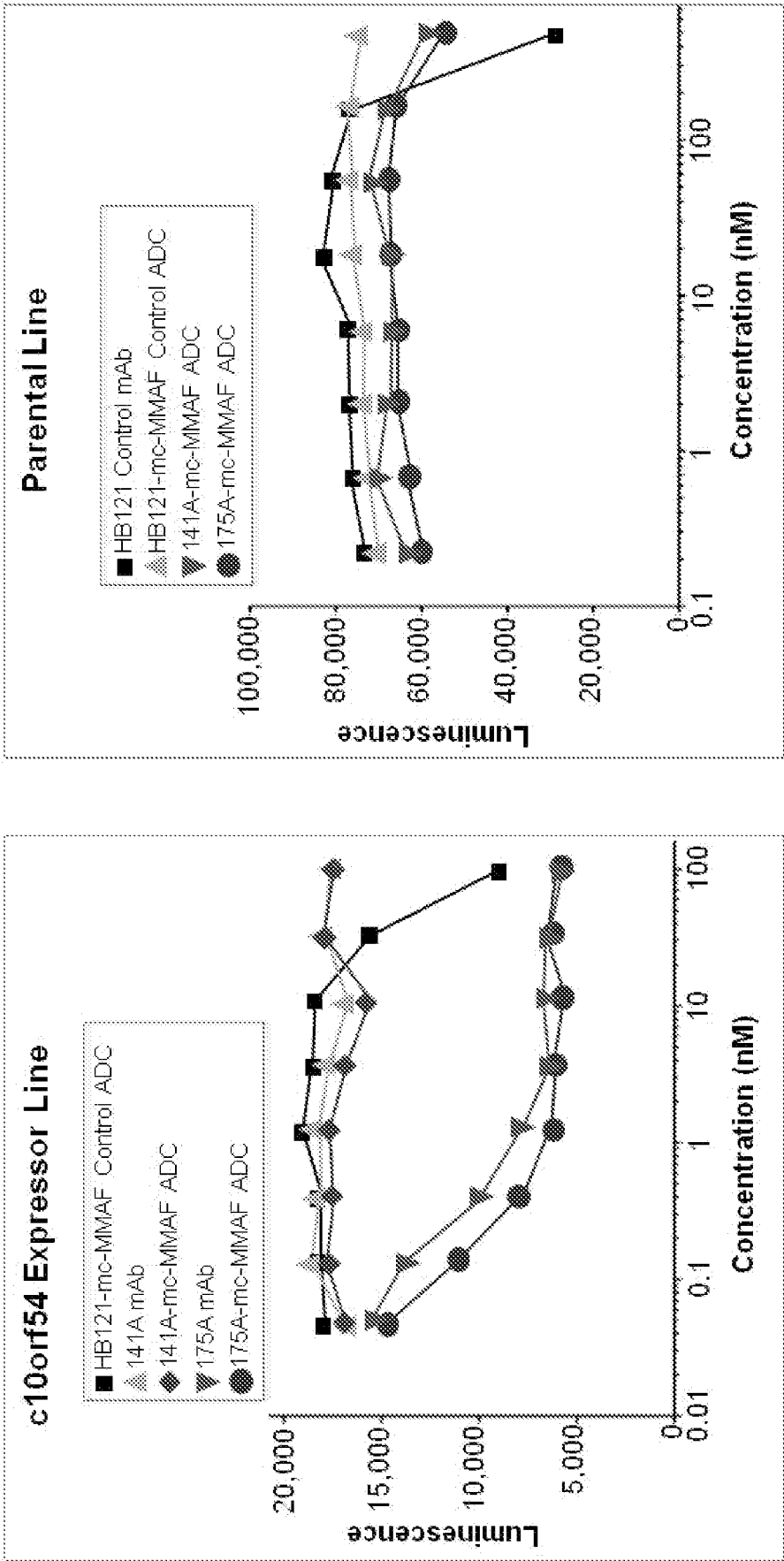


FIG. 12



|          | Free MMAF | 175A-mc-MMAF | 76E1-mc-MMAF |
|----------|-----------|--------------|--------------|
| IC50     | 1560      | 0.07166      | 0.05877      |
| R square | 0.9504    | 0.9906       | 0.9995       |

FIG. 13



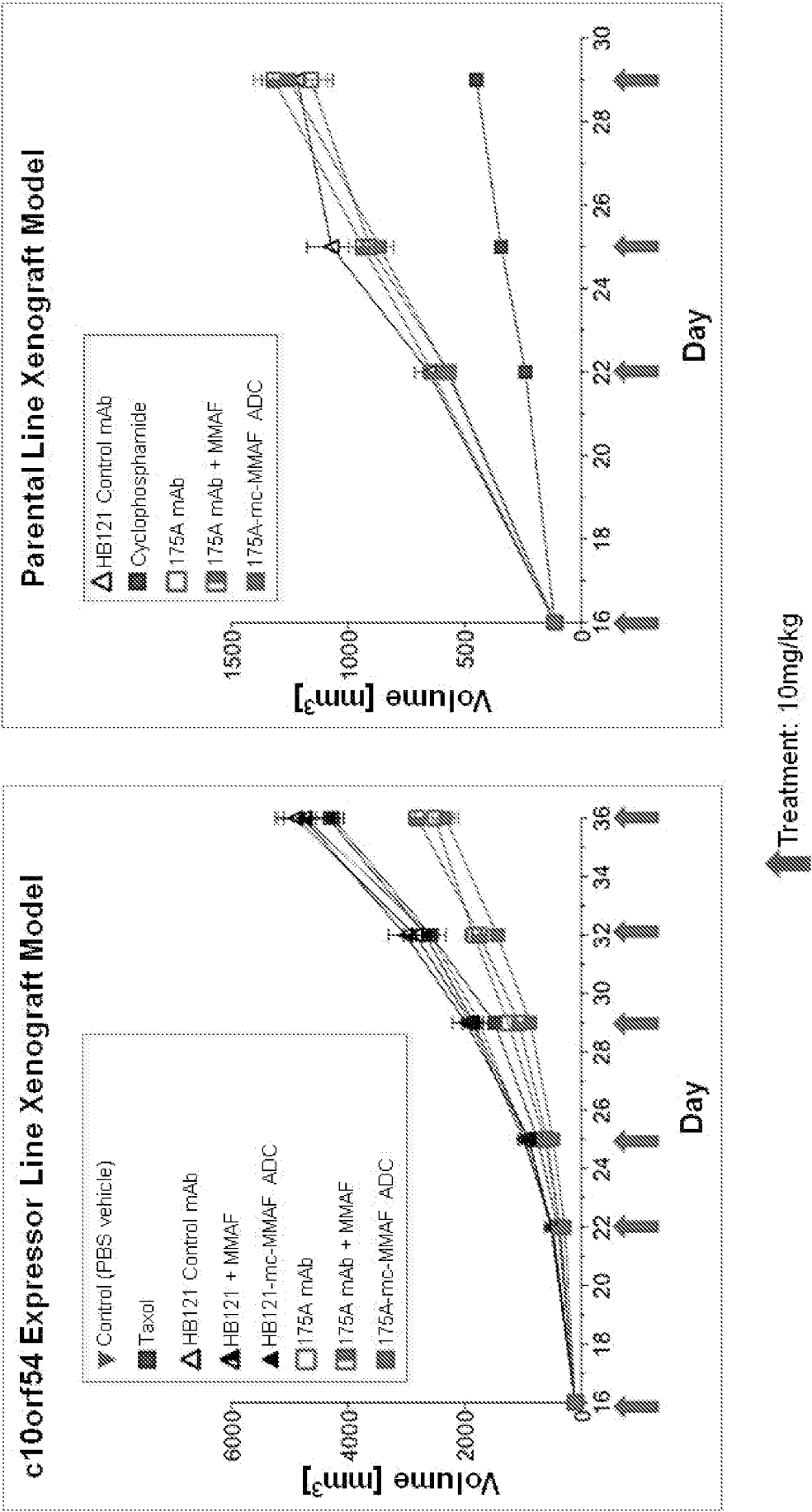


FIG. 15

R13 VH

R13-3610-76E1 MGWTWIFILILSVTTGVHS  
R13-3610-141A MEWTWVFLFLLSVTAGVHS  
R13-3610-175A MEWTWVFLFLLSVTAGVHS

|         |   |    |    |                  |    |                         |           |
|---------|---|----|----|------------------|----|-------------------------|-----------|
| Kabat   | 1 | 10 | 22 | <b>31--35</b>    | 40 | <b>50--a-----60----</b> | <b>65</b> |
| AbM     | 1 | 10 | 22 | <b>26-----35</b> | 40 | <b>50--a-----58</b>     | 65        |
| Chothia | 1 | 10 | 22 | <b>26-----32</b> | 40 | <b>a-55</b>             | 65        |
| Contact | 1 | 10 | 22 | <b>30----35</b>  | 40 | <b>47-----a-----58</b>  | 65        |
| IMGT    | 1 | 23 | 27 | <b>27-----38</b> | 41 | <b>56-----65</b>        | 74        |

76E1 EVQLLQSGPELEKPGASVKISCKAS GYSFTGYNMN WVKQSNKGKSLWIG NIDPYYDYTSYNLKFKD  
141A QVQLQQSGAELMKPGASVKISCKAT GYTFSTRYWIE WVKQRPFGHGLEWIG EILPGSGSTNYNEKFKG  
175A QVQLQQSGAELMKPGASVKISCKAT GYTFSTHWIE WVKQRPFGHGLEWIG EILPGSGSTSYNEKFKG

|         |    |    |     |                    |                        |     |
|---------|----|----|-----|--------------------|------------------------|-----|
| Kabat   | 70 | 80 | abc | 90                 | <b>95--100---102</b>   | 110 |
| AbM     | 70 | 80 | abc | 90                 | <b>95--100---102</b>   | 110 |
| Chothia | 70 | 80 | abc | 90                 | <b>96-100--101</b>     | 110 |
| Contact | 70 | 80 | abc | 90                 | <b>93-----100--101</b> | 110 |
| IMGT    | 75 | 89 |     | <b>105-----117</b> |                        |     |

76E1 KATLTVDKSSSTAYMQLKSLTSEDSAVYYCAT STMITP---FDY WQQGTTLTVSS  
141A KATFTADTSSNTAYMQLSLTSSEDSAVYYCAG EEVYDGYPWFGY WQQGTLVTVSA  
175A KATFTADTSSNTAYMQLSLTSSEDSAVYYCAR WLLYYA--MDY WQQGTSVTVSS

FIG. 16A

R13 VL

R13-3610-76E1 MKLPVRLLVLMFWIPASSS  
R13-3610-141A MDFQVQIFSFLISASVIMSRG  
R13-3610-175A MKLPVRLLVLMFWIPASSS

|         |   |    |    |                           |    |                  |
|---------|---|----|----|---------------------------|----|------------------|
| Kabat   | 1 | 10 | 20 | <b>24-27abcd-----34</b>   | 40 | <b>50-----56</b> |
| AbM     | 1 | 10 | 20 | <b>24-----30abcd---34</b> | 40 | <b>50-----56</b> |
| Chothia | 1 | 10 | 20 | <b>26--30abcd-32</b>      | 40 | <b>50--</b>      |
| Contact | 1 | 10 | 20 | <b>30abcd-----36</b>      | 40 | <b>46-----55</b> |
| IMGT    | 1 |    | 23 | <b>27-----38</b>          | 41 | <b>56-65 69</b>  |

76E1 DVLMTQTPLSLPVSIGDQASISC RSSQSIIVHSNGNTYLE WYLQKPGQSPKLLIY KVSNRFS  
141A QIVLSQSPAILSASPGKVTMT C RASSL-----SYMH WYQQKPGSSPKPWIY ATSNLAS  
175A DVLMTQTPLSLPVSIGDQASISC RSSQSIIVHSNGNTYLE WYLQKPGQSPKLLIY KLSNRFS

|         |    |    |    |                    |
|---------|----|----|----|--------------------|
| Kabat   | 60 | 70 | 80 | <b>89-----97</b>   |
| AbM     | 60 | 70 | 80 | <b>89-----97</b>   |
| Chothia | 60 | 70 | 80 | <b>91---96</b>     |
| Contact | 60 | 70 | 80 | <b>89-----96</b>   |
| IMGT    | 70 |    | 89 | <b>105-----117</b> |

76E1 GVPDRFSGSGGTDFTLKINRVEAEDLGVIYC FQGSHPWT FGGGTKLEIK  
141A GVPARFSGSGGTSYSLTISRVEAEDAATYIC QQWSSNPYT FGGGTKLEIK  
175A GVPDRFSGSGGTDFTLKISRVEAEDLGVIYC FQGSHPYT FGGGTKLEIK

FIG. 16B

R13 VH

|        |                          |                    |                |                          |    |              |    |
|--------|--------------------------|--------------------|----------------|--------------------------|----|--------------|----|
| AbM    | 1                        | 10                 | 22             | 26-----35                | 40 | 50--a-----58 | 65 |
| hu76E1 | QVQLVQSGAEVKKPGASVKVCKAS | GYSFTGYNMN         | WVRQAPGQGLEWIG | NIDPYDYTSYNLKF           | KD |              |    |
| hu141A | QVQLVQSGAEVKKPGASVKVCKAS | <b>GYTFSRYWIE</b>  | WVRQAPGQGLEWIG | <b>EILPGSGSTNYNEKFKG</b> |    |              |    |
| hu175A | QVQLVQSGAEVKKPGASVKVCKAS | <b>GYTFSSTHWIE</b> | WVRQAPGQGLEWIG | <b>EILPGSGSTSYNEKFKG</b> |    |              |    |
| consen | QVQLVQSGAEVKKPGASVKVCKAS | <b>GYTFSXXXWIE</b> | WVRQAPGQGLEWIG | <b>EILPGSGSTXYNEKFKG</b> |    |              |    |
|        |                          | <b>RY</b>          |                | <b>N</b>                 |    |              |    |
|        |                          | <b>TH</b>          |                | <b>S</b>                 |    |              |    |

|        |                                  |                     |       |        |                   |                   |       |
|--------|----------------------------------|---------------------|-------|--------|-------------------|-------------------|-------|
| AbM    | 70                               | 80                  | abc   | 90     | 95--100---102     | 110               |       |
| hu76E1 | RVTMTVDKSTSTAYMELRSLRSDDTAVYYCAT | STMITP---           | FDY   | WGQGT  | LVTVSS            | (SEQ ID NO: 1135) | 25/26 |
| hu141A | RVTMTADTSTSTAYMELRSLRSDDTAVYYCAG | <b>EEVYDGYPWFGY</b> | WGQGT | LVTVSS | (SEQ ID NO: 1136) |                   |       |
| hu175A | RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR | <b>WLLYYA--MDY</b>  | WGQGT | LVTVSS | (SEQ ID NO: 1137) |                   |       |
| consen | RVTMTADTSTSTAYMELRSLRSDDTAVYYCAR | <b>XXXXXXXXXX</b>   | WGQGT | LVTVSS | (SEQ ID NO: 1138) |                   |       |
|        |                                  | <b>MG</b>           |       |        |                   |                   |       |
|        |                                  | <b>FD</b>           |       |        |                   |                   |       |

FIG. 17A

R13 VL

|        |                           |                         |                 |                           |    |                  |
|--------|---------------------------|-------------------------|-----------------|---------------------------|----|------------------|
| AbM    | 1                         | 10                      | 20              | <b>24-----30abcd---34</b> | 40 | <b>50-----56</b> |
| hu141A | EIVLTQSPGTLISLSPGERATLSC  | RASSSL-----SYMH         | WYQQKPGQAPRPWIY | ATSNLAS                   |    |                  |
| hu76E1 | DIVMTQSPPLSLPVTTPGEPASISC | <b>RSSQSIVHSNGNTYLE</b> | WYLQKPGQSPQLLIY | <b>KVSNRFS</b>            |    |                  |
| hu175A | DIVMTQSPPLSLPVTTPGEPASISC | <b>RSSQSIVHSNGNTYLE</b> | WYLQKPGQSPQLLIY | <b>KLSNRFS</b>            |    |                  |
| consen | DIVMTQSPPLSLPVTTPGEPASISC | <b>RSSQSIVHSNGNTYLE</b> | WYLQKPGQSPQLLIY | <b>KXSNRFS</b>            |    |                  |

**V**  
**L**

|        |                                |                  |            |                   |  |  |
|--------|--------------------------------|------------------|------------|-------------------|--|--|
| AbM    | 60                             | 70               | 80         | <b>89-----97</b>  |  |  |
| hu141A | GIPDRFSGSGGTDTLTISRLEPEDFAVYYC | QQWSSNPYT        | FGQGTKLEIK | (SEQ ID NO: 1139) |  |  |
| hu76E1 | GVPDRFSGSGGTDTLTISRVEAEDVGVYYC | <b>FQGSHPVPT</b> | FGQGTKLEIK | (SEQ ID NO: 1140) |  |  |
| hu175A | GVPDRFSGSGGTDTLTISRVEAEDVGVYYC | <b>FQGSHPFPT</b> | FGQGTKLEIK | (SEQ ID NO: 1141) |  |  |
| consen | GVPDRFSGSGGTDTLTISRVEAEDVGVYYC | <b>FQGSHPXT</b>  | FGQGTKLEIK | (SEQ ID NO: 1142) |  |  |

**V W**  
**F Y**

FIG. 17B