SEQUENCE LISTING

<110> F. Hoffmann-La Roche AG

<120> HUMANIZED ANTI-HUMAN CD19 ANTIBODIES AND METHODS OF USE

<130> P33094

<150> EP15187820.4
<151> 2015-10-01

<160> 70

<170> PatentIn version 3.5

<210> 1
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<212> PRT
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<400> 1

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Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Met Ala Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
            20                  25                  30


Ile Met His Trp Val Lys Gln Lys Thr Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
    50                  55                  60


Asn Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ile Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110
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Gln Gly Thr Thr Leu Thr Val Ser Ser
        115                 120


<210>  2
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<212>  PRT
<213>  Mus musculus

<400>  2

Asp Ala Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1               5                   10                  15


Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Glu Asn Ser
            20                  25                  30


Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Leu
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  3
<211>  5
<212>  PRT
<213>  Mus musculus

<400>  3
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Asp Tyr Ile Met His
1 5

<210> 4
<211> 17
<212> PRT
<213> Mus musculus

<400> 4

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Asn
1 5 10 15

Gly

<210> 5
<211> 12
<212> PRT
<213> Mus musculus

<400> 5

Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr
1 5 10

<210> 6
<211> 16
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<213> Mus musculus

<400> 6

Arg Ser Ser Gln Ser Leu Glu Asn Ser Asn Gly Asn Thr Tyr Leu Asn
1 5 10 15

<210> 7
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<213> Mus musculus

<400> 7

Arg Val Ser Lys Arg Phe Ser
1 5

<210> 8
<211> 9
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<213> Mus musculus

<400> 8

Leu Gln Leu Thr His Val Pro Tyr Thr
1 5

<210> 9
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized VH

<400> 9

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ile Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Gly Thr Tyr Tyr Tyr Gly Ser Ala Leu Phe Asp Tyr Trp Gly
            100                 105                 110


Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  10
<211>  112
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  N27dH VL

<400>  10

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                   10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu His Ser
            20                  25                  30


Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  11
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<211> 17
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<213> Artificial Sequence

<220>
<223> humanized HVR-H2

<400> 11

Tyr Ile Asn Pro Tyr Asn Asp Gly Ser Lys Tyr Thr Glu Lys Phe Gln
1 5 10 15

Gly

<210> 12
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> N27dH HVR-L1

<400> 12

Lys Ser Ser Gln Ser Leu Glu His Ser Asn Gly Asn Thr Tyr Leu Asn
1 5 10 15

<210> 13
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> N27dQ VL

<400> 13

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Gln Ser
20 25 30

```
Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  14
<211>  16
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  N27dQ HVR-L1

<400>  14

Lys Ser Ser Gln Ser Leu Glu Gln Ser Asn Gly Asn Thr Tyr Leu Asn
1               5                   10                  15


<210>  15
<211>  112
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  S27eA VH

<400>  15

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                   10                  15
```

```
Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Ala
            20                  25                  30

Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 16
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<212> PRT
<213> Artificial Sequence

<220>
<223> S27eA HVR-L1

<400> 16

```
Lys Ser Ser Gln Ser Leu Glu Asn Ala Asn Gly Asn Thr Tyr Leu Asn
1               5                   10                  15
```

<210> 17
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> S27eV VL

<400> 17

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                   10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Val
            20                  25                  30


Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110


<210>  18
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<212>  PRT
<213>  Artificial Sequence

<220>
<223>  S27eV HVR-L1

<400>  18

Lys Ser Ser Gln Ser Leu Glu Asn Val Asn Gly Asn Thr Tyr Leu Asn
1               5                   10                  15


<210>  19
<211>  112
<212>  PRT
<213>  Artificial Sequence
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<220>
<223> S27eP VL

<400> 19

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Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                   10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Pro
            20                  25                  30


Asn Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 20
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> S27eP HVR-L1

<400> 20

```
Lys Ser Ser Gln Ser Leu Glu Asn Pro Asn Gly Asn Thr Tyr Leu Asn
1               5                   10                  15
```

<210> 21

<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> N28Q VL

<400> 21

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                  10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Ser
            20                  25                  30


Gln Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
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<210> 22
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<212> PRT
<213> Artificial Sequence

<220>
<223> N28Q HVR-L1

<400> 22

```
Lys Ser Ser Gln Ser Leu Glu Asn Ser Gln Gly Asn Thr Tyr Leu Asn
```

1 5 10 15

<210> 23
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> G29A VL

<400> 23

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Ser
20 25 30

Asn Ala Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 24
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> G29A HVR-L1

<400> 24

```
Lys Ser Ser Gln Ser Leu Glu Asn Ser Asn Ala Asn Thr Tyr Leu Asn
1               5                   10                  15
```

<210> 25
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> G29V VL

<400> 25

```
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1               5                   10                  15


Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Ser
            20                  25                  30


Asn Val Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45


Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
    50                  55                  60


Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80


Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
                85                  90                  95


Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

<210> 26
<211> 16
<212> PRT

<213> Artificial Sequence

<220>
<223> G29V HVR-L1

<400> 26

Lys Ser Ser Gln Ser Leu Glu Asn Ser Asn Val Asn Thr Tyr Leu Asn
1 5 10 15

<210> 27
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> S27eP/N28S VH

<400> 27

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Glu Asn Pro
20 25 30

Ser Gly Asn Thr Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Lys Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln Leu
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 28
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> S27eP/N28S HVR-L1

<400> 28

Lys Ser Ser Gln Ser Leu Glu Asn Pro Ser Gly Asn Thr Tyr Leu Asn
1 5 10 15

<210> 29
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> signal peptide

<400> 29

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15

Val His Ser

<210> 30
<211> 272
<212> PRT
<213> Homo sapiens

<400> 30

Pro Glu Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val
1 5 10 15

Leu Gln Cys Leu Lys Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Thr
20 25 30

```
Trp Ser Arg Glu Ser Pro Leu Lys Pro Phe Leu Lys Leu Ser Leu Gly
        35                  40                  45

Leu Pro Gly Leu Gly Ile His Met Arg Pro Leu Ala Ile Trp Leu Phe
    50                  55                  60

Ile Phe Asn Val Ser Gln Gln Met Gly Gly Phe Tyr Leu Cys Gln Pro
65                  70                  75                  80

Gly Pro Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Asn Val
                85                  90                  95

Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly
            100                 105                 110

Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro
        115                 120                 125

Ser Gly Lys Leu Met Ser Pro Lys Leu Tyr Val Trp Ala Lys Asp Arg
    130                 135                 140

Pro Glu Ile Trp Glu Gly Glu Pro Pro Cys Leu Pro Pro Arg Asp Ser
145                 150                 155                 160

Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr
                165                 170                 175

Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro
            180                 185                 190

Leu Ser Trp Thr His Val His Pro Lys Gly Pro Lys Ser Leu Leu Ser
        195                 200                 205

Leu Glu Leu Lys Asp Asp Arg Pro Ala Arg Asp Met Trp Val Met Glu
    210                 215                 220
```

Thr Gly Leu Leu Leu Pro Arg Ala Thr Ala Gln Asp Ala Gly Lys Tyr
225 230 235 240

Tyr Cys His Arg Gly Asn Leu Thr Met Ser Phe His Leu Glu Ile Thr
245 250 255

Ala Arg Pro Val Leu Trp His Trp Leu Leu Arg Thr Gly Gly Trp Lys
260 265 270

<210> 31
<211> 274
<212> PRT
<213> Macaca fascicularis

<400> 31

Pro Gln Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val
1 5 10 15

Leu Gln Cys Leu Glu Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Val
20 25 30

Trp Cys Arg Asp Ser Pro Phe Glu Pro Phe Leu Asn Leu Ser Leu Gly
35 40 45

Leu Pro Gly Met Gly Ile Arg Met Gly Pro Leu Gly Ile Trp Leu Leu
50 55 60

Ile Phe Asn Val Ser Asn Gln Thr Gly Gly Phe Tyr Leu Cys Gln Pro
65 70 75 80

Gly Leu Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Ser Val
85 90 95

Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly
100 105 110

Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro

```
        115                 120                 125

Ser Gly Lys Leu Asn Ser Ser Gln Leu Tyr Val Trp Ala Lys Asp Arg
    130                 135                 140

Pro Glu Met Trp Glu Gly Glu Pro Val Cys Gly Pro Pro Arg Asp Ser
145                 150                 155                 160

Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr
                165                 170                 175

Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro
            180                 185                 190

Leu Ser Trp Thr His Val Arg Pro Lys Gly Pro Lys Ser Ser Leu Leu
        195                 200                 205

Ser Leu Glu Leu Lys Asp Asp Arg Pro Asp Arg Asp Met Trp Val Val
    210                 215                 220

Asp Thr Gly Leu Leu Leu Thr Arg Ala Thr Ala Gln Asp Ala Gly Lys
225                 230                 235                 240

Tyr Tyr Cys His Arg Gly Asn Trp Thr Lys Ser Phe Tyr Leu Glu Ile
                245                 250                 255

Thr Ala Arg Pro Ala Leu Trp His Trp Leu Leu Arg Ile Gly Gly Trp
            260                 265                 270

Lys Val
```

<210> 32
<211> 36
<212> PRT
<213> Homo sapiens

<400> 32

Asp Thr Asp Leu Cys Asn Ala Ser Gly Ala His Ala Leu Gln Pro Ala
1 5 10 15

Ala Ala Ile Leu Ala Leu Leu Pro Ala Leu Gly Leu Leu Leu Trp Gly
20 25 30

Pro Gly Gln Leu
35

<210> 33
<211> 537
<212> PRT
<213> Homo sapiens

<400> 33

Pro Glu Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val
1 5 10 15

Leu Gln Cys Leu Lys Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Thr
20 25 30

Trp Ser Arg Glu Ser Pro Leu Lys Pro Phe Leu Lys Leu Ser Leu Gly
35 40 45

Leu Pro Gly Leu Gly Ile His Met Arg Pro Leu Ala Ile Trp Leu Phe
50 55 60

Ile Phe Asn Val Ser Gln Gln Met Gly Gly Phe Tyr Leu Cys Gln Pro
65 70 75 80

Gly Pro Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Asn Val
85 90 95

Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly
100 105 110

```
Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro
        115                 120                 125

Ser Gly Lys Leu Met Ser Pro Lys Leu Tyr Val Trp Ala Lys Asp Arg
    130                 135                 140

Pro Glu Ile Trp Glu Gly Glu Pro Pro Cys Leu Pro Pro Arg Asp Ser
145                 150                 155                 160

Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr
                165                 170                 175

Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro
            180                 185                 190

Leu Ser Trp Thr His Val His Pro Lys Gly Pro Lys Ser Leu Leu Ser
        195                 200                 205

Leu Glu Leu Lys Asp Asp Arg Pro Ala Arg Asp Met Trp Val Met Glu
    210                 215                 220

Thr Gly Leu Leu Leu Pro Arg Ala Thr Ala Gln Asp Ala Gly Lys Tyr
225                 230                 235                 240

Tyr Cys His Arg Gly Asn Leu Thr Met Ser Phe His Leu Glu Ile Thr
                245                 250                 255

Ala Arg Pro Val Leu Trp His Trp Leu Leu Arg Thr Gly Gly Trp Lys
            260                 265                 270

Val Ser Ala Val Thr Leu Ala Tyr Leu Ile Phe Cys Leu Cys Ser Leu
        275                 280                 285

Val Gly Ile Leu His Leu Gln Arg Ala Leu Val Leu Arg Arg Lys Arg
    290                 295                 300
```

```
Lys Arg Met Thr Asp Pro Thr Arg Arg Phe Phe Lys Val Thr Pro Pro
305                 310                 315                 320


Pro Gly Ser Gly Pro Gln Asn Gln Tyr Gly Asn Val Leu Ser Leu Pro
                325                 330                 335


Thr Pro Thr Ser Gly Leu Gly Arg Ala Gln Arg Trp Ala Ala Gly Leu
            340                 345                 350


Gly Gly Thr Ala Pro Ser Tyr Gly Asn Pro Ser Ser Asp Val Gln Ala
        355                 360                 365


Asp Gly Ala Leu Gly Ser Arg Ser Pro Pro Gly Val Gly Pro Glu Glu
    370                 375                 380


Glu Glu Gly Glu Gly Tyr Glu Glu Pro Asp Ser Glu Glu Asp Ser Glu
385                 390                 395                 400


Phe Tyr Glu Asn Asp Ser Asn Leu Gly Gln Asp Gln Leu Ser Gln Asp
                405                 410                 415


Gly Ser Gly Tyr Glu Asn Pro Glu Asp Glu Pro Leu Gly Pro Glu Asp
            420                 425                 430


Glu Asp Ser Phe Ser Asn Ala Glu Ser Tyr Glu Asn Glu Asp Glu Glu
        435                 440                 445


Leu Thr Gln Pro Val Ala Arg Thr Met Asp Phe Leu Ser Pro His Gly
    450                 455                 460


Ser Ala Trp Asp Pro Ser Arg Glu Ala Thr Ser Leu Gly Ser Gln Ser
465                 470                 475                 480


Tyr Glu Asp Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg Ser
                485                 490                 495
```

```
Ile Arg Gly Gln Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser Tyr
            500                 505                 510


Glu Asn Met Asp Asn Pro Asp Gly Pro Asp Pro Ala Trp Gly Gly Gly
        515                 520                 525


Gly Arg Met Gly Thr Trp Ser Thr Arg
    530                 535
```

<210> 34
<211> 538
<212> PRT
<213> Homo sapiens

<400> 34

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Pro Glu Glu Pro Leu Val Val Lys Val Glu Glu Gly Asp Asn Ala Val
1               5                   10                  15


Leu Gln Cys Leu Lys Gly Thr Ser Asp Gly Pro Thr Gln Gln Leu Thr
            20                  25                  30


Trp Ser Arg Glu Ser Pro Leu Lys Pro Phe Leu Lys Leu Ser Leu Gly
        35                  40                  45


Leu Pro Gly Leu Gly Ile His Met Arg Pro Leu Ala Ile Trp Leu Phe
    50                  55                  60


Ile Phe Asn Val Ser Gln Gln Met Gly Gly Phe Tyr Leu Cys Gln Pro
65                  70                  75                  80


Gly Pro Pro Ser Glu Lys Ala Trp Gln Pro Gly Trp Thr Val Asn Val
                85                  90                  95


Glu Gly Ser Gly Glu Leu Phe Arg Trp Asn Val Ser Asp Leu Gly Gly
            100                 105                 110
```

```
Leu Gly Cys Gly Leu Lys Asn Arg Ser Ser Glu Gly Pro Ser Ser Pro
        115                 120                 125

Ser Gly Lys Leu Met Ser Pro Lys Leu Tyr Val Trp Ala Lys Asp Arg
    130                 135                 140

Pro Glu Ile Trp Glu Gly Glu Pro Pro Cys Leu Pro Pro Arg Asp Ser
145                 150                 155                 160

Leu Asn Gln Ser Leu Ser Gln Asp Leu Thr Met Ala Pro Gly Ser Thr
                165                 170                 175

Leu Trp Leu Ser Cys Gly Val Pro Pro Asp Ser Val Ser Arg Gly Pro
            180                 185                 190

Leu Ser Trp Thr His Val His Pro Lys Gly Pro Lys Ser Leu Leu Ser
        195                 200                 205

Leu Glu Leu Lys Asp Asp Arg Pro Ala Arg Asp Met Trp Val Met Glu
    210                 215                 220

Thr Gly Leu Leu Leu Pro Arg Ala Thr Ala Gln Asp Ala Gly Lys Tyr
225                 230                 235                 240

Tyr Cys His Arg Gly Asn Leu Thr Met Ser Phe His Leu Glu Ile Thr
                245                 250                 255

Ala Arg Pro Val Leu Trp His Trp Leu Leu Arg Thr Gly Gly Trp Lys
            260                 265                 270

Val Ser Ala Val Thr Leu Ala Tyr Leu Ile Phe Cys Leu Cys Ser Leu
        275                 280                 285

Val Gly Ile Leu His Leu Gln Arg Ala Leu Val Leu Arg Arg Lys Arg
    290                 295                 300
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```
Lys Arg Met Thr Asp Pro Thr Arg Arg Phe Phe Lys Val Thr Pro Pro
305                 310                 315                 320


Pro Gly Ser Gly Pro Gln Asn Gln Tyr Gly Asn Val Leu Ser Leu Pro
                325                 330                 335


Thr Pro Thr Ser Gly Leu Gly Arg Ala Gln Arg Trp Ala Ala Gly Leu
            340                 345                 350


Gly Gly Thr Ala Pro Ser Tyr Gly Asn Pro Ser Ser Asp Val Gln Ala
        355                 360                 365


Asp Gly Ala Leu Gly Ser Arg Ser Pro Pro Gly Val Gly Pro Glu Glu
    370                 375                 380


Glu Glu Gly Glu Gly Tyr Glu Glu Pro Asp Ser Glu Glu Asp Ser Glu
385                 390                 395                 400


Phe Tyr Glu Asn Asp Ser Asn Leu Gly Gln Asp Gln Leu Ser Gln Asp
                405                 410                 415


Gly Ser Gly Tyr Glu Asn Pro Glu Asp Glu Pro Leu Gly Pro Glu Asp
            420                 425                 430


Glu Asp Ser Phe Ser Asn Ala Glu Ser Tyr Glu Asn Glu Asp Glu Glu
        435                 440                 445


Leu Thr Gln Pro Val Ala Arg Thr Met Asp Phe Leu Ser Pro His Gly
    450                 455                 460


Ser Ala Trp Asp Pro Ser Arg Glu Ala Thr Ser Leu Ala Gly Ser Gln
465                 470                 475                 480


Ser Tyr Glu Asp Met Arg Gly Ile Leu Tyr Ala Ala Pro Gln Leu Arg
                485                 490                 495
```

Ser Ile Arg Gly Gln Pro Gly Pro Asn His Glu Glu Asp Ala Asp Ser
500 505 510

Tyr Glu Asn Met Asp Asn Pro Asp Gly Pro Asp Pro Ala Trp Gly Gly
515 520 525

Gly Gly Arg Met Gly Thr Trp Ser Thr Arg
530 535

<210> 35
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> antibody fragment for MS analysis

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> X = S, P, A

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> X = G or A

<400> 35

Ser Ser Gln Ser Leu Glu Asn Xaa Asn Xaa Asn Thr Tyr Leu Asn Trp
1 5 10 15

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Arg
20 25 30

<210> 36
<211> 6
<212> PRT
<213> Mus musculus

<400> 36

Asn Ser Asn Gly Asn Thr
1 5

<210> 37
<211> 4
<212> PRT
<213> Mus musculus

<400> 37

Lys Phe Asn Gly
1

<210> 38
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized HVR-H2 fragment with N64Q mutation

<400> 38

Thr Glu Lys Phe Gln Gly
1 5

<210> 39
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized HVR-L2 fragment with S27eP mutation

<400> 39

Leu Glu Asn Pro Asn Gly Asn Thr
1 5

<210> 40
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized HVR-L2 fragment with S27eP/N28S mutation

<400> 40

Leu Glu Asn Pro Ser Gly Asn Thr
1   5

<210> 41
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 41

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
1   5   10   15

Gly Ser

<210> 42
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> human transferrin receptor fragment

<400> 42

Ile Gly Gln Asn Met Val Thr Ile Val Gln Ser Asn Gly Asn Leu
1   5   10   15

<210> 43
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> human transferrin receptor fragment

<400> 43

Asn Met Val Thr Ile Val Gln Ser Asn Gly Asn Leu Asp Pro Val
1 5 10 15

<210> 44
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> human transferrin receptor fragment

<400> 44

Gln Ser Asn Gly Asn Leu Asp Pro Val Glu Ser Pro Glu Gly Tyr
1 5 10 15

<210> 45
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> peptidic linker

<400> 45

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

<210> 46
<211> 118
<212> PRT
<213> Mus musculus

<400> 46

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Asn
1 5 10 15

```
Ser Leu Thr Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asn Tyr
            20                  25                  30

Gly Met His Trp Ile Arg Gln Ala Pro Lys Lys Gly Leu Glu Trp Ile
        35                  40                  45

Ala Met Ile Tyr Tyr Asp Ser Ser Lys Met Asn Tyr Ala Asp Thr Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Glu Met Asn Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

Ala Val Pro Thr Ser His Tyr Val Val Asp Val Trp Gly Gln Gly Val
            100                 105                 110

Ser Val Thr Val Ser Ser
        115
```

<210> 47
<211> 107
<212> PRT
<213> Mus musculus

<400> 47

```
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu
1               5                   10                  15

Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
        35                  40                  45
```

```
Tyr Gly Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Arg Ser Gly Thr Gln Phe Ser Leu Lys Ile Ser Arg Val Gln Val
65                  70                  75                  80


Glu Asp Ile Gly Ile Tyr Tyr Cys Leu Gln Ala Tyr Asn Thr Pro Trp
                85                  90                  95


Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
            100                 105


<210>  48
<211>  107
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  L104V and L106I variant of SEQ ID NO: 57

<400>  48

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Leu Glu
1               5                   10                  15


Glu Ile Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Gly Asn Trp
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
        35                  40                  45


Tyr Gly Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Arg Ser Gly Thr Gln Phe Ser Leu Lys Ile Ser Arg Val Gln Val
65                  70                  75                  80


Glu Asp Ile Gly Ile Tyr Tyr Cys Leu Gln Ala Tyr Asn Thr Pro Trp
```

85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 49
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> 299-023 VH humanization variant_DASG

<400> 49

Gln Ser Met Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr
1 5 10 15

Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Tyr Ala
20 25 30

Met Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Tyr Ile Trp Ser Gly Gly Ser Thr Asp Tyr Ala Ser Trp Ala Lys Ser
50 55 60

Arg Val Thr Ile Ser Lys Thr Ser Thr Thr Val Ser Leu Lys Leu Ser
65 70 75 80

Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Arg Tyr
85 90 95

Gly Thr Ser Tyr Pro Asp Tyr Gly Asp Ala Ser Gly Phe Asp Pro Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 50
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> 299-009 VL humanization variant_NYA

<400> 50

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Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45


Tyr Arg Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60


Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Asn Tyr Ala Ser Ser Asn
                85                  90                  95


Val Asp Asn Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105                 110
```

<210> 51
<211> 7
<212> PRT
<213> Oryctolagus cuniculus

<400> 51

```
Gly Phe Ser Leu Ser Ser Tyr
1               5
```

<210> 52
<211> 5
<212> PRT
<213> Oryctolagus cuniculus

<400> 52

Trp Ser Gly Gly Ser
1 5

<210> 53
<211> 17
<212> PRT
<213> Oryctolagus cuniculus

<400> 53

Arg Tyr Gly Thr Ser Tyr Pro Asp Tyr Gly Asp Ala Asn Gly Phe Asp
1 5 10 15

Pro

<210> 54
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> 299-000 HVR-H3 DASG

<400> 54

Arg Tyr Gly Thr Ser Tyr Pro Asp Tyr Gly Asp Ala Ser Gly Phe Asp
1 5 10 15

Pro

<210> 55
<211> 17

<212> PRT
<213> Artificial Sequence

<220>
<223> 299-000 HVR-H3 DAQG

<400> 55

Arg Tyr Gly Thr Ser Tyr Pro Asp Tyr Gly Asp Ala Gln Gly Phe Asp
1 5 10 15

Pro

<210> 56
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> 299-000 HVR-L1 RAA

<400> 56

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Ala
1 5 10

<210> 57
<211> 7
<212> PRT
<213> Oryctolagus cuniculus

<400> 57

Arg Ala Ser Thr Leu Ala Ser
1 5

<210> 58
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> 299-000 HVR-L3 NYA

<400> 58

Gln Gln Asn Tyr Ala Ser Ser Asn Val Asp Asn Thr
1   5   10

<210> 59
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 0

<400> 59

Gln Ser Leu Glu Asn Ser Asn Gly Asn Thr Tyr Leu
1   5   10

<210> 60
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 1

<400> 60

Gln Ser Leu Glu His Ser Asn Gly Asn Thr Tyr Leu
1   5   10

<210> 61
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 2

<400> 61

Gln Ser Leu Glu Gln Ser Asn Gly Asn Thr Tyr Leu
1   5   10

<210> 62
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 3

<400> 62

Gln Ser Leu Glu Asn Ala Asn Gly Asn Thr Tyr Leu
1   5   10

<210> 63
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 4

<400> 63

Gln Ser Leu Glu Asn Val Asn Gly Asn Thr Tyr Leu
1   5   10

<210> 64
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 5

<400> 64

Gln Ser Leu Glu Asn Pro Asn Gly Asn Thr Tyr Leu
1   5   10

<210> 65
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 6

<400> 65

Gln Ser Leu Glu Asn Ser Gln Gly Asn Thr Tyr Leu
1   5   10

<210> 66
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 7

<400> 66

Gln Ser Leu Glu Asn Ser Asn Ala Asn Thr Tyr Leu
1   5   10

<210> 67
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 8

<400> 67

Gln Ser Leu Glu Asn Ser Asn Val Asn Thr Tyr Leu
1   5   10

<210> 68
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence LC variant 9

<400> 68

Gln Ser Leu Glu Asn Pro Ser Gly Asn Thr Tyr Leu

1 5 10

<210> 69
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence HC variant 0

<400> 69

Thr Glu Lys Phe Asn Gly Lys Ala Thr Leu
1 5 10

<210> 70
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> sequence HC variant 1

<400> 70

Thr Glu Lys Phe Gln Gly Arg Val Thr Met
1 5 10