

SEQUENCE LISTING

<110> Roche Glycart AG

<120> Combination therapy of an afucosylated antibody and one or more of the cytokines GM-CSF, M-CSF and IL-3

<130> 25390 WO

<150> EP 09004754.9

<151> 2009-03-31

<160> 31

<170> PatentIn version 3.2

<210> 1

<211> 112

<212> PRT

<213> Mus sp.

<220>

<221> MISC_FEATURE

<223> amino acid sequence of variable region of the heavy chain (VH) of murine monoclonal anti-CD20 antibody B-Ly1

<400> 1

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

Ala Ser Gly Tyr Ala Phe Ser Tyr Ser Trp Met Asn Trp Val Lys Leu
20 25 30

Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Arg Ile Phe Pro Gly Asp
35 40 45

Gly Asp Thr Asp Tyr Asn Gly Lys Phe Lys Gly Lys Ala Thr Leu Thr
50 55 60

Ala Asp Lys Ser Ser Asn Thr Ala Tyr Met Gln Leu Thr Ser Leu Thr
65 70 75 80

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

Tyr Trp Leu Val Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala
100 105 110

<210> 2
<211> 103
<212> PRT
<213> Mus sp.

<220>
<221> MISC_FEATURE
<223> amino acid sequence of variable region of the light chain (VL) of
murine monoclonal anti-CD20 antibody B-Ly1

<400> 2

Asn Pro Val Thr Leu Gly Thr Ser Ala Ser Ile Ser Cys Arg Ser Ser
1 5 10 15

Lys Ser Leu Leu His Ser Asn Gly Ile Thr Tyr Leu Tyr Trp Tyr Leu
20 25 30

Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Gln Met Ser Asn
35 40 45

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

Asp Phe Thr Leu Arg Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
65 70 75 80

Tyr Tyr Cys Ala Gln Asn Leu Glu Leu Pro Tyr Thr Phe Gly Gly Gly
85 90 95

Thr Lys Leu Glu Ile Lys Arg
100

<210> 3
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HH2)

<400> 3

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser

1 5 10 15

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

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

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 4
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Lyl antibody (B-HH3)

<400> 4

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

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

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

Gly Arg Ile Phe Pro Gly Asp Gly Asp Thr Asp Tyr Asn Gly Lys Phe

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly

100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 6
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HH5)

<400> 6

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

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

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

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 7
<211> 119
<212> PRT
<213> Artificial

<220>

<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HH6)

<400> 7

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

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

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

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 8

<211> 119

<212> PRT

<213> Artificial

<220>

<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HH7)

<400> 8

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

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

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

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 9
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Lyl antibody (B-HH8)

<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 Tyr Ser
20 25 30

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

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 10
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Lyl antibody (B-HH9)

<400> 10

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 Ser Tyr Ser
20 25 30

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

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 11
<211> 119
<212> PRT
<213> Artificial

<220>

<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL8)

<400> 11

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 12
<211> 119
<212> PRT
<213> Artificial

<220>

<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL10)

<400> 12

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Tyr Ser
20 25 30

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 13
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL11)

<400> 13

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 14
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL12)

<400> 14

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 15
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL13)

<400> 15

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 16
<211> 119
<212> PRT

<213> Artificial

<220>

<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Lyl antibody (B-HL14)

<400> 16

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 17

<211> 119

<212> PRT

<213> Artificial

<220>

<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Lyl antibody (B-HL15)

<400> 17

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 18
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL16)

<400> 18

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 19
<211> 119
<212> PRT
<213> Artificial

<220>
<223> amino acid sequences of variable region of the heavy chain (VH)
of humanized B-Ly1 antibody (B-HL17)

<400> 19

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

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

Trp Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

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

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

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

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100 105 110

,

Thr Leu Val Thr Val Ser Ser
115

<210> 20

<211> 115

<212> PRT

<213> Artificial

<220>

<223> amino acid sequences of variable region of the light chain (VL)
of humanized B-Ly1 antibody B-KV1

<400> 20

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

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

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

Pro Gln Leu Leu Ile Tyr Gln Met Ser Asn Leu Val 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 Ala Gln Asn
85 90 95

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

Arg Thr Val
115

<210> 21

<211> 144

<212> PRT

<213> Homo sapiens

<400> 21

Met Trp Leu Gln Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile

1 5 10 15

Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His
20 25 30

Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp
35 40 45

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe
50 55 60

Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys
65 70 75 80

Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met
85 90 95

Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser
100 105 110

Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys
115 120 125

Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu
130 135 140

<210> 22
<211> 144
<212> PRT
<213> Homo sapiens

<400> 22

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

Ser Ala Pro Gly Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His
20 25 30

Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp
35 40 45

Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe

| | | | | | | | | | | | | | | | | | | | | | | |
|-----------|--------------|------------|------------|-----------|-----------|------------|------------|------------|-----------|-----------|------------|-----------|-----------|-----------|-----------|--|--|--|--|--|--|----|
| 50 | | | | | | | | | | | 55 | | | | | | | | | | | 60 |
| Asp 65 | Leu | Gln | Glu | Pro | Thr 70 | Cys | Leu | Gln | Thr | Arg 75 | Leu | Glu | Leu | Tyr | Lys 80 | | | | | | | |
| Gln | Gly | Leu | Arg | Gly 85 | Ser | Leu | Thr | Lys | Leu 90 | Lys | Gly | Pro | Leu | Thr 95 | Met | | | | | | | |
| Met | Ala | Ser | His 100 | Tyr | Lys | Gln | His | Cys 105 | Pro | Pro | Thr | Pro | Glu | Thr | Ser | | | | | | | |
| Cys | Ala | Thr 115 | Gln | Thr | Ile | Thr | Phe 120 | Glu | Ser | Phe | Lys | Glu | Asn | Leu | Lys | | | | | | | |
| Asp | Phe 130 | Leu | Leu | Val | Ile | Pro 135 | Phe | Asp | Cys | Trp | Glu 140 | Pro | Val | Gln | Glu | | | | | | | |
| <210> | 23 | | | | | | | | | | | | | | | | | | | | | |
| <211> | 152 | | | | | | | | | | | | | | | | | | | | | |
| <212> | PRT | | | | | | | | | | | | | | | | | | | | | |
| <213> | Homo sapiens | | | | | | | | | | | | | | | | | | | | | |
| <400> | 23 | | | | | | | | | | | | | | | | | | | | | |
| Met 1 | Ser | Arg | Leu | Pro 5 | Val | Leu | Leu | Leu | Leu 10 | Gln | Leu | Leu | Val | Arg 15 | Pro | | | | | | | |
| Gly | Leu | Gln | Ala 20 | Pro | Met | Thr | Gln | Thr 25 | Thr | Pro | Leu | Lys | Thr 30 | Ser | Trp | | | | | | | |
| Val | Asn | Cys 35 | Ser | Asn | Met | Ile | Asp 40 | Glu | Ile | Ile | Thr | His 45 | Leu | Lys | Gln | | | | | | | |
| Pro 50 | Pro | Leu | Pro | Leu | Leu | Asp 55 | Phe | Asn | Asn | Leu | Asn 60 | Gly | Glu | Asp | Gln | | | | | | | |
| Asp 65 | Ile | Leu | Met | Glu | Asn 70 | Asn | Leu | Arg | Arg | Pro 75 | Asn | Leu | Glu | Ala | Phe 80 | | | | | | | |
| Asn | Arg | Ala | Val | Lys 85 | Ser | Leu | Gln | Asn | Ala 90 | Ser | Ala | Ile | Glu | Ser | Ile | | | | | | | |
| Leu | Lys | Asn | Leu | Leu | Pro | Cys | Leu | Pro | Leu | Ala | Thr | Ala | Ala | Pro | Thr | | | | | | | |

100 105 110

Arg`His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
115 120 125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
130 135 140

Thr Thr Leu Ser Leu Ala Ile Phe
145 150

<210> 24
<211> 152
<212> PRT
<213> Homo sapiens

<400> 24

Met Ser Arg Leu Pro Val Leu Leu Leu Leu Gln Leu Leu Val Arg Pro
1 5 10 15

Gly Leu Gln Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp
20 25 30

Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
35 40 45

Pro Pro Leu Pro Leu Leu Asp Phe Asn Ser Leu Asn Gly Glu Asp Gln
50 55 60

Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe
65 70 75 80

Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile
85 90 95

Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr
100 105 110

Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
115 120 125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln

130 135 140

Thr Thr Leu Ser Leu Ala Ile Phe
145 150

<210> 25
<211> 152
<212> PRT
<213> Homo sapiens

<400> 25

Met Ser Arg Leu Pro Val Leu Leu Leu Leu Gln Leu Leu Val Arg Pro
1 5 10 15

Gly Leu Gln Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp
20 25 30

Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr Arg Leu Lys Gln
35 40 45

Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln
50 55 60

Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe
65 70 75 80

Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile
85 90 95

Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr
100 105 110

Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
115 120 125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
130 135 140

Thr Thr Leu Ser Leu Ala Ile Phe
145 150

<210> 26

<211> 554
<212> PRT
<213> Homo sapiens

<400> 26

Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu
1 5 10 15

Gly Ser Leu Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr
20 25 30

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
35 40 45

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
50 55 60

Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
65 70 75 80

Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
85 90 95

Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
100 105 110

Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
115 120 125

Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
130 135 140

Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
145 150 155 160

Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
165 170 175

Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu
180 185 190

Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His

| 195 | | | | | 200 | | | | | 205 | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gln | Pro | Leu | Ala | Pro | Ser | Met | Ala | Pro | Val | Ala | Gly | Leu | Thr | Trp | Glu |
| 210 | | | | | | 215 | | | | | 220 | | | | |
| Asp | Ser | Glu | Gly | Thr | Glu | Gly | Ser | Ser | Leu | Leu | Pro | Gly | Glu | Gln | Pro |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Leu | His | Thr | Val | Asp | Pro | Gly | Ser | Ala | Lys | Gln | Arg | Pro | Pro | Arg | Ser |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Thr | Cys | Gln | Ser | Phe | Glu | Pro | Pro | Glu | Thr | Pro | Val | Val | Lys | Asp | Ser |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Thr | Ile | Gly | Gly | Ser | Pro | Gln | Pro | Arg | Pro | Ser | Val | Gly | Ala | Phe | Asn |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Pro | Gly | Met | Glu | Asp | Ile | Leu | Asp | Ser | Ala | Met | Gly | Thr | Asn | Trp | Val |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Pro | Glu | Glu | Ala | Ser | Gly | Glu | Ala | Ser | Glu | Ile | Pro | Val | Pro | Gln | Gly |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Thr | Glu | Leu | Ser | Pro | Ser | Arg | Pro | Gly | Gly | Gly | Ser | Met | Gln | Thr | Glu |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Pro | Ala | Arg | Pro | Ser | Asn | Phe | Leu | Ser | Ala | Ser | Ser | Pro | Leu | Pro | Ala |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Ser | Ala | Lys | Gly | Gln | Gln | Pro | Ala | Asp | Val | Thr | Gly | Thr | Ala | Leu | Pro |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Arg | Val | Gly | Pro | Val | Arg | Pro | Thr | Gly | Gln | Asp | Trp | Asn | His | Thr | Pro |
| | 370 | | | | | 375 | | | | | 380 | | | | |
| Gln | Lys | Thr | Asp | His | Pro | Ser | Ala | Leu | Leu | Arg | Asp | Pro | Pro | Glu | Pro |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Gly | Ser | Pro | Arg | Ile | Ser | Ser | Leu | Arg | Pro | Gln | Gly | Leu | Ser | Asn | Pro |
| | | | | 405 | | | | | 410 | | | | | 415 | |

Ser Thr Leu Ser Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly
420 425 430

Ser Val Leu Pro Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp
435 440 445

Arg Arg Ser Pro Ala Glu Pro Glu Gly Gly Pro Ala Ser Glu Gly Ala
450 455 460

Ala Arg Pro Leu Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly
465 470 475 480

His Glu Arg Gln Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser
485 490 495

Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val
500 505 510

Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro
515 520 525

Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr
530 535 540

Gln Asp Asp Arg Gln Val Glu Leu Pro Val
545 550

<210> 27
<211> 554
<212> PRT
<213> Homo sapiens

<400> 27

Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu
1 5 10 15

Gly Ser Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr
20 25 30

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
35 40 45

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
50 55 60

Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
65 70 75 80

Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
85 90 95

Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
100 105 110

Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
115 120 125

Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
130 135 140

Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
145 150 155 160

Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
165 170 175

Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu
180 185 190

Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His
195 200 205

Gln Pro Leu Ala Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu
210 215 220

Asp Ser Glu Gly Thr Glu Gly Ser Ser Leu Leu Pro Gly Glu Gln Pro
225 230 235 240

Leu His Thr Val Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser
245 250 255

Thr Cys Gln Ser Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser
260 265 270

Thr Ile Gly Gly Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn
275 280 285

Pro Gly Met Glu Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val
290 295 300

Pro Glu Glu Ala Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly
305 310 315 320

Thr Glu Leu Ser Pro Ser Arg Pro Gly Gly Gly Ser Met Gln Thr Glu
325 330 335

Pro Ala Arg Pro Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala
340 345 350

Ser Ala Lys Gly Gln Gln Pro Ala Asp Val Thr Gly Thr Ala Leu Pro
355 360 365

Arg Val Gly Pro Val Arg Pro Thr Gly Gln Asp Trp Asn His Thr Pro
370 375 380

Gln Lys Thr Asp His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro
385 390 395 400

Gly Ser Pro Arg Ile Ser Ser Leu Arg Pro Gln Gly Leu Ser Asn Pro
405 410 415

Ser Thr Leu Ser Ala Gln Pro Gln Leu Ser Arg Ser His Ser Ser Gly
420 425 430

Ser Val Leu Pro Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp
435 440 445

Arg Arg Ser Pro Ala Glu Pro Glu Gly Gly Pro Ala Ser Glu Gly Ala
450 455 460

Ala Arg Pro Leu Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly
465 470 475 480

His Glu Arg Gln Ser Glu Gly Ser Phe Ser Pro Gln Leu Gln Glu Ser
485 490 495

Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val
500 505 510

Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro
515 520 525

Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr
530 535 540

Gln Asp Asp Arg Gln Val Glu Leu Pro Val
545 550

<210> 28
<211> 120
<212> PRT
<213> Artificial

<220>
<223> heavy chain variable domain, humanized <EGFR>ICR62-I-HHD

<400> 28

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

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

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

Gly Tyr Phe Asn Pro Asn Ser Gly Tyr Ser Thr Tyr Ala Gln Lys Phe
50 55 60

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

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

Ala Arg Leu Ser Pro Gly Gly Tyr Tyr Val Met Asp Ala Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 29
<211> 108
<212> PRT
<213> Artificial

<220>
<223> light chain variable domain, humanized <EGFR>ICR62 -I-KC

<400> 29

Asp Ile Gln Met 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 Gly Ile Asn Asn Tyr
20 25 30

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

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

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

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

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr
100 105

<210> 30
<211> 118
<212> PRT
<213> Homo sapiens

<400> 30

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

Ser Gln Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

29 20 25 30

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

Ala Ile Ile Trp Phe Asp Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

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

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

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

Leu Val Ser Val Ser Ser
 115

<210> 31
<211> 108
<212> PRT
<213> Homo sapiens

<400> 31

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
 20 25 30

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

Tyr Asp Ala Ser Lys Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Lys Trp Pro Pro

- 29 -

85

90

95

| | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Trp | Thr | Phe | Gly | Gln | Gly | Thr | Lys | Val | Glu | Ser | Lys |
| | | | 100 | | | | | 105 | | | |