

SEQUENCE LISTING

<110> Numab Innovation AG
 <120> Anti-TNFalpha-antibodies and functional fragments thereof
 <130> 112257P877PC
 <150> EP16000653.2
 <151> 2016-03-17
 <160> 39
 <170> PatentIn version 3.5
 <210> 1
 <211> 11
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> artificial CDR sequence; positions "X" indicate positions of limited diversity
 <220>
 <221> MISC_FEATURE
 <222> (4)..(4)
 <223> X (or Xaa) is placeholder for limited diversity consisting of amino acid residues E and Q
 <220>
 <221> MISC_FEATURE
 <222> (8)..(8)
 <223> X (or Xaa) is placeholder for limited diversity consisting of amino acid residues N and S
 <220>
 <221> MISC_FEATURE
 <222> (11)..(11)
 <223> X (or Xaa) is placeholder for limited diversity consisting of amino acid residues A and S
 <400> 1
 Gln Ala Ser Xaa Ser Ile Ser Xaa Trp Leu Xaa
 1 5 10

<210> 2
 <211> 7
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> artificial CDR sequence

 <400> 2

Lys Ala Ser Thr Leu Ala Ser
 1 5

<210> 3
 <211> 13
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> artificial CDR sequence; positions "X" indicate positions of
 limited diversity

<220>
 <221> MISC_FEATURE
 <222> (7)..(7)
 <223> X (or Xaa) is placeholder for limited diversity consisting of
 amino acid residues N and S

<400> 3

Gln Gly Tyr Tyr Tyr Ser Xaa Ser Gly Asp Asp Asn Ala
 1 5 10

<210> 4
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial CDR sequence; positions "X" indicate positions of
 limited diversity

<220>
 <221> MISC_FEATURE
 <222> (6)..(6)

3

<223> X (or Xaa) is placeholder for limited diversity consisting of amino acid residues R, S and T

<400> 4

Gly	Ile	Asp	Phe	Ser	Xaa	Tyr	Gly	Ile	Ser
1				5				10	

<210> 5

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence; positions "X" indicate positions of limited diversity

<220>

<221> MISC_FEATURE

<222> (8)..(8)

<223> X (or Xaa) is placeholder for limited diversity consisting of amino acid residues I and T

<220>

<221> MISC_FEATURE

<222> (13)..(13)

<223> X (or Xaa) is placeholder for limited diversity consisting of amino acid residues N and S

<400> 5

Tyr	Ile	Tyr	Pro	Asp	Tyr	Gly	Xaa	Thr	Asp	Tyr	Ala	Xaa	Trp	Val	Asn
1				5				10						15	

Gly

<210> 6

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence; positions "X" indicate positions of limited diversity

<220>
 <221> MISC_FEATURE
 <222> (8)..(8)
 <223> X (or Xaa) is placeholder for limited diversity consisting of
 amino acid residues R and S

<220>
 <221> MISC_FEATURE
 <222> (13)..(13)
 <223> X (or Xaa) is placeholder for limited diversity consisting of
 amino acid residues E and H

<400> 6

Arg Ser Gly Ser Tyr Tyr Ser Xaa Gly Trp Gly Ala Xaa Tyr Phe Asn
 1 5 10 15

Leu

<210> 7
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial CDR sequence

<400> 7

Gln Ala Ser Glu Ser Ile Ser Ser Trp Leu Ala
 1 5 10

<210> 8
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial CDR sequence

<400> 8

Gln Gly Tyr Tyr Leu Asp Ser Ser Val Asp Asp Asn Val

1 5 10 5

<210> 9
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> artificial CDR sequence

<400> 9

Gly Ile Asp Phe Ser Thr Tyr Gly Ile Ser
1 5 10

<210> 10
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> artificial CDR sequence

<400> 10

Tyr Ile Tyr Pro Asp Tyr Gly Ile Thr Asp Tyr Ala Ser Trp Val Asn
1 5 10 15

Gly

<210> 11
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> artificial CDR sequence

<400> 11

Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp Gly Ala His Tyr Phe Asn
1 5 10 15

Leu

<210> 12
 <211> 125
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody VH sequence

<400> 12

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

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

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

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

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

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

Ala Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp Gly Ala His Tyr Phe
 100 105 110

Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120 125

<210> 13
 <211> 125
 <212> PRT

<213> Artificial Sequence

<220>

<223> artificial antibody VH sequence

<400> 13

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

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

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

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

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

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

Ala Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp Gly Ala His Tyr Phe
100 105 110

Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 14

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial antibody VH sequence

<400> 14

8
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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

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

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

Asn Gly Arg Phe Thr Ile Ser Leu Asp Asn Ala Gln Asn Thr Val Tyr
65 70 75 80

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

Ala Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp Gly Ala His Tyr Phe
100 105 110

Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

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

<220>
<223> artificial antibody VL sequence

<400> 15

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 Gln Ala Ser Glu Ser Ile Ser Ser Trp
20 25 30

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

Tyr Lys 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 Gly Tyr Tyr Leu Asp Ser Ser
 85 90 95

Val Asp Asp Asn Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
 100 105 110

<210> 16

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial antibody VL sequence

<400> 16

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 Asn Cys Gln Ala Ser Glu Ser Ile Ser Ser Trp
 20 25 30

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

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

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

Ala Asp Phe Ala Thr Tyr Tyr Cys Gln Gly Tyr Tyr Leu Asp Ser Ser
 85 90 95

Val Asp Asp Asn Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
 100 105 110

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

<220>
 <223> artificial antibody VL sequence

<400> 17

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 Asn Cys Gln Ala Ser Glu Ser Ile Ser Ser Trp
 20 25 30

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

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

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

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

Val Asp Asp Asn Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
 100 105 110

<210> 18

<211> 258
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody scFv sequence

<400> 18

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

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

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

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

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

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

Ser Val Asp Asp Asn Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
 130 135 140

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile
 145 150 155 160

Asp Phe Ser Thr Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Lys
165 170 175

Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Pro Asp Tyr Gly Ile Thr Asp
180 185 190

Tyr Ala Ser Trp Val Asn Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
195 200 205

Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
210 215 220

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp
225 230 235 240

Gly Ala His Tyr Phe Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val
245 250 255

Ser Ser

<210> 19
<211> 258
<212> PRT
<213> Artificial Sequence

<220>
<223> artificial antibody scFv sequence

<400> 19

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

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

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

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

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

Pro Ala Asp Phe Ala Thr Tyr Tyr Cys Gln Gly Tyr Tyr Leu Asp Ser
 85 90 95

Ser Val Asp Asp Asn Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
 130 135 140

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Ile
 145 150 155 160

Asp Phe Ser Thr Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Lys
 165 170 175

Gly Leu Glu Trp Ile Ala Tyr Ile Tyr Pro Asp Tyr Gly Ile Thr Asp
 180 185 190

Tyr Ala Ser Trp Val Asn Gly Arg Phe Thr Ile Ser Leu Asp Asn Ser
 195 200 205

Lys Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
 210 215 220

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp
 225 230 235 240

Gly Ala His Tyr Phe Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val
 245 250 255

Ser Ser

<210> 20
 <211> 258
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody scFv sequence

<400> 20

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

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

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

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

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
 65 70 75 80

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

Ser Val Asp Asp Asn Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
 130 135 140

Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile
 145 150 155 160

Asp Phe Ser Thr Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Lys
 165 170 175

Gly Leu Glu Trp Ile Ala Tyr Ile Tyr Pro Asp Tyr Gly Ile Thr Asp
 180 185 190

Tyr Ala Ser Trp Val Asn Gly Arg Phe Thr Ile Ser Leu Asp Asn Ala
 195 200 205

Gln Asn Thr Val Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
 210 215 220

Ala Val Tyr Tyr Cys Ala Arg Ser Gly Ser Tyr Tyr Ser Arg Gly Trp
 225 230 235 240

Gly Ala His Tyr Phe Asn Leu Trp Gly Gln Gly Thr Leu Val Thr Val
 245 250 255

Ser Ser

<210> 21

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence

<400> 21

Gln Ala Ser Gln Ser Ile Ser Ser Trp Leu Ser
 1 5 10

<210> 22
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial CDR sequence

<400> 22

Gln Ala Ser Gln Ser Ile Ser Asn Trp Leu Ala
 1 5 10

<210> 23
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial CDR sequence

<400> 23

Gln Gly Tyr Tyr Tyr Ser Ser Ser Gly Asp Asp Asn Ala
 1 5 10

<210> 24
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial CDR sequence

<400> 24

Gln Gly Tyr Tyr Tyr Ser Asn Ser Gly Asp Asp Asn Ala
 1 5 10

<210> 25
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>

<223> artificial CDR sequence

<400> 25

Gly	Ile	Asp	Phe	Ser	Ser	Tyr	Gly	Ile	Ser
1				5					10

<210> 26

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence

<400> 26

Gly	Ile	Asp	Phe	Ser	Arg	Tyr	Gly	Ile	Ser
1				5					10

<210> 27

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence

<400> 27

Tyr	Ile	Tyr	Pro	Asp	Tyr	Gly	Thr	Thr	Asp	Tyr	Ala	Ser	Trp	Val	Asn
1				5					10					15	

Gly

<210> 28

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence

<400> 28

Tyr	Ile	Tyr	Pro	Asp	Tyr	Gly	Thr	Thr	Asp	Tyr	Ala	Asn	Trp	Val	Asn
1				5					10					15	

Gly

<210> 29

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial CDR sequence

<400> 29

Arg	Ser	Gly	Ser	Tyr	Tyr	Ser	Ser	Gly	Trp	Gly	Ala	Glu	Tyr	Phe	Asn
1				5					10					15	

Leu

<210> 30

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial linker sequence

<400> 30

Gly	Gly	Gly	Gly	Ser
1				5

<210> 31

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> artificial linker sequence

<220>
 <221> REPEAT
 <222> (1)..(5)
 <223> generic linker sequence (GGGGS)_n, with n being selected from 2,
 3, 4, 5, and 6

<400> 31

Gly Gly Gly Gly Ser
 1 5

<210> 32
 <211> 20
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial linker sequence

<400> 32

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

Gly Gly Gly Ser
 20

<210> 33
 <211> 23
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 33

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
 20

<210> 34
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 34

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5				10					15	

<210> 35
 <211> 32
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 35

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5				10					15		

Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys
			20				25						30		

<210> 36
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 36

Phe	Gly	Thr	Gly	Thr	Lys	Val	Thr	Val	Leu
1				5					10

<210> 37
 <211> 10

<212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 37

Phe	Gly	Gly	Gly	Thr	Lys	Leu	Thr	Val	Leu
1				5					10

<210> 38
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 38

Phe	Gly	Gly	Gly	Thr	Gln	Leu	Ile	Ile	Leu
1				5					10

<210> 39
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> artificial antibody framework sequence

<400> 39

Phe	Gly	Ser	Gly	Thr	Lys	Val	Thr	Val	Leu
1				5					10