

SEQUENCE LISTING

<110> Tillotts Pharma AG
 <120> Anti-TNF-alpha antibodies and functional fragments thereof
 <130> PW000279TIL
 <150> EP16160918.5
 <151> 2016-03-17
 <160> 37
 <170> PatentIn version 3.5
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 <223> Generic CDR L1
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 <222> (7)..(7)
 <223> Xaa is Ser or Gly
 <220>
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 <222> (8)..(8)
 <223> Xaa is Ser or Asn
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 <222> (11)..(11)
 <223> Xaa is Ala or Ser
 <400> 1
 Gln Ala Ser Gln Ser Ile Xaa Xaa Tyr Leu Xaa
 1 5 10
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<220>
<223> Generic CDR L2

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa is Arg, Gln or Lys

<400> 2

Xaa Ala Ser Thr Leu Ala Ser
1 5

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

<220>
<223> Generic CDR L3

<220>
<221> misc_feature
<222> (2)..(2)
<223> Xaa can be any naturally occurring amino acid

<400> 3

Gln Xaa Thr Tyr Tyr Glu Pro Ser Tyr Val Phe Arg Ala
1 5 10

<210> 4
<211> 11
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<220>
<223> Generic CDR H1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa is Arg or Gly

<400> 4

Xaa Ile Asp Phe Ser Ala Gly Tyr Asp Met Cys
1 5 10

<210> 5
<211> 17
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<220>
<223> Generic CDR H2

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is Arg, Asn or Ser

<220>
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<222> (7)..(7)
<223> Xaa is Asp or Glu

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa is Asn, Asp or Glu

<220>
<221> MISC_FEATURE
<222> (9)..(9)
<223> Xaa is Ser or Thr

<400> 5

Cys Ile Asp Ser Arg Xaa Xaa Xaa Xaa Asp Tyr Ala Ser Trp Ala Lys
1 5 10 15

Gly

<210> 6
<211> 14
<212> PRT
<213> Artificial Sequence

<220>

<223> CDR H3 of clones 17-22-B03, 16-12-E09, 16-13-E01, 16-15-E11,
16-17-C08, 16-17-G01, 17-18-D10 and 17-22-B01

<400> 6

Gly Gly Tyr Gly Gly Asp Gly Val Asp Gly Ala Phe Asp Pro
1 5 10

<210> 7

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> CDR L1 of clones 17-22-B03, 16-12-E09, 16-13-E01, 16-15-E11 and
17-18-D10

<400> 7

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

<210> 8

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> CDR L2 of clones 17-22-B03, 16-12-E09, 16-15-E11, 16-17-C08,
16-17-G01 and 17-18-D10

<400> 8

Lys Ala Ser Thr Leu Ala Ser
1 5

<210> 9

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> CDR L3 of clones 17-22-B03, 16-12-E09, 16-13-E01, 16-15-E11,
16-17-C08, 16-17-G01, 17-18-D10 and 17-22-B01

<400> 9

Gln Cys Thr Tyr Tyr Glu Pro Ser Tyr Val Phe Arg Ala
1 5 10

<210> 10
<211> 11
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<213> Artificial Sequence

<220>
<223> CDR H1 of clones 17-22-B03, 16-12-E09, 16-13-E01, 16-15-E11,
16-17-C08, 17-18-D10 and 17-22-B01

<400> 10

Gly Ile Asp Phe Ser Ala Gly Tyr Asp Met Cys
1 5 10

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

<220>
<223> CDR H2 of clones 17-22-B03 and 16-17-C08

<400> 11

Cys Ile Asp Ser Arg Arg Glu Glu Ser Asp Tyr Ala Ser Trp Ala Lys
1 5 10 15

Gly

<210> 12
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2 of clone 16-12-E09

<400> 12

Cys Ile Asp Ser Arg Ser Asp Asn Thr Asp Tyr Ala Ser Trp Ala Lys
1 5 10 15

Gly

<210> 13
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L2 of clone 16-13-E01

<400> 13

Gln Ala Ser Thr Leu Ala Ser
1 5

<210> 14
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2 of clones 16-13-E01 and 17-18-D10

<400> 14

Cys Ile Asp Ser Arg Arg Glu Asp Ser Asp Tyr Ala Ser Trp Ala Lys
1 5 10 15

Gly

<210> 15
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2 of clones 16-15-E11, 16-17-G01 and 17-22-B01

<400> 15

Cys Ile Asp Ser Arg Asn Asp Asn Thr Asp Tyr Ala Ser Trp Ala Lys
1 5 10 15

Gly

<210> 16
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L1 of clone 16-17-C08

<400> 16

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

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

<220>
<223> CDR L1 of clone 16-17-G01

<400> 17

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

<210> 18
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H1 of clone 16-17-G01

<400> 18

Arg Ile Asp Phe Ser Ala Gly Tyr Asp Met Cys
1 5 10

<210> 19
<211> 11
<212> PRT

<213> Artificial Sequence

<220>

<223> CDR L1 of clone 17-22-B01

<400> 19

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

<210> 20

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> CDR L2 of clone 17-22-B01

<400> 20

Arg Ala Ser Thr Leu Ala Ser
1 5

<210> 21

<211> 124

<212> PRT

<213> Artificial Sequence

<220>

<223> VH of humanized scFv of clones 17-22-B03-sc02, 17-22-B03-sc08,
17-22-B03-sc12

<400> 21

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 Ala Gly
20 25 30

Tyr Asp Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Ala Cys Ile Asp Ser Arg Arg Glu Glu Ser Asp Tyr Ala Ser Trp
50 55 60

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

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

Cys Ala Arg Gly Gly Tyr Gly Gly Asp Gly Val Asp Gly Ala Phe Asp
100 105 110

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

<210> 22

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> VL of humanized scFv of clone 17-22-B03-sc02

<400> 22

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 Lys Cys Gln 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 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 Asp Leu Glu Pro
65 70 75 80

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

Tyr Val Phe Arg Ala Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

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

<220>
<223> VL of humanized scFv of clone 17-22-B03-sc08

<400> 23

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 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 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 Cys Thr Tyr Tyr Glu Pro Ser
85 90 95

Tyr Val Phe Arg Ala Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 24
<211> 112
<212> PRT
<213> Artificial Sequence

<220>

<223> VL of humanized scFv of clone 17-22-B03-sc12

<400> 24

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 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 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 Ser Thr Tyr Tyr Glu Pro Ser
85 90 95

Tyr Val Phe Arg Ala Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 25

<211> 257

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized scFv of clone 17-22-B03-sc02

<400> 25

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 Lys Cys Gln Ala Ser Gln Ser Ile Ser Ser
20 25 30

Tyr 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 Asp Leu Glu
65 70 75 80

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

Ser Tyr Val Phe Arg Ala 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 Ala Gly Tyr Asp Met Cys Trp Val Arg Gln Ala Pro Gly
165 170 175

Lys Gly Leu Glu Trp Ile Ala Cys Ile Asp Ser Arg Arg Glu Glu Ser
180 185 190

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

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

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Gly Tyr Gly Gly Asp Gly Val
225 230 235 240

Asp Gly Ala Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser
245 250 255

Ser

<210> 26
<211> 257
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized scFv of clone 17-22-B03-sc08

<400> 26

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 Gln Ser Ile Ser Ser
20 25 30

Tyr 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 Cys Thr Tyr Tyr Glu Pro
85 90 95

Ser Tyr Val Phe Arg Ala 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 Ala Gly Tyr Asp Met Cys Trp Val Arg Gln Ala Pro Gly
165 170 175

Lys Gly Leu Glu Trp Ile Ala Cys Ile Asp Ser Arg Arg Glu Glu Ser
180 185 190

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

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

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Gly Tyr Gly Gly Asp Gly Val
225 230 235 240

Asp Gly Ala Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser
245 250 255

Ser

<210> 27
<211> 257
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized scFv of clone 17-22-B03-sc12

<400> 27

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 Gln Ser Ile Ser Ser
20 25 30

Tyr 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 Ser Thr Tyr Tyr Glu Pro
85 90 95

Ser Tyr Val Phe Arg Ala 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 Ala Gly Tyr Asp Met Cys Trp Val Arg Gln Ala Pro Gly
165 170 175

Lys Gly Leu Glu Trp Ile Ala Cys Ile Asp Ser Arg Arg Glu Glu Ser
180 185 190

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

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

Thr Ala Val Tyr Tyr Cys Ala Arg Gly Gly Tyr Gly Gly Asp Gly Val
225 230 235 240

Asp Gly Ala Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser
245 250 255

Ser

<210> 28
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic CDR L3 where Cys2 (Xaa) is limited to Arg, His, Pro, Phe,
Gln, Gly or Tyr

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Arg, His, Pro, Phe, Gln, Gly or Tyr

<400> 28

Gln Xaa Thr Tyr Tyr Glu Pro Ser Tyr Val Phe Arg Ala
1 5 10

<210> 29
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker sequence in scFv

<400> 29

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> 30
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker sequence in diabody

<400> 30

Gly Gly Gly Gly Ser
1 5

<210> 31
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Vk1 consensus sequence of framework I (Kabat positions 1-23)

<400> 31

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> 32
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Vk1 consensus sequence of framework II (Kabat positions 35-49)

<400> 32

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

<210> 33
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Vk1 consensus sequence of framework III (Kabat positions 57-88)

<400> 33

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> 34
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> V lamda germline-based sequence of framework IV

<400> 34

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

<210> 35
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> V lamda germline-based sequence of framework IV

<400> 35

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

<210> 36
<211> 10
<212> PRT

<213> Artificial Sequence

<220>

<223> V lamda germline-based sequence of framework IV

<400> 36

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

<210> 37

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> V lamda germline-based sequence of framework IV

<400> 37

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