SEQUENCE LISTING

<110> Tillotts Pharma AG

<120> Anti-TNF-alpha antibodies and functional fragments thereof

<130> PWO00279TIL

<150> EP16160918.5
<151> 2016-03-17

<160> 37

<170> PatentIn version 3.5

<210> 1
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic CDR L1

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa is Ser or Gly

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa is Ser or Asn

<220>
<221> MISC_FEATURE
<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

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

<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
<212> PRT
<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
<212> PRT
<213> Artificial Sequence

<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
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic CDR H2

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

<220>
<221> MISC_FEATURE
<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
<212> PRT
<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