SEQUENCE LISTING

<110> Micromet AG

<120> Novel treatment of pediatric acute lymphoblastic leukemia

<130> R2201 PCT S3

<150> 61/112,323
<151> 2008-11-07

<150> 61/221,269
<151> 2009-06-29

<150> 61/183,291
<151> 2009-06-02

<160> 22

<170> PatentIn version 3.3

<210> 1
<211> 498
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: CD19xCD3 bispecific single chain antibody"

<400> 1

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

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

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

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

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

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly
100 105 110

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Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val
        115                 120                 125

Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser Ser Val
    130                 135                 140

Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr Trp Met
145                 150                 155                 160

Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Gln
                165                 170                 175

Ile Trp Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys Gly
            180                 185                 190

Lys Ala Thr Leu Thr Ala Asp Glu Ser Ser Ser Thr Ala Tyr Met Gln
        195                 200                 205

Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Phe Cys Ala Arg
    210                 215                 220

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr Trp
225                 230                 235                 240

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Asp
                245                 250                 255

Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala Ser
            260                 265                 270

Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr Thr
        275                 280                 285

Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly
    290                 295                 300

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
305                 310                 315                 320

Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr Met
                325                 330                 335

Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala
            340                 345                 350
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Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly Thr
        355                 360                 365

Thr Leu Thr Val Ser Ser Val Glu Gly Gly Ser Gly Gly Ser Gly Gly
    370                 375                 380

Ser Gly Gly Ser Gly Gly Val Asp Asp Ile Gln Leu Thr Gln Ser Pro
385                 390                 395                 400

Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg
                405                 410                 415

Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln Lys Ser Gly
            420                 425                 430

Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Val Ala Ser Gly
        435                 440                 445

Val Pro Tyr Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
    450                 455                 460

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln
465                 470                 475                 480

Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu
                485                 490                 495

Leu Lys
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<210> 2
<211> 1494
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: CD19xCD3 bispecific single chain antibody"

<400> 2

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gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc     60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac    120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct    180

gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat    240
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cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300

acgttcggtg gagggaccaa gctcgagatc aaaggtggtg gtggttctgg cggcggcggc 360

tccggtggtg gtggttctca ggtgcagctg cagcagtctg gggctgagct ggtgaggcct 420

gggtcctcag tgaagatttc ctgcaaggct tctggctatg cattcagtag ctactggatg 480

aactgggtga agcagaggcc tggacagggt cttgagtgga ttggacagat ttggcctgga 540

gatggtgata ctaactacaa tggaaagttc aagggtaaag ccactctgac tgcagacgaa 600

tcctccagca cagcctacat gcaactcagc agcctagcat ctgaggactc tgcggtctat 660

ttctgtgcaa gacgggagac tacgacggta ggccgttatt actatgctat ggactactgg 720

ggccaaggga ccacggtcac cgtctcctcc ggaggtggtg gatccgatat caaactgcag 780

cagtcagggg ctgaactggc aagacctggg gcctcagtga agatgtcctg caagacttct 840

ggctacacct ttactaggta cacgatgcac tgggtaaaac agaggcctgg acagggtctg 900

gaatggattg gatacattaa tcctagccgt ggttatacta attacaatca gaagttcaag 960

gacaaggcca cattgactac agacaaatcc tccagcacag cctacatgca actgagcagc 1020

ctgacatctg aggactctgc agtctattac tgtgcaagat attatgatga tcattactgc 1080

cttgactact ggggccaagg caccactctc acagtctcct cagtcgaagg tggaagtgga 1140

ggttctggtg gaagtggagg ttcaggtgga gtcgacgaca ttcagctgac ccagtctcca 1200

gcaatcatgt ctgcatctcc aggggagaag gtcaccatga cctgcagagc cagttcaagt 1260

gtaagttaca tgaactggta ccagcagaag tcaggcacct cccccaaaag atggatttat 1320

gacacatcca aagtggcttc tggagtccct tatcgcttca gtggcagtgg gtctgggacc 1380

tcatactctc tcacaatcag cagcatggag gctgaagatg ctgccactta ttactgccaa 1440

cagtggagta gtaacccgct cacgttcggt gctgggacca agctggagct gaaa 1494

<210> 3
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: VH anti CD19"

<400> 3

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

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

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

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

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

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

Ala Arg Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp
            100                 105                 110

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120
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<210> 4
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: VH anti CD19"

<400> 4

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caggtgcagc tgcagcagtc tggggctgag ctggtgaggc ctgggtcctc agtgaagatt     60

tcctgcaagg cttctggcta tgcattcagt agctactgga tgaactgggt gaagcagagg    120

cctggacagg gtcttgagtg gattggacag atttggcctg gagatggtga tactaactac    180

aatggaaagt tcaagggtaa agccactctg actgcagacg aatcctccag cacagcctac    240

atgcaactca gcagcctagc atctgaggac tctgcggtct atttctgtgc aagacgggag    300

actacgacgg taggccgtta ttactatgct atggactact ggggccaagg gaccacggtc    360

accgtctcct cc                                                        372
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<210> 5
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: VL anti CD19"

<400> 5

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

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

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

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Val Ser Gly Ile Pro Pro
50 55 60

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

Pro Val Glu Lys Val Asp Ala Ala Thr Tyr His Cys Gln Gln Ser Thr
85 90 95

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 6
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: VL anti CD19"

<400> 6
gatatccagc tgacccagtc tccagcttct ttggctgtgt ctctagggca gagggccacc 60

atctcctgca aggccagcca aagtgttgat tatgatggtg atagttattt gaactggtac 120

caacagattc caggacagcc acccaaactc ctcatctatg atgcatccaa tctagtttct 180

gggatcccac ccaggtttag tggcagtggg tctgggacag acttcaccct caacatccat 240

cctgtggaga aggtggatgc tgcaacctat cactgtcagc aaagtactga ggatccgtgg 300

acgttcggtg gagggaccaa gctcgagatc aaa 333

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

<220>
<221> source

<223> VH anti CD3

<400> 7

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Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1               5                   10                  15

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

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

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

Lys Asp Lys Ala Thr Leu Thr Thr Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

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

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Thr Leu Thr Val Ser Ser
        115
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<210> 8
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: VH anti CD3"

<400> 8

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gatatcaaac tgcagcagtc aggggctgaa ctggcaagac ctggggcctc agtgaagatg     60

tcctgcaaga cttctggcta cacctttact aggtacacga tgcactgggt aaaacagagg    120

cctggacagg gtctggaatg gattggatac attaatccta gccgtggtta tactaattac    180

aatcagaagt tcaaggacaa ggccacattg actacagaca aatcctccag cacagcctac    240

atgcaactga gcagcctgac atctgaggac tctgcagtct attactgtgc aagatattat    300

gatgatcatt actgccttga ctactggggc caaggcacca ctctcacagt ctcctca       357
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<210> 9

<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of artificial sequence: VL anti CD3"

<400> 9

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

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

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

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

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

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

<210> 10
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<220>
<221> source

<400> 10
gacattcagc tgacccagtc tccagcaatc atgtctgcat ctccagggga gaaggtcacc 60

atgacctgca gagccagttc aagtgtaagt tacatgaact ggtaccagca gaagtcaggc 120

acctccccca aaagatggat ttatgacaca tccaaagtgg cttctggagt cccttatcgc 180

ttcagtggca gtgggtctgg gacctcatac tctctcacaa tcagcagcat ggaggctgaa 240

gatgctgcca cttattactg ccaacagtgg agtagtaacc cgctcacgtt cggtgctggg 300

accaagctgg agctgaaa 318

<210> 11
<211> 15
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD19 L1"

<400> 11

Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Leu Asn
1 5 10 15

<210> 12
<211> 7
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD19 L2"

<400> 12

Asp Ala Ser Asn Leu Val Ser
1 5

<210> 13
<211> 9
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD19 L3"

<400> 13

Gln Gln Ser Thr Glu Asp Pro Trp Thr
1 5

<210> 14
<211> 5
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD19 H1"

<400> 14

Ser Tyr Trp Met Asn
1 5

<210> 15
<211> 17
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD19 H2"

<400> 15

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

Gly

<210> 16
<211> 15
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD19 H3"

<400> 16

Arg Glu Thr Thr Thr Val Gly Arg Tyr Tyr Tyr Ala Met Asp Tyr
1 5 10 15

<210> 17
<211> 5
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD3 H1"

<400> 17

Arg Tyr Thr Met His
1 5

<210> 18
<211> 17
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD3 H2"

<400> 18

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

Asp

<210> 19
<211> 10
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD3 H3"

<400> 19

Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr
1 5 10

<210> 20
<211> 10
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD3 L1"

<400> 20

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
1 5 10

<210> 21
<211> 7
<212> PRT
<213> artificial sequence

<220>
<221> source
<223> /note="Description of artificial sequence: anti-CD3 L2"

<400> 21

Asp Thr Ser Lys Val Ala Ser
1 5

<210> 22
<211> 9
<212> PRT
<213> artificial sequence

<220>

<221> source
<223> /note="Description of artificial sequence: anti-CD3 L3"

<400> 22

Gln Gln Trp Ser Ser Asn Pro Leu Thr
1 5