

1301\_0116PCT\_Sequence\_Listing\_ST25  
SEQUENCE LISTING

<110> MacroGenics, Inc.  
Johnson, Leslie  
Bonvini, Ezio  
Lam, Chia-Ying Kao  
Moore, Paul  
Liu, Liqin  
Koenig, Scott

<120> Bi-Specific Monovalent Diabodies That Are Capable of Binding CD19  
and CD3, and Uses Thereof

<130> 1301.0116PCT

<150> US 62/0255,695  
<151> 2014-09-26

<160> 48

<170> PatentIn version 3.5

<210> 1  
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<212> PRT  
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<223> Intervening Spacer Peptide (Linker 1)

<400> 1  
Gly Gly Gly Ser Gly Gly Gly Gly  
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<210> 2  
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<400> 2  
Ala Ser Thr Lys Gly  
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<223> Cysteine-Containing Linker

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Gly Gly Cys Gly Gly Gly  
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<210> 4  
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<212> PRT  
<213> Homo sapiens

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<220>  
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 <223> IgG1 Hinge Domain

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Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
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<400> 5

Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
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<210> 6  
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<220>  
 <223> Heterodimer-Promoting Domain

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Gly Val Glu Pro Lys Ser Cys  
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<210> 7  
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<220>  
 <223> Heterodimer-Promoting Domain

<400> 7

Val Glu Pro Lys Ser Cys  
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<220>  
 <223> Heterodimer-Promoting Domain

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Gly Phe Asn Arg Gly Glu Cys  
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<210> 9  
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Phe Asn Arg Gly Glu Cys  
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<210> 10  
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 <223> E-coil Heterodimer-Promoting Domain

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Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys Glu Val  
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Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys  
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 <223> K-coil Heterodimer-Promoting Domain

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Lys Val Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu Lys Val  
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Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu  
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 <223> Cysteine-Containing E-coil Heterodimer-Promoting Domain

<400> 12

Glu Val Ala Ala Cys Glu Lys Glu Val Ala Ala Leu Glu Lys Glu Val  
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Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys  
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Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu  
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 <223> CH2-CH3 Domain of Human IgG1

<400> 14

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys  
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Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val  
 20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr  
 35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu  
 50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His  
 65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys  
 85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln  
 100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met  
 115 120 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro  
 130 135 140

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Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn  
145 150 155 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu  
165 170 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val  
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln  
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys  
210 215

<210> 15

<211> 217

<212> PRT

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<220>

<223> "Knob-Bearing" CH2-CH3 Domain

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

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val  
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr  
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu  
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His  
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys  
85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln  
100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met  
115 120 125

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro  
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn  
145 150 155 160

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Tyr Lys Thr Thr Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu  
165 170 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val  
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln  
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys  
210 215

<210> 16

<211> 217

<212> PRT

<213> Artificial Sequence

<220>

<223> "Hole-Bearing" CH2-CH3 Domain

<400> 16

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys  
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Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val  
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr  
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu  
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His  
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys  
85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln  
100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met  
115 120 125

Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro  
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn  
145 150 155 160

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Tyr Lys Thr Thr Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu  
165 170 175

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val  
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln  
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys  
210 215

<210> 17  
<211> 106  
<212> PRT  
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<223> Variable Light Chain of Anti-CD19 Antibody

<400> 17

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

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

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

Asp Ala Ser Asn Arg Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser  
50 55 60

Gly Ser Gly Thr Asp His Thr Leu Thr Ile Ser Ser Leu Glu Ala Glu  
65 70 75 80

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

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

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

<220>  
<223> CDR1 of Variable Light Chain of Anti-CD19 Antibody

<400> 18

Arg Ala Ser Gln Ser Val Ser Tyr Met His  
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<210> 19

<211> 7

<212> PRT

<213> Artificial sequence

<220>

<223> CDR2 of Variable Light Chain of Anti-CD19 Antibody

<400> 19

Asp Ala Ser Asn Arg Ala Ser  
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<210> 20

<211> 9

<212> PRT

<213> Artificial sequence

<220>

<223> CDR3 of Variable Light Chain of Anti-CD19 Antibody

<400> 20

Phe Gln Gly Ser Val Tyr Pro Phe Thr  
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<210> 21

<211> 120

<212> PRT

<213> Artificial sequence

<220>

<223> Variable Heavy Chain of Anti-CD19 Antibody

<400> 21

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

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser  
20 25 30

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

Trp Leu Ala His Ile Trp Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ala  
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val  
65 70 75 80

Phe Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr  
85 90 95

Cys Ala Arg Met Glu Leu Trp Ser Tyr Tyr Phe Asp Tyr Trp Gly Gln  
100 105 110

Gly Thr Thr Val Thr Val Ser Ser  
115 120

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

<220>  
 <223> CDR1 of Variable Heavy Chain of Anti-CD19 Antibody  
 <400> 22

Thr Ser Gly Met Gly Val Gly  
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<210> 23  
 <211> 16  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> CDR2 of Variable Heavy Chain of Anti-CD19 Antibody  
 <400> 23

His Ile Trp Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ala Leu Lys Ser  
 1 5 10 15

<210> 24  
 <211> 10  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> CDR3 of Variable Heavy Chain of Anti-CD19 Antibody  
 <400> 24

Met Glu Leu Trp Ser Tyr Tyr Phe Asp Tyr  
 1 5 10

<210> 25  
 <211> 110  
 <212> PRT  
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 <223> Variable Light Chain of Anti-CD3 Antibody  
 <400> 25

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

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

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

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe  
 50 55 60

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Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala  
65 70 75 80

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

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly  
100 105 110

<210> 26  
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<223> CDR1 of Variable Light Chain of Anti-CD3 Antibody  
<400> 26

Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn  
1 5 10

<210> 27  
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<212> PRT  
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<223> CDR2 of Variable Light Chain of Anti-CD3 Antibody  
<400> 27

Gly Thr Asn Lys Arg Ala Pro  
1 5

<210> 28  
<211> 9  
<212> PRT  
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<223> CDR3 of Variable Light Chain of Anti-CD3 Antibody  
<400> 28

Ala Leu Trp Tyr Ser Asn Leu Trp Val  
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<210> 29  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> variable Heavy Chain of Anti-CD3 Antibody  
<400> 29

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

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

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

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

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

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

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe  
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser  
115 120 125

<210> 30  
<211> 5  
<212> PRT  
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<223> CDR1 of Variable Heavy Chain of Anti-CD3 Antibody  
<400> 30

Thr Tyr Ala Met Asn  
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<210> 31  
<211> 19  
<212> PRT  
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<220>  
<223> CDR2 of Variable Heavy Chain of Anti-CD3 Antibody  
<400> 31

Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser  
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Val Lys Gly

<210> 32  
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<220>

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<223> CDR3 of Variable Heavy Chain of Anti-CD3 Antibody

<400> 32

His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr  
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<210> 33

<211> 4

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<213> Artificial Sequence

<220>

<223> Linker 4

<400> 33

Gly Gly Gly Ser  
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<210> 34

<211> 46

<212> PRT

<213> Artificial Sequence

<220>

<223> Albumin-Binding Domain (ABD)

<400> 34

Leu Ala Glu Ala Lys Val Leu Ala Asn Arg Glu Leu Asp Lys Tyr Gly  
1 5 10 15

Val Ser Asp Tyr Tyr Lys Asn Leu Ile Asp Asn Ala Lys Ser Ala Glu  
20 25 30

Gly Val Lys Ala Leu Ile Asp Glu Ile Leu Ala Ala Leu Pro  
35 40 45

<210> 35

<211> 502

<212> PRT

<213> Artificial Sequence

<220>

<223> First Polypeptide Chain of DART-A

<400> 35

Glu Asn Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Thr Pro Gly  
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Glu Lys Ala Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Tyr Met  
20 25 30

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

Asp Ala Ser Asn Arg Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser  
50 55 60

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Gly Ser Gly Thr Asp His Thr Leu Thr Ile Ser Ser Leu Glu Ala Glu  
 65 70 75 80  
 Asp Ala Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Val Tyr Pro Phe Thr  
 85 90 95  
 Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro  
 115 120 125  
 Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser  
 130 135 140  
 Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu  
 145 150 155 160  
 Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr  
 165 170 175  
 Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys  
 180 185 190  
 Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala  
 195 200 205  
 Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser  
 210 215 220  
 Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala  
 225 230 235 240  
 Ser Thr Lys Gly Glu Val Ala Ala Cys Glu Lys Glu Val Ala Ala Leu  
 245 250 255  
 Glu Lys Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys  
 260 265 270  
 Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu  
 275 280 285  
 Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp  
 290 295 300  
 Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp  
 305 310 315 320  
 Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly  
 325 330 335

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Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn  
340 345 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp  
355 360 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro  
370 375 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu  
385 390 395 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn  
405 410 415

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile  
420 425 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr  
435 440 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys  
450 455 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys  
465 470 475 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu  
485 490 495

Ser Leu Ser Pro Gly Lys  
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<210> 36  
<211> 1506  
<212> DNA  
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<220>  
<223> Polynucleotide Encoding DART-A (SEQ ID NO:35)

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caagctccca ggttgctgat ctatgacgcg agcaaccggg ctagtggcgt tccatcccgg 180  
ttttctggct caggatctgg cactgaccac accctcacca tatccagcct tgaagccgaa 240  
gatgccgcaa cctactactg ctttcagggg agtgtgtatc cttcacatt cggtcagggt 300  
acaaagctgg agattaaggg tggaggatcc ggcggcggag gcgaggtgca gctggtggag 360  
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<210> 37  
 <211> 271  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Second Polypeptide Chain of DART-A

<400> 37

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

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

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

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe  
 50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala  
 65 70 75 80

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

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly  
100 105 110

Gly Ser Gly Gly Gly Gly Gln Val Thr Leu Arg Glu Ser Gly Pro Ala  
115 120 125

Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly  
130 135 140

Phe Ser Leu Ser Thr Ser Gly Met Gly Val Gly Trp Ile Arg Gln Pro  
145 150 155 160

Pro Gly Lys Ala Leu Glu Trp Leu Ala His Ile Trp Trp Asp Asp Asp  
165 170 175

Lys Arg Tyr Asn Pro Ala Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp  
180 185 190

Thr Ser Lys Asn Gln Val Phe Leu Thr Met Thr Asn Met Asp Pro Val  
195 200 205

Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Met Glu Leu Trp Ser Tyr Tyr  
210 215 220

Phe Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser  
225 230 235 240

Thr Lys Gly Lys Val Ala Ala Cys Lys Glu Lys Val Ala Ala Leu Lys  
245 250 255

Glu Lys Val Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu  
260 265 270

<210> 38

<211> 813

<212> DNA

<213> Artificial Sequence

<220>

<223> Polynucleotide Encoding Second Polypeptide Chain of DART-A (SEQ ID NO:37)

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aagccaggac aggcaccaag gggcctgatc ggggggtacaa aaaaaagggc tccctggacc 180

cctgcacggt tttctggaag tctgctgggc ggaaaggccg ctctgactat taccggggca 240

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| acactgaggg aatctggtcc agctctggtg aaaccctc agacgctcac tctcacttgc   | 420 |
| acctttagtg ggttctcact gtccacatct ggcatgggag taggctggat tcgacagcca | 480 |
| cctgggaaag ccttgagtg gcttgccac atctggtggg atgacgacaa gcggtataat   | 540 |
| cccgcactga agagcagact gaccatcagc aaggatacat ccaagaacca ggtgtttctg | 600 |
| accatgacca acatggaccc tgtcgataca gccacctact attgtgctcg catggagttg | 660 |
| tggtcctact acttcgacta ttggggacaa ggcacaaccg tgactgtctc atccgcctcc | 720 |
| accaagggca aagtggccgc atgtaaggag aaagttgctg ctttgaaaga gaaggtcgcc | 780 |
| gcacttaagg aaaaggtcgc agccctgaaa gag                              | 813 |

<210> 39  
 <211> 227  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Third Polypeptide Chain of DART-A

<400> 39

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Lys | Thr | His | Thr | Cys | Pro | Pro | Cys | Pro | Ala | Pro | Glu | Ala | Ala | Gly |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Pro | Ser | Val | Phe | Leu | Phe | Pro | Pro | Lys | Pro | Lys | Asp | Thr | Leu | Met |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Ser | Arg | Thr | Pro | Glu | Val | Thr | Cys | Val | Val | Val | Asp | Val | Ser | His |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Asp | Pro | Glu | Val | Lys | Phe | Asn | Trp | Tyr | Val | Asp | Gly | Val | Glu | Val |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Asn | Ala | Lys | Thr | Lys | Pro | Arg | Glu | Glu | Gln | Tyr | Asn | Ser | Thr | Tyr |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Arg | Val | Val | Ser | Val | Leu | Thr | Val | Leu | His | Gln | Asp | Trp | Leu | Asn | Gly |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | Glu | Tyr | Lys | Cys | Lys | Val | Ser | Asn | Lys | Ala | Leu | Pro | Ala | Pro | Ile |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Lys | Thr | Ile | Ser | Lys | Ala | Lys | Gly | Gln | Pro | Arg | Glu | Pro | Gln | Val |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tyr | Thr | Leu | Pro | Pro | Ser | Arg | Glu | Glu | Met | Thr | Lys | Asn | Gln | Val | Ser |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Ser | Cys | Ala | Val | Lys | Gly | Phe | Tyr | Pro | Ser | Asp | Ile | Ala | Val | Glu |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

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145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro  
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val  
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met  
195 200 205

His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser  
210 215 220

Pro Gly Lys  
225

<210> 40  
<211> 681  
<212> DNA  
<213> Artificial sequence

<220>  
<223> Polynucleotide Encoding Third Polypeptide Chain of DART-A

<400> 40  
gacaaaactc acacatgccc accgtgcccga gcacctgaag ccgcgggggg accgtcagtc 60  
ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 120  
tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 180  
ggcgtggagg tgcataatgc caagacaaag ccgcggggagg agcagtacaa cagcacgtac 240  
cgtgtggtca gcgtcctcac cgctcctgcac caggactggc tgaatggcaa ggagtacaag 300  
tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 360  
gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 420  
aaccaggtca gcctgagttg cgcagtcaaa ggcttctatc ccagcgacat cgccgtggag 480  
tgggagagca atgggcagcc ggagaacaac tacaagacca cgctcccggt gctggactcc 540  
gacggctcct tcttcctcgt cagcaagctc accgtggaca agagcaggtg gcagcagggg 600  
aacgtcttct catgctccgt gatgcatgag gctctgcaca accgctacac gcagaagagc 660  
ctctccctgt ctccgggtaa a 681

<210> 41  
<211> 112  
<212> PRT  
<213> Artificial sequence

<220>  
<223> Variable Light Chain Domain of Anti-Fluorescein Antibody 4-4-20

<400> 41

Asp Val Val Met Thr Gln Thr Pro Phe Ser Leu Pro Val Ser Leu Gly

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1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
20 25 30

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

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Phe 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 Leu Gly Val Tyr Phe Cys Ser Gln Ser  
85 90 95

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

<210> 42  
<211> 118  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> variable Heavy Chain Domain Of Anti-Fluorescein Antibody 4-4-20

<400> 42

Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg  
1 5 10 15

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

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

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp  
50 55 60

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

Val Tyr Leu Gln Met Asn Asn Leu Arg Val Glu Asp Met Gly Ile Tyr  
85 90 95

Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp Tyr Trp Gly Gln Gly Thr  
100 105 110

Ser Val Thr Val Ser Ser  
115

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<210> 43  
 <211> 508  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> First Polypeptide Chain of Control DART 1

<400> 43

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

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
 20 25 30

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

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Phe 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 Leu Gly Val Tyr Phe Cys Ser Gln Ser  
 85 90 95

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

Gly Gly Gly Ser Gly Gly Gly Gly Glu Val Gln Leu Val Glu Ser Gly  
 115 120 125

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

Ser Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn Trp Val Arg Gln Ala  
 145 150 155 160

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

Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile  
 180 185 190

Ser Arg Asp Asp Ser Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu  
 195 200 205

Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe  
 210 215 220

Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu  
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225 230 235 240

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Glu Val Ala Ala Cys Glu  
245 250 255

Lys Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu Glu Lys Glu  
260 265 270

Val Ala Ala Leu Glu Lys Gly Gly Gly Asp Lys Thr His Thr Cys Pro  
275 280 285

Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe  
290 295 300

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val  
305 310 315 320

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe  
325 330 335

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro  
340 345 350

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr  
355 360 365

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val  
370 375 380

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala  
385 390 395 400

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg  
405 410 415

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly  
420 425 430

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro  
435 440 445

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser  
450 455 460

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln  
465 470 475 480

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His  
485 490 495

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

<210> 44  
<211> 269  
<212> PRT  
<213> Artificial sequence

<220>  
<223> Second Polypeptide Chain of Control DART 1  
<400> 44

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

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

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

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe  
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala  
65 70 75 80

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

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly  
100 105 110

Gly Ser Gly Gly Gly Gly Glu Val Lys Leu Asp Glu Thr Gly Gly Gly  
115 120 125

Leu Val Gln Pro Gly Arg Pro Met Lys Leu Ser Cys Val Ala Ser Gly  
130 135 140

Phe Thr Phe Ser Asp Tyr Trp Met Asn Trp Val Arg Gln Ser Pro Glu  
145 150 155 160

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

Glu Thr Tyr Tyr Ser Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg  
180 185 190

Asp Asp Ser Lys Ser Ser Val Tyr Leu Gln Met Asn Asn Leu Arg Val  
195 200 205

Glu Asp Met Gly Ile Tyr Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp  
210 215 220

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Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys  
225 230 235 240

Gly Lys Val Ala Ala Cys Lys Glu Lys Val Ala Ala Leu Lys Glu Lys  
245 250 255

Val Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu  
260 265

<210> 45  
<211> 495  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Frst Polypeptide Chain of Control DART 2

<400> 45

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

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

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

Asp Ala Ser Asn Arg Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser  
50 55 60

Gly Ser Gly Thr Asp His Thr Leu Thr Ile Ser Ser Leu Glu Ala Glu  
65 70 75 80

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

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Ser Gly Gly  
100 105 110

Gly Gly Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro  
115 120 125

Gly Arg Pro Met Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser  
130 135 140

Asp Tyr Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu  
145 150 155 160

Trp Val Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr  
165 170 175

Ser Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys  
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180

185

190

Ser Ser Val Tyr Leu Gln Met Asn Asn Leu Arg Val Glu Asp Met Gly  
195 200 205

Ile Tyr Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp Tyr Trp Gly Gln  
210 215 220

Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Glu Val Ala  
225 230 235 240

Ala Cys Glu Lys Glu Val Ala Ala Leu Glu Lys Glu Val Ala Ala Leu  
245 250 255

Glu Lys Glu Val Ala Ala Leu Glu Lys Gly Gly Gly Asp Lys Thr His  
260 265 270

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val  
275 280 285

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr  
290 295 300

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu  
305 310 315 320

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys  
325 330 335

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser  
340 345 350

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys  
355 360 365

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile  
370 375 380

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro  
385 390 395 400

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu  
405 410 415

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn  
420 425 430

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser  
435 440 445

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg

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450

455

460

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu  
 465 470 475 480

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
 485 490 495

&lt;210&gt; 46

&lt;211&gt; 269

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Second Polypeptide Chain of Control DART 2

&lt;400&gt; 46

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

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

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

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe  
 50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala  
 65 70 75 80

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

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly Gly  
 100 105 110

Gly Ser Gly Gly Gly Gly Glu Val Lys Leu Asp Glu Thr Gly Gly Gly  
 115 120 125

Leu Val Gln Pro Gly Arg Pro Met Lys Leu Ser Cys Val Ala Ser Gly  
 130 135 140

Phe Thr Phe Ser Asp Tyr Trp Met Asn Trp Val Arg Gln Ser Pro Glu  
 145 150 155 160

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

Glu Thr Tyr Tyr Ser Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg  
 180 185 190

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Asp Asp Ser Lys Ser Ser Val Tyr Leu Gln Met Asn Asn Leu Arg Val  
195 200 205

Glu Asp Met Gly Ile Tyr Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp  
210 215 220

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys  
225 230 235 240

Gly Lys Val Ala Ala Cys Lys Glu Lys Val Ala Ala Leu Lys Glu Lys  
245 250 255

Val Ala Ala Leu Lys Glu Lys Val Ala Ala Leu Lys Glu  
260 265

<210> 47  
<211> 5  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Intervening Spacer Peptide (Linker 4)

<400> 47

Ala Pro Ser Ser Ser  
1 5

<210> 48  
<211> 8  
<212> PRT  
<213> Artificial sequence

<220>  
<223> Intervening Spacer Peptide (Linker 4)

<400> 48

Ala Pro Ser Ser Ser Pro Met Glu  
1 5