

INFORMAL SEQUENCE LISTING

SEQUENCE LISTING

<110> Pastan, Ira H.
Weldon, John
Hasan, Raffit

<120> Recombinant Immunotoxin Targeting
Mesothelin

<130> 77867-803685

<140> US Not yet assigned

<141> Not yet assigned

<160> 73

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 613

<212> PRT

<213> Pseudomonas aeruginosa

<220>

<223> native Pseudomonas exotoxin A (PE)

<400> 1

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Leu	Asp	Leu	Lys	Asp	Gly	Val	Arg	Ser	Ser	Arg	Met	Ser	Val	Asp	Pro
			20					25					30		
Ala	Ile	Ala	Asp	Thr	Asn	Gly	Gln	Gly	Val	Leu	His	Tyr	Ser	Met	Val
		35				40					45				
Leu	Glu	Gly	Gly	Asn	Asp	Ala	Leu	Lys	Leu	Ala	Ile	Asp	Asn	Ala	Leu
	50				55					60					
Ser	Ile	Thr	Ser	Asp	Gly	Leu	Thr	Ile	Arg	Leu	Glu	Gly	Gly	Val	Glu
65				70					75					80	
Pro	Asn	Lys	Pro	Val	Arg	Tyr	Ser	Tyr	Thr	Arg	Gln	Ala	Arg	Gly	Ser
			85					90					95		
Trp	Ser	Leu	Asn	Trp	Leu	Val	Pro	Ile	Gly	His	Glu	Lys	Pro	Ser	Asn
		100					105						110		
Ile	Lys	Val	Phe	Ile	His	Glu	Leu	Asn	Ala	Gly	Asn	Gln	Leu	Ser	His
	115				120					125					
Met	Ser	Pro	Ile	Tyr	Thr	Ile	Glu	Met	Gly	Asp	Glu	Leu	Leu	Ala	Lys
	130				135				140						
Leu	Ala	Arg	Asp	Ala	Thr	Phe	Phe	Val	Arg	Ala	His	Glu	Ser	Asn	Glu
145				150					155					160	
Met	Gln	Pro	Thr	Leu	Ala	Ile	Ser	His	Ala	Gly	Val	Ser	Val	Val	Met
			165					170					175		
Ala	Gln	Thr	Gln	Pro	Arg	Arg	Glu	Lys	Arg	Trp	Ser	Glu	Trp	Ala	Ser
		180					185					190			
Gly	Lys	Val	Leu	Cys	Leu	Leu	Asp	Pro	Leu	Asp	Gly	Val	Tyr	Asn	Tyr
	195				200					205					
Leu	Ala	Gln	Gln	Arg	Cys	Asn	Leu	Asp	Asp	Thr	Trp	Glu	Gly	Lys	Ile
	210			215						220					
Tyr	Arg	Val	Leu	Ala	Gly	Asn	Pro	Ala	Lys	His	Asp	Leu	Asp	Ile	Lys
225				230					235					240	
Pro	Thr	Val	Ile	Ser	His	Arg	Leu	His	Phe	Pro	Glu	Gly	Gly	Ser	Leu
			245					250					255		
Ala	Ala	Leu	Thr	Ala	His	Gln	Ala	Cys	His	Leu	Pro	Leu	Glu	Thr	Phe
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Thr Arg His Arg Gln Pro Arg Gly Trp Glu Gln Leu Glu Gln Cys Gly
275                280                285
Tyr Pro Val Gln Arg Leu Val Ala Leu Tyr Leu Ala Ala Arg Leu Ser
290                295                300
Trp Asn Gln Val Asp Gln Val Ile Arg Asn Ala Leu Ala Ser Pro Gly
305                310                315                320
Ser Gly Gly Asp Leu Gly Glu Ala Ile Arg Glu Gln Pro Glu Gln Ala
325                330                335
Arg Leu Ala Leu Thr Leu Ala Ala Ala Glu Ser Glu Arg Phe Val Arg
340                345                350
Gln Gly Thr Gly Asn Asp Glu Ala Gly Ala Ala Asn Ala Asp Val Val
355                360                365
Ser Leu Thr Cys Pro Val Ala Ala Gly Glu Cys Ala Gly Pro Ala Asp
370                375                380
Ser Gly Asp Ala Leu Leu Glu Arg Asn Tyr Pro Thr Gly Ala Glu Phe
385                390                395                400
Leu Gly Asp Gly Gly Asp Val Ser Phe Ser Thr Arg Gly Thr Gln Asn
405                410                415
Trp Thr Val Glu Arg Leu Leu Gln Ala His Arg Gln Leu Glu Glu Arg
420                425                430
Gly Tyr Val Phe Val Gly Tyr His Gly Thr Phe Leu Glu Ala Ala Gln
435                440                445
Ser Ile Val Phe Gly Gly Val Arg Ala Arg Ser Gln Asp Leu Asp Ala
450                455                460
Ile Trp Arg Gly Phe Tyr Ile Ala Gly Asp Pro Ala Leu Ala Tyr Gly
465                470                475                480
Tyr Ala Gln Asp Gln Glu Pro Asp Ala Arg Gly Arg Ile Arg Asn Gly
485                490                495
Ala Leu Leu Arg Val Tyr Val Pro Arg Ser Ser Leu Pro Gly Phe Tyr
500                505                510
Arg Thr Ser Leu Thr Leu Ala Ala Pro Glu Ala Ala Gly Glu Val Glu
515                520                525
Arg Leu Ile Gly His Pro Leu Pro Leu Arg Leu Asp Ala Ile Thr Gly
530                535                540
Pro Glu Glu Glu Gly Gly Arg Leu Glu Thr Ile Leu Gly Trp Pro Leu
545                550                555                560
Ala Glu Arg Thr Val Val Ile Pro Ser Ala Ile Pro Thr Asp Pro Arg
565                570                575
Asn Val Gly Gly Asp Leu Asp Pro Ser Ser Ile Pro Asp Lys Glu Gln
580                585                590
Ala Ile Ser Ala Leu Pro Asp Tyr Ala Ser Gln Pro Gly Lys Pro Pro
595                600                605
Arg Glu Asp Leu Lys
610

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<210> 2
 <211> 230
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic Pseudomonas exotoxin A with reduced immunogenicity

<220>
 <221> VARIANT
 <222> (1)...(230)
 <223> Xaa = Gly, Ala or Ser

<400> 2
 Arg His Arg Gln Pro Arg Gly Trp Glu Gln Leu Pro Thr Gly Ala Glu
 1 5 10 15

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Phe Leu Gly Asp Gly Gly Xaa Val Ser Phe Ser Thr Arg Gly Thr Gln
      20      25      30
Asn Trp Thr Val Glu Arg Leu Leu Gln Ala His Arg Gln Leu Glu Glu
      35      40      45
Xaa Gly Tyr Val Phe Val Gly Tyr His Gly Thr Phe Leu Glu Ala Ala
      50      55      60
Gln Ser Ile Val Phe Gly Gly Val Arg Ala Arg Ser Gln Asp Leu Asp
      65      70      75      80
Ala Ile Trp Xaa Gly Phe Tyr Ile Ala Gly Asp Pro Ala Leu Ala Tyr
      85      90      95
Gly Tyr Ala Gln Asp Gln Glu Pro Asp Ala Xaa Gly Arg Ile Arg Asn
      100      105      110
Gly Ala Leu Leu Arg Val Tyr Val Pro Arg Ser Ser Leu Pro Gly Phe
      115      120      125
Tyr Xaa Thr Ser Leu Thr Leu Ala Ala Pro Glu Ala Ala Gly Glu Val
      130      135      140
Glu Arg Leu Ile Gly His Pro Leu Pro Leu Arg Leu Asp Ala Ile Thr
      145      150      155      160
Gly Pro Glu Glu Xaa Gly Gly Arg Leu Glu Thr Ile Leu Gly Trp Pro
      165      170      175
Leu Ala Glu Arg Thr Val Val Ile Pro Ser Ala Ile Pro Thr Asp Pro
      180      185      190
Arg Asn Val Gly Gly Asp Leu Asp Pro Ser Ser Ile Pro Asp Xaa Glu
      195      200      205
Xaa Ala Ile Ser Ala Leu Pro Asp Tyr Ala Ser Gln Pro Gly Lys Pro
      210      215      220
Pro Arg Glu Asp Leu Lys
      225      230

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<210> 3
<211> 233
<212> PRT
<213> Artificial Sequence

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<220>
<223> synthetic modified Pseudomonas exotoxin A
      PE-LR/GGS/8M

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<400> 3
Arg His Arg Gln Pro Arg Gly Trp Glu Gln Leu Gly Gly Ser Pro Thr
  1      5      10      15
Gly Ala Glu Phe Leu Gly Asp Gly Gly Ala Val Ser Phe Ser Thr Arg
      20      25      30
Gly Thr Gln Asn Trp Thr Val Glu Arg Leu Leu Gln Ala His Arg Gln
      35      40      45
Leu Glu Glu Gly Gly Tyr Val Phe Val Gly Tyr His Gly Thr Phe Leu
      50      55      60
Glu Ala Ala Gln Ser Ile Val Phe Gly Gly Val Arg Ala Arg Ser Gln
      65      70      75      80
Asp Leu Asp Ala Ile Trp Ala Gly Phe Tyr Ile Ala Gly Asp Pro Ala
      85      90      95
Leu Ala Tyr Gly Tyr Ala Gln Asp Gln Glu Pro Asp Ala Ala Gly Arg
      100      105      110
Ile Arg Asn Gly Ala Leu Leu Arg Val Tyr Val Pro Arg Ser Ser Leu
      115      120      125
Pro Gly Phe Tyr Ala Thr Ser Leu Thr Leu Ala Ala Pro Glu Ala Ala
      130      135      140
Gly Glu Val Glu Arg Leu Ile Gly His Pro Leu Pro Leu Arg Leu Asp
      145      150      155      160
Ala Ile Thr Gly Pro Glu Glu Ser Gly Gly Arg Leu Glu Thr Ile Leu
      165      170      175
Gly Trp Pro Leu Ala Glu Arg Thr Val Val Ile Pro Ser Ala Ile Pro

```

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                180                185                190
Thr Asp Pro Arg Asn Val Gly Gly Asp Leu Asp Pro Ser Ser Ile Pro
                195                200                205
Asp Ser Glu Ala Ala Ile Ser Ala Leu Pro Asp Tyr Ala Ser Gln Pro
                210                215                220
Gly Lys Pro Pro Arg Glu Asp Leu Lys
225                230

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<210> 4
 <211> 238
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic modified Pseudomonas exotoxin A
 PE-LR/FL/8X

<220>
 <221> VARIANT
 <222> (12)...(14)
 <223> Xaa = Gly or Ser

<220>
 <221> VARIANT
 <222> (15)...(19)
 <223> Xaa = Gly or Ser, may be present or absent

<220>
 <221> VARIANT
 <222> (20)...(230)
 <223> Xaa = Gly, Ala or Ser

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<400> 4
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Xaa Xaa Xaa Pro Thr Gly Ala Glu Phe Leu Gly Asp Gly Gly Xaa Val
                20                25                30
Ser Phe Ser Thr Arg Gly Thr Gln Asn Trp Thr Val Glu Arg Leu Leu
                35                40                45
Gln Ala His Arg Gln Leu Glu Glu Xaa Gly Tyr Val Phe Val Gly Tyr
 50                55                60
His Gly Thr Phe Leu Glu Ala Ala Gln Ser Ile Val Phe Gly Gly Val
65                70                75                80
Arg Ala Arg Ser Gln Asp Leu Asp Ala Ile Trp Xaa Gly Phe Tyr Ile
                85                90                95
Ala Gly Asp Pro Ala Leu Ala Tyr Gly Tyr Ala Gln Asp Gln Glu Pro
                100                105                110
Asp Ala Xaa Gly Arg Ile Arg Asn Gly Ala Leu Leu Arg Val Tyr Val
                115                120                125
Pro Arg Ser Ser Leu Pro Gly Phe Tyr Xaa Thr Ser Leu Thr Leu Ala
                130                135                140
Ala Pro Glu Ala Ala Gly Glu Val Glu Arg Leu Ile Gly His Pro Leu
145                150                155                160
Pro Leu Arg Leu Asp Ala Ile Thr Gly Pro Glu Glu Xaa Gly Gly Arg
                165                170                175
Leu Glu Thr Ile Leu Gly Trp Pro Leu Ala Glu Arg Thr Val Val Ile
                180                185                190
Pro Ser Ala Ile Pro Thr Asp Pro Arg Asn Val Gly Gly Asp Leu Asp
                195                200                205
Pro Ser Ser Ile Pro Asp Xaa Glu Xaa Ala Ile Ser Ala Leu Pro Asp
                210                215                220
Tyr Ala Ser Gln Pro Gly Lys Pro Pro Arg Glu Asp Leu Lys

```

225

230

235

<210> 5
 <211> 238
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic modified Pseudomonas exotoxin A
 PE-LR/FL/8M

<220>
 <221> VARIANT
 <222> (12)...(14)
 <223> Xaa = Gly or Ser

<220>
 <221> VARIANT
 <222> (15)...(19)
 <223> Xaa = Gly or Ser, may be present or absent

<400> 5
 Arg His Arg Gln Pro Arg Gly Trp Glu Gln Leu Xaa Xaa Xaa Xaa Xaa
 1 5 10 15
 Xaa Xaa Xaa Pro Thr Gly Ala Glu Phe Leu Gly Asp Gly Gly Ala Val
 20 25 30
 Ser Phe Ser Thr Arg Gly Thr Gln Asn Trp Thr Val Glu Arg Leu Leu
 35 40 45
 Gln Ala His Arg Gln Leu Glu Gly Gly Tyr Val Phe Val Gly Tyr
 50 55 60
 His Gly Thr Phe Leu Glu Ala Ala Gln Ser Ile Val Phe Gly Gly Val
 65 70 75 80
 Arg Ala Arg Ser Gln Asp Leu Asp Ala Ile Trp Ala Gly Phe Tyr Ile
 85 90 95
 Ala Gly Asp Pro Ala Leu Ala Tyr Gly Tyr Ala Gln Asp Gln Glu Pro
 100 105 110
 Asp Ala Ala Gly Arg Ile Arg Asn Gly Ala Leu Leu Arg Val Tyr Val
 115 120 125
 Pro Arg Ser Ser Leu Pro Gly Phe Tyr Ala Thr Ser Leu Thr Leu Ala
 130 135 140
 Ala Pro Glu Ala Ala Gly Glu Val Glu Arg Leu Ile Gly His Pro Leu
 145 150 155 160
 Pro Leu Arg Leu Asp Ala Ile Thr Gly Pro Glu Glu Ser Gly Gly Arg
 165 170 175
 Leu Glu Thr Ile Leu Gly Trp Pro Leu Ala Glu Arg Thr Val Val Ile
 180 185 190
 Pro Ser Ala Ile Pro Thr Asp Pro Arg Asn Val Gly Gly Asp Leu Asp
 195 200 205
 Pro Ser Ser Ile Pro Asp Ser Glu Ala Ala Ile Ser Ala Leu Pro Asp
 210 215 220
 Tyr Ala Ser Gln Pro Gly Lys Pro Pro Arg Glu Asp Leu Lys
 225 230 235

<210> 6
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody SS1
 variable light chain (VL)

<400> 6

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Met Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro
 1           5           10           15
Gly Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr
      20           25           30
Met His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile
      35           40           45
Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Gly Arg Phe Ser Gly
      50           55           60
Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala
65           70           75           80
Glu Asp Asp Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Lys His Pro Leu
      85           90           95
Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys
      100           105

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<210> 7

<211> 355

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody SS1
variable heavy chain (VH)

<400> 7

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Met Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly
 1           5           10           15
Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly
      20           25           30
Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Cys Leu Glu Trp
      35           40           45
Ile Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys
      50           55           60
Phe Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala
65           70           75           80
Tyr Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
      85           90           95
Cys Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln
      100           105           110
Gly Thr Thr Val Thr Val Ser Ser Lys
      115           120

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<210> 8

<211> 358

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
recombinant immunotoxin SS1-LR/GGS/8M variable
heavy chain (VH-PE)

<400> 8

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Met Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly
 1           5           10           15
Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly
      20           25           30
Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Cys Leu Glu Trp
      35           40           45
Ile Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys
      50           55           60

```

```

Phe Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala
65      70      75      80
Tyr Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
      85      90      95
Cys Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln
      100     105     110
Gly Thr Thr Val Thr Val Ser Ser Lys Ala Ser Gly Gly Arg His Arg
      115     120     125
Gln Pro Arg Gly Trp Glu Gln Leu Gly Gly Ser Pro Thr Gly Ala Glu
      130     135     140
Phe Leu Gly Asp Gly Gly Ala Val Ser Phe Ser Thr Arg Gly Thr Gln
145     150     155     160
Asn Trp Thr Val Glu Arg Leu Leu Gln Ala His Arg Gln Leu Glu Glu
      165     170     175
Gly Gly Tyr Val Phe Val Gly Tyr His Gly Thr Phe Leu Glu Ala Ala
      180     185     190
Gln Ser Ile Val Phe Gly Gly Val Arg Ala Arg Ser Gln Asp Leu Asp
      195     200     205
Ala Ile Trp Ala Gly Phe Tyr Ile Ala Gly Asp Pro Ala Leu Ala Tyr
      210     215     220
Gly Tyr Ala Gln Asp Gln Glu Pro Asp Ala Ala Gly Arg Ile Arg Asn
225     230     235     240
Gly Ala Leu Leu Arg Val Tyr Val Pro Arg Ser Ser Leu Pro Gly Phe
      245     250     255
Tyr Ala Thr Ser Leu Thr Leu Ala Ala Pro Glu Ala Ala Gly Glu Val
      260     265     270
Glu Arg Leu Ile Gly His Pro Leu Pro Leu Arg Leu Asp Ala Ile Thr
      275     280     285
Gly Pro Glu Glu Ser Gly Gly Arg Leu Glu Thr Ile Leu Gly Trp Pro
      290     295     300
Leu Ala Glu Arg Thr Val Val Ile Pro Ser Ala Ile Pro Thr Asp Pro
305     310     315     320
Arg Asn Val Gly Gly Asp Leu Asp Pro Ser Ser Ile Pro Asp Ser Glu
      325     330     335
Ala Ala Ile Ser Ala Leu Pro Asp Tyr Ala Ser Gln Pro Gly Lys Pro
      340     345     350
Pro Arg Glu Asp Leu Lys
      355

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<210> 9
<211> 358
<212> PRT
<213> Artificial Sequence

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<220>
<223> synthetic anti-mesothelin monoclonal antibody
      recombinant immunotoxin SS1-LR/GGS/8X variable heavy
      chain (VH-PE)

```

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<400> 9
Met Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly
1      5      10      15
Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly
      20      25      30
Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Cys Leu Glu Trp
      35      40      45
Ile Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys
      50      55      60
Phe Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala
65      70      75      80
Tyr Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
      85      90      95

```

Cys Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln
 100 105 110
 Gly Thr Thr Val Thr Val Ser Ser Lys Ala Ser Gly Gly Arg His Arg
 115 120 125
 Gln Pro Arg Gly Trp Glu Gln Leu Gly Gly Ser Pro Thr Gly Ala Glu
 130 135 140
 Phe Leu Gly Asp Gly Gly Asp Val Ser Phe Ser Thr Arg Gly Thr Gln
 145 150 155 160
 Asn Trp Thr Val Glu Arg Leu Leu Gln Ala His Arg Gln Leu Glu Glu
 165 170 175
 Arg Gly Tyr Val Phe Val Gly Tyr His Gly Thr Phe Leu Glu Ala Ala
 180 185 190
 Gln Ser Ile Val Phe Gly Gly Val Arg Ala Arg Ser Gln Asp Leu Asp
 195 200 205
 Ala Ile Trp Arg Gly Phe Tyr Ile Ala Gly Asp Pro Ala Leu Ala Tyr
 210 215 220
 Gly Tyr Ala Gln Asp Gln Glu Pro Asp Ala Arg Gly Arg Ile Arg Asn
 225 230 235 240
 Gly Ala Leu Leu Arg Val Tyr Val Pro Arg Ser Ser Leu Pro Gly Phe
 245 250 255
 Tyr Arg Thr Ser Leu Thr Leu Ala Ala Pro Glu Ala Ala Gly Glu Val
 260 265 270
 Glu Arg Leu Ile Gly His Pro Leu Pro Leu Arg Leu Asp Ala Ile Thr
 275 280 285
 Gly Pro Glu Glu Glu Gly Gly Arg Leu Glu Thr Ile Leu Gly Trp Pro
 290 295 300
 Leu Ala Glu Arg Thr Val Val Ile Pro Ser Ala Ile Pro Thr Asp Pro
 305 310 315 320
 Arg Asn Val Gly Gly Asp Leu Asp Pro Ser Ser Ile Pro Asp Lys Glu
 325 330 335
 Gln Ala Ile Ser Ala Leu Pro Asp Tyr Ala Ser Gln Pro Gly Lys Pro
 340 345 350
 Pro Arg Glu Asp Leu Lys
 355

<210> 10
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody SS1
 variable light chain (V-L)

<400> 10
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 ggcacctccc ccaaaagatg gatttatgac acatccaaac tggcttcttg agtcccaggt 180
 cgcttcagtg gcagtgggtc tggaaactct tactctctca caatcagcag cgtggagggt 240
 gaagatgatg caacttatta ctgccagcag tggccaagc accctctcac gttcggttgc 300
 gggacaaaag tggaaataaa ataa 324

<210> 11
 <211> 1068
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody
 recombinant immunotoxin SS1-LR variable heavy
 chain (VH-PE)

<400> 11

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 atatcctcga aggcactcgg ttactcattc actggtaca ccatgaactg ggtgaagcag 120
 agtcatgaa agtgccttga gtgattga ctattactc cttaaatg tgctcttagc 180
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 atatcctcga aggcactcgg ttactcattc actggtaca ccatgaactg ggtgaagcag 120
 agtcatgaa agtgccttga gtgattga ctattactc cttaaatg tgctcttagc 180
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 recombinant immunotoxin SSI-LR/8M variable heavy chain (VH-PE)
 <213> Artificial Sequence
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 <211> 1068
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 ctccgctcgc cgtgcacgtg gtcacacgtg gtgattccct cggcgatccc caccgaaccg 960
 ccgcctcgc ttgaaacccat caccggccc gcgaggtcag gcggcgccct ggaagacatt 900
 ctgaacctgg ccggcccgga ggcggccggc gaagtccgaac ggtgattcgg ccatccgctg 840
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 cgcgcgcga gccaggaacct cgacgcgatt tctatatcgc cggcgatccc cggcgatccc 660
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 ggttacagcg ggaagggttt tgactactgg ggcacaaggga ccaaggtcac cgtctcctca 360
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 taccaaccga agttcagggg caagggccaca ttaactgttag acaagtctac cagcacaagc 240
 agtcatgaa agtgccttga gtgattga ctattactc cttaaatg tgctcttagc 180
 atatcctcga aggcactcgg ttactcattc actggtaca ccatgaactg ggtgaagcag 120
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 <223> synthetic anti-mesothelin monoclonal antibody
 recombinant immunotoxin SSI-LR/GGS/8M variable heavy chain (VH-PE)
 <213> Artificial Sequence
 <212> DNA
 <211> 1077
 <210> 12
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 ctggtatcca tcaccggccc agaggaaggag ggcgtgctgc ttgaaacacat tctgggctgg 900
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 tacggttatg ccaggaacca gtaaccggat gctcgcgcgc gcatcgttaa ttgttgcgctg 720
 tctcaagacc ttgattcgat ttgcgcgttg ttctacatg cagcgcatcc agcgcttgca 660
 taccaagca cttctctgga agcagctcag ttctacgtgt ttggttggtg cgttgcccg 600
 gtgagagcgc ttgctgcagc acatcgtcag cttggaagag gttgctatgt attcgttgcc 540
 gaattcctgg gcgaacgttg cgaattgtcc tttaagcacc gttgtaccga gaaacttgagc 480
 aaagctctcg gaagtctca ccgtcaacca ccggtttggg aaacgctgcc aaacggtgccc 420
 ggttacagcg ggaagggttt tgactactgg ggcacaaggga ccaaggtcac cgtctcctca 360
 tacatggacc tccctcagct gaactctgaa gactctgcag tctattcttg ttcaagggtg 300
 taccaaccga agttcagggg caagggccaca ttaactgttag acaagtctac cagcacaagc 240
 agtcatgaa agtgccttga gtgattga ctattactc cttaaatg tgctcttagc 180
 atatcctcga aggcactcgg ttactcattc actggtaca ccatgaactg ggtgaagcag 120
 atgcaggtac aactgcagca gtctggccct gactgagaga agcctggcgc ttcagtgaag 60

tacaaccaga agttcagggg caaggccaca ttaactgtag acaagtcac cagcacagcc 240
tacatggacc tcctcagtct gacatctgaa gactctgcag tctatttctg tgcaaggggg 300
ggttacgacg ggagggggtt tgactactgg ggccaaggga ccacggtcac cgtctcctca 360
aaagcttccg gaggtcgtca tcgccagccg cgcggctggg aacaactgcc cactggcgcg 420
gagttcctcg gcgacggcgg cgcagtcagc ttcagcaccg gcggcacgca gaactggacg 480
gtggagcggc tgctccaggc gcaccgcca ctggaggagg gcggctatgt gttcgtcggc 540
taccacggca ccttcctcga agcggcgcaa agcatcgtct tcggcggggt gcgcgcgcgc 600
agccaggacc tcgacgcgat ctgggcccgt ttctatatcg ccggcgatcc ggcgctggcc 660
tacggctacg cccaggacca ggaaccgcag gcagccggcc gtatccgcaa cggtgccctg 720
ctgcgggtct atgtgccggc ctcgagcctg cggggcttct acgccaccag cctgaccctg 780
gccgcgccgg agggggcggg cgaggtcgaa cggctgatcg gccatccgct gccgctgcgc 840
ctggacgcca tcaccggccc cgaggagtca ggccggcgcc tggagaccat tctcggctgg 900
ccgctggcgg agcgcaccgt ggtgattccc tcggcgatcc ccaccgacc gcgcaacgctc 960
ggcggcgacc tcgaccgcgc cagcatcccc gacagcgaag cagcgatcag cgccctgccc 1020
gactacgcca gccagcccgg caaacgcggc cgcgaggacc tgaagtaa 1068

<210> 14
<211> 241
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin Fv antibody (SS scFv)

<400> 14
Met Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly
1 5 10 15
Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly
20 25 30
Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp
35 40 45
Ile Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys
50 55 60
Phe Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala
65 70 75 80
Tyr Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95
Cys Ala Arg Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln
100 105 110
Gly Thr Thr Val Thr Val Ser Ser Gly Val Gly Gly Ser Gly Gly Gly
115 120 125
Gly Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Ala
130 135 140
Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Ser Ala
145 150 155 160
Ser Ser Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Ser Gly Thr
165 170 175
Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val
180 185 190
Pro Gly Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr
195 200 205
Ile Ser Ser Val Glu Ala Glu Asp Asp Ala Thr Tyr Tyr Cys Gln Gln
210 215 220
Trp Ser Gly Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
225 230 235 240
Lys

<210> 15
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic C-terminal residues of native PE

<400> 15
Arg Glu Asp Leu Lys
1 5

<210> 16
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic canonical endoplasmic reticulum
retention signal

<400> 16
Lys Asp Glu Leu
1

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

<220>
<223> synthetic furin cleavage site (FCS)

<400> 17
Arg His Arg Gln Pro Arg Gly Trp Glu Gln Leu
1 5 10

<210> 18
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic flexible linker (FL)

<400> 18
Gly Gly Ser Gly Gly Ser
1 5

<210> 19
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic short peptide linker

<400> 19
Ala Ser Gly Gly
1

<210> 20
<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic short peptide linker and furin cleavage
site for SS1-LR

<400> 20

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

<210> 21

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic short peptide linker and furin cleavage
site for SS1-LR/GGS

<400> 21

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

Gly Ser

<210> 22

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic short peptide linker and furin cleavage
site for SS1-LR/GGSx2

<400> 22

Ala	Ser	Gly	Gly	Ser	Gly	Gly	Gly	Arg	His	Arg	Gln	Pro	Arg	Gly	Trp
1				5					10					15	

Glu	Gln	Leu	Gly	Gly	Ser	Gly	Gly	Gly	Ser
			20					25	

<210> 23

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic short peptide linker and furin cleavage
site for SS1-LR/2xFurin

<400> 23

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

Gly	Ser	Arg	His	Arg	Gln	Pro	Arg	Gly	Trp	Glu	Gln	Leu	Gly	Gly	Ser
			20					25					30		

<210> 24

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic short peptide linker and furin cleavage
site for SS1-LR/GGS R279G

<400> 24

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

<210> 25

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic scFv linker peptide

<400> 25

Gly Val Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
1 5 10

<210> 26

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic carboxyl terminus endoplasmic reticulum
retention signal

<400> 26

Arg Glu Asp Leu
1

<210> 27

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic mutated terminal residues of PE

<400> 27

Arg Glu Glu Leu
1

<210> 28

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic mutated terminal residues of PE

<400> 28

Arg Asp Glu Leu
1

<210> 29
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic substituted furin cleavage site

<400> 29
 Arg His Arg Ser Lys Arg Gly Trp Glu Gln Leu
 1 5 10

<210> 30
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic minimal furin cleavage site

<400> 30
 Arg Lys Lys Arg
 1

<210> 31
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic minimal furin cleavage site

<400> 31
 Arg Arg Arg Arg
 1

<210> 32
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic minimal furin cleavage site

<400> 32
 Arg Lys Ala Arg
 1

<210> 33
 <211> 6
 <212> PRT
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<220>
 <223> synthetic furin cleavage site

<400> 33
 Ser Arg Val Ala Arg Ser
 1 5

<210> 34
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic furin cleavage site

<400> 34
Thr Ser Ser Arg Lys Arg Arg Phe Trp
1 5

<210> 35
<211> 9
<212> PRT
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<220>
<223> synthetic furin cleavage site

<400> 35
Ala Ser Arg Arg Lys Ala Arg Ser Trp
1 5

<210> 36
<211> 8
<212> PRT
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<220>
<223> synthetic furin cleavage site

<400> 36
Arg Arg Val Lys Lys Arg Phe Trp
1 5

<210> 37
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic furin cleavage site

<400> 37
Arg Asn Val Val Arg Arg Asp Trp
1 5

<210> 38
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> synthetic furin cleavage site

<400> 38
Thr Arg Ala Val Arg Arg Arg Ser Trp

1 5

<210> 39
 <211> 4
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> synthetic furin cleavage site

 <400> 39
 Arg Gln Pro Arg
 1

<210> 40
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> synthetic furin cleavage site

 <400> 40
 Arg His Arg Gln Pro Arg Gly Trp
 1 5

<210> 41
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> synthetic furin cleavage site

 <400> 41
 Arg His Arg Gln Pro Arg Gly Trp Glu
 1 5

<210> 42
 <211> 9
 <212> PRT
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 <220>
 <223> synthetic furin cleavage site

 <400> 42
 His Arg Gln Pro Arg Gly Trp Glu Gln
 1 5

<210> 43
 <211> 7
 <212> PRT
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 <220>
 <223> synthetic furin cleavage site

<400> 43
 Arg Gln Pro Arg Gly Trp Glu
 1 5

<210> 44
 <211> 4
 <212> PRT
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<220>
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<400> 44
 Arg Ser Lys Arg
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<210> 45
 <211> 8
 <212> PRT
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<220>
 <223> synthetic furin cleavage site

<400> 45
 Arg His Arg Ser Lys Arg Gly Trp
 1 5

<210> 46
 <211> 8
 <212> PRT
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<220>
 <223> synthetic furin cleavage site

<400> 46
 His Arg Ser Lys Arg Gly Trp Glu
 1 5

<210> 47
 <211> 9
 <212> PRT
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<220>
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<400> 47
 Arg Ser Lys Arg Gly Trp Glu Gln Leu
 1 5

<210> 48
 <211> 10
 <212> PRT
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<220>

<223> synthetic furin cleavage site

<400> 48

His Arg Ser Lys Arg Gly Trp Glu Gln Leu
1 5 10

<210> 49

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic furin cleavage site

<400> 49

Arg His Arg Ser Lys Arg
1 5

<210> 50

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic scFv peptide linker

<400> 50

Gly Gly Gly Ser
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<210> 51

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable heavy chain CDR1

<400> 51

Gly Tyr Thr Met Asn
1 5

<210> 52

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable heavy chain CDR2

<400> 52

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

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<210> 53
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin monoclonal antibody
        variable heavy chain CDR3

<400> 53
Gly Gly Tyr Asp Gly Arg Gly Phe Asp Tyr
 1             5             10

<210> 54
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin monoclonal antibody
        variable light chain CDR1

<400> 54
Ser Ala Ser Ser Ser Val Ser Tyr Met His
 1             5             10

<210> 55
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin monoclonal antibody
        variable light chain CDR2

<400> 55
Asp Thr Ser Lys Leu Ala Ser
 1             5

<210> 56
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin monoclonal antibody
        variable light chain CDR3

<400> 56
Gln Gln Trp Ser Gly Tyr Pro Leu Thr
 1             5

<210> 57
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin monoclonal antibody

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variable light chain CDR3

<400> 57

Gln Gln Trp Ser Lys His Pro Leu Thr

1

5

<210> 58

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable light chain CDR3

<400> 58

Gln Gln Trp Ser Gly His Pro Leu Thr

1

5

<210> 59

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable light chain CDR3

<400> 59

Gln Gln Trp Ser Ala His Pro Leu Thr

1

5

<210> 60

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable light chain CDR3

<400> 60

Gln Gln Trp Ser Gln Ile Pro Leu Thr

1

5

<210> 61

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable light chain CDR3

<400> 61

Gln Gln Trp Gly Phe Asn Pro Leu Thr

1

5

<210> 62
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody
 variable light chain CDR3

<400> 62
 Gln Gln Trp Gly Thr Asn Pro Leu Thr
 1 5

<210> 63
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody
 variable light chain CDR3

<400> 63
 Gln Gln Trp Gly Ser His Pro Leu Thr
 1 5

<210> 64
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody
 variable light chain CDR3

<400> 64
 Gln Gln Trp Gly Asp Phe Pro Leu Thr
 1 5

<210> 65
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody
 variable light chain CDR3

<400> 65
 Gln Gln Trp Gly Asp His Pro Leu Thr
 1 5

<210> 66
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic anti-mesothelin monoclonal antibody

variable light chain CDR3

<400> 66

Gln Gln Trp Ser Ala His Pro Leu Thr
1 5

<210> 67

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic anti-mesothelin monoclonal antibody
variable light chain CDR3

<400> 67

Gln Gln Trp Ser Gly Tyr Pro Thr Thr
1 5

<210> 68

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic linker joining carboxyl terminus of
antibody to N-terminus of the furin cleavage site

<400> 68

Ala Ser Gly Gly Ser Gly Gly Gly
1 5

<210> 69

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic flexible linker

<400> 69

Gly Gly Gly Ser Gly
1 5

<210> 70

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic flexible linker

<400> 70

Gly Gly Gly Gly Ser Gly
1 5

<210> 71

<211> 4

<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic flexible linker (FL)

<400> 71
Gly Ser Gly Gly
1

<210> 72
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic flexible linker (FL)

<400> 72
Gly Gly Ser Gly Gly
1 5

<210> 73
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic flexible linker (FL)

<400> 73
Gly Gly Ser Gly
1

<210> 74
<211> 355
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic anti-mesothelin monoclonal antibody
recombinant immunotoxin SS1-LR variable heavy
chain (VH-PE)

<400> 74
Met Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly
1 5 10 15
Ala Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly
20 25 30
Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Cys Leu Glu Trp
35 40 45
Ile Gly Leu Ile Thr Pro Tyr Asn Gly Ala Ser Ser Tyr Asn Gln Lys
50 55 60
Phe Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala
65 70 75 80
Tyr Met Asp Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe
85 90 95
Cys Ala Arg Gly Tyr Asp Gly Arg Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Lys Ala Ser Gly Gly Arg His Arg
115 120 125
Gln Pro Arg Gly Trp Glu Gln Leu Pro Thr Gly Ala Glu Phe Leu Gly
130 135 140
Asp Gly Gly Asp Val Ser Phe Ser Thr Arg Gly Thr Gln Asn Trp Thr
145 150 155 160
Val Glu Arg Leu Leu Gln Ala His Arg Gln Leu Glu Glu Arg Gly Tyr
165 170 175
Val Phe Val Gly Tyr His Gly Thr Phe Leu Glu Ala Ala Gln Ser Ile
180 185 190
Val Phe Gly Gly Val Arg Ala Arg Ser Gln Asp Leu Asp Ala Ile Trp
195 200 205
Arg Gly Phe Tyr Ile Ala Gly Asp Pro Ala Leu Ala Tyr Gly Tyr Ala
210 215 220
Gln Asp Gln Glu Pro Asp Ala Arg Gly Arg Ile Arg Asn Gly Ala Leu
225 230 235 240
Leu Arg Val Tyr Val Pro Arg Ser Ser Leu Pro Gly Phe Tyr Arg Thr
245 250 255
Ser Leu Thr Leu Ala Ala Pro Glu Ala Ala Gly Glu Val Glu Arg Leu
260 265 270
Ile Gly His Pro Leu Pro Leu Arg Leu Asp Ala Ile Thr Gly Pro Glu
275 280 285
Glu Glu Gly Gly Arg Leu Glu Thr Ile Leu Gly Trp Pro Leu Ala Glu
290 295 300
Arg Thr Val Val Ile Pro Ser Ala Ile Pro Thr Asp Pro Arg Asn Val
305 310 315 320
Gly Gly Asp Leu Asp Pro Ser Ser Ile Pro Asp Lys Glu Gln Ala Ile
325 330 335
Ser Ala Leu Pro Asp Tyr Ala Ser Gln Pro Gly Lys Pro Pro Arg Glu
340 345 350
Asp Leu Lys
355