

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

Ala	Glu	Glu	Ala	Phe	Asp	Leu	Trp	Asn	Glu	Cys	Ala	Lys	Ala	Cys	Val
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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
			260					265						270	

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

<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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<220>
<223> synthetic modified Pseudomonas exotoxin A
      PE-LR/FL/8X
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<220>
<221> VARIANT
<222> (15)...(19)
<223> Xaa = Gly or Ser, may be present or absent
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<400>																
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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

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```

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 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

<220>

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

<400> 9

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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

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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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 accatgacct gcagtgccag ctcaagtgtg agttacatgc actggtacca gcagaagtca 120
 ggcacctccc ccaaagatg gatttatgac acatccaaac tggcttcttg agtcccaggt 180
 cgcttcagtg gcagtgggtc tggaaactct tactctctca caatcagcag cgtggaggct 240
 gaagatgatg caacttatta ctgccagcag tggccaagc accctctcac gttcggttgc 300
 gggacaaaagt 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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atgcaggtac aactgcagca gtctgggcct gagctggaga agcctggcgc ttcagtgaag 60
atatacctgca aggcacatctgg ttactcattc actggctaca ccatgaactg ggtgaagcag 120
agtcacatggaa agtgccttga gtggattgga cttattactc cttacaatgg tgcttctagc 180
tacaaccaga agttcagggg caaggccaca ttaactgtag acaagtcac cagcacagcc 240
tacatggacc tcctcagtc gacatctgaa gactctgcag tctatttctg tgcaaggggg 300
ggttacgacg ggagggggtt tgactactgg ggccaaggga ccacggtcac cgtctcctca 360
aaagcttccg gaggtcgtca ccgtcaacca cgcgggtggg aacagctgcc aaccggtgcc 420
gagttcctgg gcgacgggtg cgatgtgtcc tttagcacc gtggtaccca gaactggacg 480
gtagagcgcc tgctgcaggc acatcgtcag ctggaagagc gtggctatgt attcgttggc 540
taccacggca cttttctgga agcagctcag tccatcgtgt ttggtggtgt ccgtgcccg 600
tctcaagacc tggatgcgat ttggcgtggt ttctacattg caggcgatcc agcgtggca 660
tacggttatg cgcaggacca ggaaccggat gctcgcggtc gcattcgtaa tgggtgcgtg 720
ctgcgcgat atgtgcccg ttccagcctg cggggttct accgcactag cctgaccctg 780
gccgcgccgg agggggcggg tgaagtggaa cgtctgattg gtcatectct gcctctgcgc 840
ctggatgcc taccggccc agaggaggag ggcggtcgtc tggaaacccat tctgggctgg 900
ccgtggctg aacgtacgg cgttattcc agcgcgattc ctaccgatcc tcgtaacggt 960
ggcggcgatc tggacccatc ttctattcca gataaggagc aggaatctc cgcgctgccg 1020
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<210> 12

<211> 1077

<212> DNA

<213> Artificial Sequence

<220>

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

<400> 12

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atgcaggtac aactgcagca gtctgggcct gagctggaga agcctggcgc ttcagtgaag 60
atatacctgca aggcacatctgg ttactcattc actggctaca ccatgaactg ggtgaagcag 120
agtcacatggaa agtgccttga gtggattgga cttattactc cttacaatgg tgcttctagc 180
tacaaccaga agttcagggg caaggccaca ttaactgtag acaagtcac cagcacagcc 240
tacatggacc tcctcagtc gacatctgaa gactctgcag tctatttctg tgcaaggggg 300
ggttacgacg ggagggggtt tgactactgg ggccaaggga ccacggtcac cgtctcctca 360
aaagcttccg gaggtcgtca tcgccagccg cgcggctggg aacaactggg tggaaagtccc 420
actggcgcgg agttcctcgg cgacggcggc gcagtcagct tcagcaccgg cggcacgcag 480
aactggacgg tggagcggct gctccaggcg caccgccaac tggaggaggg cggctatgtg 540
ttcgtcggct accacggcac ctctctcgaa gcggcgcaa gcacgtctt cggcggggtg 600
cgcgcgcgca gccaggacct cgacgcgac tgggcccgtt tctatatcgc cggcgatccg 660
gcgctggcct acggctacgc ccaggaccag gaaccgcagc cagccggccg tatccgcaac 720
ggtgccctgc tgcgggtcta tgtgccgcgc tcgagcctgc cgggcttcta cgccaccagc 780
ctgaccctgg ccgcgccgga ggccggcggg gaggtcgaac ggctgatcgg ccatccgctg 840
ccgctgcgcc tggacgccat caccggcccc gagagtcag gcgggcgcct ggagaccatt 900
ctcggctggc cgtggccga gcgcaccgtg gtgattccct cggcgatccc caccgaccgg 960
cgcaacgctg gcggcgacct cgacccgtcc agcatccccg acagcgaagc agcgatcagc 1020
gccctgccgg actacgccag ccagcccggc aaaccgccgc gcgaggacct gaagtaa 1077

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<210> 13

<211> 1068

<212> DNA

<213> Artificial Sequence

<220>

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

<400> 13

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atgcaggtac aactgcagca gtctgggcct gagctggaga agcctggcgc ttcagtgaag 60
atatacctgca aggcacatctgg ttactcattc actggctaca ccatgaactg ggtgaagcag 120
agtcacatggaa agtgccttga gtggattgga cttattactc cttacaatgg tgcttctagc 180

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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 gcaccgccaa ctggaggagg gcggctatgt gttcgtcggc 540
taccacggca ccttcctcga agcggcgcaa agcatcgtct tcggcggggg gcgcgcgcgc 600
agccaggacc tcgacgcgat ctgggcccgt ttctatatcg ccggcgatcc ggcgctggcc 660
tacggctacg cccaggacca ggaaccgcag gcagccggcc gtatccgcaa cggtgccctg 720
ctgcgggtct atgtgccgg ctcgagcctg ccgggcttct acgccaccag cctgaccctg 780
gccgcgcggg agggcgcggg cgaggtcgaa cggctgatcg gccatccgct gccgctgcgc 840
ctggacgcca tcaccggccc cgaggagtca ggccggcgcc tggagaccat tctcggctgg 900
ccgctggcgg agcgcaccgt ggtgattccc tcggcgatcc ccaccgaccc gcgcaacgtc 960
ggcggcgacc tcgacccgtc cagcatcccc gacagcgaag cagcgatcag cgccctgccc 1020
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<210> 14

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

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

<400> 14

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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 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 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

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<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
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<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
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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											
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<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
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<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
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<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
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<210> 35
<211> 9
<212> PRT
<213> Artificial Sequence

<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
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<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
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<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

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<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

<213> Artificial Sequence

<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

<213> Artificial Sequence

<220>

<223> synthetic furin cleavage site

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

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

<400> 49
Arg His Arg Ser Lys Arg
1 5

<210> 50
<211> 4
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<220>
<223> synthetic scFv peptide linker

<400> 50
Gly Gly Gly Ser
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<210> 51
<211> 5
<212> PRT
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<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

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

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

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

<220>
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        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>
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        variable light chain CDR3

<400> 63
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<210> 64
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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        variable light chain CDR3

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

<210> 65
<211> 9
<212> PRT
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<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

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

<400> 71
Gly Ser Gly Gly
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<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
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<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