<110> Genentech, Inc. et al.

<120> TREATMENT OF DISORDERS WITH ALTERED VASCULAR BARRIER FUNCTION

<130> P4616R1-WO

<141> 2012-03-09

<150> US 61/451,540
<151> 2011-03-10

<160> 2

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<211> 963
<212> PRT
<213> Homo sapiens

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Met Leu Ser Gly Glu Arg Lys Glu Gly Gly Ser Pro Arg Phe Gly
  1               5                  10                  15

Lys Leu His Leu Pro Val Gly Leu Trp Ile Asn Ser Pro Arg Lys
             20                  25                  30

Gln Leu Ala Lys Leu Gly Arg Arg Trp Pro Ser Ala Ala Ser Val
             35                  40                  45

Lys Ser Ser Ser Ser Asp Thr Gly Ser Arg Ser Ser Glu Pro Leu
             50                  55                  60

Pro Pro Pro Pro Pro His Val Glu Leu Arg Arg Val Gly Ala Val
             65                  70                  75

Lys Ala Ala Gly Gly Ala Ser Gly Ser Arg Ala Lys Arg Ile Ser
             80                  85                  90

Gln Leu Phe Arg Gly Ser Gly Thr Gly Thr Thr Gly Ser Ser Gly
             95                 100                 105

Ala Gly Gly Pro Gly Thr Pro Gly Gly Ala Gln Arg Trp Ala Ser
            110                 115                 120

Glu Lys Lys Leu Pro Glu Leu Ala Ala Gly Val Ala Pro Glu Pro
            125                 130                 135

Pro Leu Ala Thr Arg Ala Thr Ala Pro Pro Gly Val Leu Lys Ile
            140                 145                 150

Phe Gly Ala Gly Leu Ala Ser Gly Ala Asn Tyr Lys Ser Val Leu
            155                 160                 165

Ala Thr Ala Arg Ser Thr Ala Arg Glu Leu Val Ala Glu Ala Leu
            170                 175                 180

Glu Arg Tyr Gly Leu Ala Gly Ser Pro Gly Gly Gly Pro Gly Glu
            185                 190                 195

Ser Ser Cys Val Asp Ala Phe Ala Leu Cys Asp Ala Leu Gly Arg
            200                 205                 210
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Pro Ala Ala Ala Gly Val Gly Ser Gly Glu Trp Arg Ala Glu His
                215                 220                 225

Leu Arg Val Leu Gly Asp Ser Glu Arg Pro Leu Leu Val Gln Glu
                230                 235                 240

Leu Trp Arg Ala Arg Pro Gly Trp Ala Arg Arg Phe Glu Leu Arg
                245                 250                 255

Gly Arg Glu Glu Ala Arg Arg Leu Glu Gln Glu Ala Phe Gly Ala
                260                 265                 270

Ala Asp Ser Glu Gly Thr Gly Ala Pro Ser Trp Arg Pro Gln Lys
                275                 280                 285

Asn Arg Ser Arg Ala Ala Ser Gly Gly Ala Ala Leu Ala Ser Pro
                290                 295                 300

Gly Pro Gly Thr Gly Ser Gly Ala Pro Ala Gly Ser Gly Gly Lys
                305                 310                 315

Glu Arg Ser Glu Asn Leu Ser Leu Arg Arg Ser Val Ser Glu Leu
                320                 325                 330

Ser Leu Gln Gly Arg Arg Arg Arg Gln Gln Glu Arg Arg Gln Gln
                335                 340                 345

Ala Leu Ser Met Ala Pro Gly Ala Ala Asp Ala Gln Ile Gly Thr
                350                 355                 360

Ala Asp Pro Gly Asp Phe Asp Gln Leu Thr Gln Cys Leu Ile Gln
                365                 370                 375

Ala Pro Ser Asn Arg Pro Tyr Phe Leu Leu Leu Gln Gly Tyr Gln
                380                 385                 390

Asp Ala Gln Asp Phe Val Val Tyr Val Met Thr Arg Glu Gln His
                395                 400                 405

Val Phe Gly Arg Gly Gly Asn Ser Ser Gly Arg Gly Gly Ser Pro
                410                 415                 420

Ala Pro Tyr Val Asp Thr Phe Leu Asn Ala Pro Asp Ile Leu Pro
                425                 430                 435

Arg His Cys Thr Val Arg Ala Gly Pro Glu His Pro Ala Met Val
                440                 445                 450

Arg Pro Ser Arg Gly Ala Pro Val Thr His Asn Gly Cys Leu Leu
                455                 460                 465

Leu Arg Glu Ala Glu Leu His Pro Gly Asp Leu Leu Gly Leu Gly
                470                 475                 480

Glu His Phe Leu Phe Met Tyr Lys Asp Pro Arg Thr Gly Gly Ser
                485                 490                 495

Gly Pro Ala Arg Pro Pro Trp Leu Pro Ala Arg Pro Gly Ala Thr
                500                 505                 510

Pro Pro Gly Pro Gly Trp Ala Phe Ser Cys Arg Leu Cys Gly Arg
                515                 520                 525
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Gly Leu Gln Glu Arg Gly Glu Ala Leu Ala Ala Tyr Leu Asp Gly
                530                 535                 540

Arg Glu Pro Val Leu Arg Phe Arg Pro Arg Glu Glu Glu Ala Leu
                545                 550                 555

Leu Gly Glu Ile Val Arg Ala Ala Ala Ala Gly Ser Gly Asp Leu
                560                 565                 570

Pro Pro Leu Gly Pro Ala Thr Leu Leu Ala Leu Cys Val Gln His
                575                 580                 585

Ser Ala Arg Glu Leu Glu Leu Gly His Leu Pro Arg Leu Leu Gly
                590                 595                 600

Arg Leu Ala Arg Leu Ile Lys Glu Ala Val Trp Glu Lys Ile Lys
                605                 610                 615

Glu Ile Gly Asp Arg Gln Pro Glu Asn His Pro Glu Gly Val Pro
                620                 625                 630

Glu Val Pro Leu Thr Pro Glu Ala Val Ser Val Glu Leu Arg Pro
                635                 640                 645

Leu Met Leu Trp Met Ala Asn Thr Thr Glu Leu Leu Ser Phe Val
                650                 655                 660

Gln Glu Lys Val Leu Glu Met Glu Lys Glu Ala Asp Gln Glu Asp
                665                 670                 675

Pro Gln Leu Cys Asn Asp Leu Glu Leu Cys Asp Glu Ala Met Ala
                680                 685                 690

Leu Leu Asp Glu Val Ile Met Cys Thr Phe Gln Gln Ser Val Tyr
                695                 700                 705

Tyr Leu Thr Lys Thr Leu Tyr Ser Thr Leu Pro Ala Leu Leu Asp
                710                 715                 720

Ser Asn Pro Phe Thr Ala Gly Ala Glu Leu Pro Gly Pro Gly Ala
                725                 730                 735

Glu Leu Gly Ala Met Pro Pro Gly Leu Arg Pro Thr Leu Gly Val
                740                 745                 750

Phe Gln Ala Ala Leu Glu Leu Thr Ser Gln Cys Glu Leu His Pro
                755                 760                 765

Asp Leu Val Ser Gln Thr Phe Gly Tyr Leu Phe Phe Phe Ser Asn
                770                 775                 780

Ala Ser Leu Leu Asn Ser Leu Met Glu Arg Gly Gln Gly Arg Pro
                785                 790                 795

Phe Tyr Gln Trp Ser Arg Ala Val Gln Ile Arg Thr Asn Leu Asp
                800                 805                 810

Leu Val Leu Asp Trp Leu Gln Gly Ala Gly Leu Gly Asp Ile Ala
                815                 820                 825

Thr Glu Phe Phe Arg Lys Leu Ser Met Ala Val Asn Leu Leu Cys
                830                 835                 840
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Val Pro Arg Thr Ser Leu Leu Lys Ala Ser Trp Ser Ser Leu Arg
845 850 855

Thr Asp His Pro Thr Leu Thr Pro Ala Gln Leu His His Leu Leu
860 865 870

Ser His Tyr Gln Leu Gly Pro Gly Arg Gly Pro Pro Ala Ala Trp
875 880 885

Asp Pro Pro Pro Ala Glu Arg Glu Ala Val Asp Thr Gly Asp Ile
890 895 900

Phe Glu Ser Phe Ser Ser His Pro Pro Leu Ile Leu Pro Leu Gly
905 910 915

Ser Ser Arg Leu Arg Leu Thr Gly Pro Val Thr Asp Asp Ala Leu
920 925 930

His Arg Glu Leu Arg Arg Leu Arg Arg Leu Leu Trp Asp Leu Glu
935 940 945

Gln Gln Glu Leu Pro Ala Asn Tyr Arg His Gly Pro Pro Val Ala
950 955 960

Thr Ser Pro

<210> 2
<211> 961
<212> PRT
<213> Mus musculus

<400> 2
Met Leu Ser Gly Glu Arg Lys Glu Gly Gly Ser Pro Arg Phe Gly
1 5 10 15

Lys Leu His Leu Pro Val Gly Leu Trp Ile Asn Ser Pro Arg Lys
20 25 30

Gln Leu Ala Lys Leu Gly Arg Arg Trp Pro Ser Ala Ala Ser Val
35 40 45

Lys Ser Ser Ser Ser Asp Thr Gly Ser Arg Ser Ser Glu Pro Leu
50 55 60

Pro Pro Pro Pro Pro Pro Pro His Val Glu Leu Arg Arg Val Gly
65 70 75

Ala Val Lys Ala Ala Gly Gly Ala Ser Gly Ser Arg Ala Lys Arg
80 85 90

Ile Ser Gln Leu Phe Arg Gly Ser Gly Ala Gly Gly Ala Gly Gly
95 100 105

Pro Gly Thr Pro Gly Gly Ala Gln Arg Trp Ala Ser Glu Lys Lys
110 115 120

Leu Pro Glu Leu Ala Ala Gly Val Ala Pro Glu Pro Pro Leu Pro
125 130 135

Thr Arg Ala Ala Val Pro Pro Gly Val Leu Lys Ile Phe Ala Ser
140 145 150

```
Gly Leu Ala Ser Gly Ala Asn Tyr Lys Ser Val Leu Ala Thr Glu
                155                 160                 165

Arg Ser Thr Ala Arg Glu Leu Val Ala Glu Ala Leu Glu Arg Tyr
                170                 175                 180

Gly Leu Thr Gly Gly Arg Gly Ala Gly Asp Ser Gly Cys Val Asp
                185                 190                 195

Ala Tyr Ala Leu Cys Asp Ala Leu Gly Arg Pro Ala Val Gly Val
                200                 205                 210

Gly Gly Gly Glu Trp Arg Ala Glu His Leu Arg Val Leu Ala Asp
                215                 220                 225

Ala Glu Arg Pro Leu Leu Val Gln Asp Leu Trp Arg Ala Arg Pro
                230                 235                 240

Gly Trp Ala Arg Arg Phe Glu Leu Arg Gly Arg Glu Glu Ala Arg
                245                 250                 255

Arg Leu Glu Gln Glu Ala Phe Gly Ala Ala Asp Ala Asp Gly Thr
                260                 265                 270

Asn Ala Pro Ser Trp Arg Thr Gln Lys Asn Arg Ser Arg Ala Ala
                275                 280                 285

Ser Gly Gly Ala Ala Leu Ala Ser Pro Gly Pro Gly Ser Gly Ser
                290                 295                 300

Gly Thr Pro Thr Gly Ser Gly Gly Lys Glu Arg Ser Glu Asn Leu
                305                 310                 315

Ser Leu Arg Arg Ser Val Ser Glu Leu Ser Leu Gln Gly Arg Arg
                320                 325                 330

Arg Arg Gln Gln Glu Arg Arg Gln Gln Ala Leu Ser Met Ala Pro
                335                 340                 345

Gly Ala Ala Asp Ala Gln Met Val Pro Thr Asp Pro Gly Asp Phe
                350                 355                 360

Asp Gln Leu Thr Gln Cys Leu Ile Gln Ala Pro Ser Asn Arg Pro
                365                 370                 375

Tyr Phe Leu Leu Leu Gln Gly Tyr Gln Asp Ala Gln Asp Phe Val
                380                 385                 390

Val Tyr Val Met Thr Arg Glu Gln His Val Phe Gly Arg Gly Gly
                395                 400                 405

Pro Ser Ser Ser Arg Gly Gly Ser Pro Ala Pro Tyr Val Asp Thr
                410                 415                 420

Phe Leu Asn Ala Pro Asp Ile Leu Pro Arg His Cys Thr Val Arg
                425                 430                 435

Ala Gly Pro Glu Pro Pro Ala Met Val Arg Pro Ser Arg Gly Ala
                440                 445                 450

Pro Val Thr His Asn Gly Cys Leu Leu Leu Arg Glu Ala Glu Leu
                455                 460                 465
```

```
His Pro Gly Asp Leu Leu Gly Leu Gly Glu His Phe Leu Phe Met
                470                 475                 480

Tyr Lys Asp Pro Arg Ser Gly Gly Ser Gly Pro Ala Arg Pro Ser
                485                 490                 495

Trp Leu Pro Ala Arg Pro Gly Ala Ala Pro Pro Gly Pro Gly Trp
                500                 505                 510

Ala Phe Ser Cys Arg Leu Cys Gly Arg Gly Leu Gln Glu Arg Gly
                515                 520                 525

Glu Ala Leu Ala Ala Tyr Leu Asp Gly Arg Glu Pro Val Leu Arg
                530                 535                 540

Phe Arg Pro Arg Glu Glu Glu Ala Leu Leu Gly Glu Ile Val Arg
                545                 550                 555

Ala Ala Ala Ser Gly Ala Gly Asp Leu Pro Pro Leu Gly Pro Ala
                560                 565                 570

Thr Leu Leu Ala Leu Cys Val Gln His Ser Ala Arg Glu Leu Glu
                575                 580                 585

Leu Gly His Leu Pro Arg Leu Leu Gly Arg Leu Ala Arg Leu Ile
                590                 595                 600

Lys Glu Ala Val Trp Glu Lys Ile Lys Glu Ile Gly Asp Arg Gln
                605                 610                 615

Pro Glu Asn His Pro Glu Gly Val Pro Glu Val Pro Leu Thr Pro
                620                 625                 630

Glu Ala Val Ser Val Glu Leu Arg Pro Leu Ile Leu Trp Met Ala
                635                 640                 645

Asn Thr Thr Glu Leu Leu Ser Phe Val Gln Glu Lys Val Leu Glu
                650                 655                 660

Met Glu Lys Glu Ala Asp Gln Glu Gly Leu Ser Ser Asp Pro Gln
                665                 670                 675

Leu Cys Asn Asp Leu Glu Leu Cys Asp Glu Ala Leu Ala Leu Leu
                680                 685                 690

Asp Glu Val Ile Met Cys Thr Phe Gln Gln Ser Val Tyr Tyr Leu
                695                 700                 705

Thr Lys Thr Leu Tyr Ser Thr Leu Pro Ala Leu Leu Asp Ser Asn
                710                 715                 720

Pro Phe Thr Ala Gly Ala Glu Leu Pro Gly Pro Gly Ala Glu Leu
                725                 730                 735

Glu Ala Met Pro Pro Gly Leu Arg Pro Thr Leu Gly Val Phe Gln
                740                 745                 750

Ala Ala Leu Glu Leu Thr Ser Gln Cys Glu Leu His Pro Asp Leu
                755                 760                 765

Val Ser Gln Thr Phe Gly Tyr Leu Phe Phe Phe Ser Asn Ala Ser
                770                 775                 780
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```
Leu Leu Asn Ser Leu Met Glu Arg Gly Gln Gly Arg Pro Phe Tyr
                785                 790                 795

Gln Trp Ser Arg Ala Val Gln Ile Arg Thr Asn Leu Asp Leu Val
                800                 805                 810

Leu Asp Trp Leu Gln Gly Ala Gly Leu Gly Asp Ile Ala Thr Glu
                815                 820                 825

Phe Phe Arg Lys Leu Ser Ile Ala Val Asn Leu Leu Cys Val Pro
                830                 835                 840

Arg Thr Ser Leu Leu Lys Ala Ser Trp Ser Ser Leu Arg Thr Asp
                845                 850                 855

Tyr Pro Thr Leu Thr Pro Ala Gln Leu His His Leu Leu Ser His
                860                 865                 870

Tyr Gln Leu Gly Pro Gly Arg Gly Pro Pro Pro Ala Trp Asp Pro
                875                 880                 885

Pro Pro Ala Glu Arg Asp Ala Val Asp Thr Gly Asp Ile Phe Glu
                890                 895                 900

Ser Phe Ser Ser His Pro Pro Leu Ile Leu Pro Leu Gly Ser Ser
                905                 910                 915

Arg Leu Arg Leu Thr Gly Pro Val Thr Asp Asp Ala Leu His Arg
                920                 925                 930

Glu Leu Arg Arg Leu Arg Arg Leu Leu Trp Asp Leu Glu Gln Gln
                935                 940                 945

Glu Leu Pro Ala Asn His Arg His Gly Pro Pro Val Ala Ser Thr
                950                 955                 960

Pro
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