

18JIN2622346-Rothe-F  
SEQUENCE LISTING

<110> AdrenoMed AG  
<120> Therapy monitoring under treatment with an anti-Adrenomedullin  
(ADM) binder  
<130> A75177WO  
<150> EP17197177.3  
<151> 2017-10-18  
<160> 27  
<170> PatentIn version 3.5  
<210> 1  
<211> 52  
<212> PRT  
<213> Homo sapiens  
<400> 1

Tyr Arg Gln Ser Met Asn Asn Phe Gln Gly Leu Arg Ser Phe Gly Cys  
1 5 10 15

Arg Phe Gly Thr Cys Thr Val Gln Lys Leu Ala His Gln Ile Tyr Gln  
20 25 30

Phe Thr Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys Ile Ser  
35 40 45

Pro Gln Gly Tyr  
50

<210> 2  
<211> 185  
<212> PRT  
<213> Homo sapiens

<400> 2

Met Lys Leu Val Ser Val Ala Leu Met Tyr Leu Gly Ser Leu Ala Phe  
1 5 10 15

Leu Gly Ala Asp Thr Ala Arg Leu Asp Val Ala Ser Glu Phe Arg Lys  
20 25 30

18JIN2622346-Rothe-F

Lys Trp Asn Lys Trp Ala Leu Ser Arg Gly Lys Arg Glu Leu Arg Met  
 35 40 45

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

Gln Thr Leu Ile Arg Pro Gln Asp Met Lys Gly Ala Ser Arg Ser Pro  
 65 70 75 80

Glu Asp Ser Ser Pro Asp Ala Ala Arg Ile Arg Val Lys Arg Tyr Arg  
 85 90 95

Gln Ser Met Asn Asn Phe Gln Gly Leu Arg Ser Phe Gly Cys Arg Phe  
 100 105 110

Gly Thr Cys Thr Val Gln Lys Leu Ala His Gln Ile Tyr Gln Phe Thr  
 115 120 125

Asp Lys Asp Lys Asp Asn Val Ala Pro Arg Ser Lys Ile Ser Pro Gln  
 130 135 140

Gly Tyr Gly Arg Arg Arg Arg Arg Ser Leu Pro Glu Ala Gly Pro Gly  
 145 150 155 160

Arg Thr Leu Val Ser Ser Lys Pro Gln Ala His Gly Ala Pro Ala Pro  
 165 170 175

Pro Ser Gly Ser Ala Pro His Phe Leu  
 180 185

<210> 3  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 3

Ala Arg Leu Asp Val Ala Ser Glu Phe Arg Lys Lys Trp Asn Lys Trp  
 1 5 10 15

18JIN2622346-Rothe-F

Ala Leu Ser Arg  
20

<210> 4  
<211> 48  
<212> PRT  
<213> Homo sapiens

<400> 4

Glu Leu Arg Met Ser Ser Ser Tyr Pro Thr Gly Leu Ala Asp Val Lys  
1 5 10 15

Ala Gly Pro Ala Gln Thr Leu Ile Arg Pro Gln Asp Met Lys Gly Ala  
20 25 30

Ser Arg Ser Pro Glu Asp Ser Ser Pro Asp Ala Ala Arg Ile Arg Val  
35 40 45

<210> 5  
<211> 38  
<212> PRT  
<213> Homo sapiens

<400> 5

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

Val Ser Ser Lys Pro Gln Ala His Gly Ala Pro Ala Pro Pro Ser Gly  
20 25 30

Ser Ala Pro His Phe Leu  
35

<210> 6  
<211> 8  
<212> PRT  
<213> Homo sapiens

<400> 6

Gly Tyr Thr Phe Ser Arg Tyr Trp  
1 5

<210> 7  
 <211> 8  
 <212> PRT  
 <213> Homo sapiens

<400> 7

Ile Leu Pro Gly Ser Gly Ser Thr  
 1 5

<210> 8  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 8

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr  
 1 5 10

<210> 9  
 <211> 11  
 <212> PRT  
 <213> Homo sapiens

<400> 9

Gln Ser Ile Val Tyr Ser Asn Gly Asn Thr Tyr  
 1 5 10

<210> 10  
 <211> 9  
 <212> PRT  
 <213> Homo sapiens

<400> 10

Phe Gln Gly Ser His Ile Pro Tyr Thr  
 1 5

<210> 11  
 <211> 219  
 <212> PRT  
 <213> Homo sapiens

<400> 11

18JIN2622346-Rothe-F

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

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

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

Gly Glu Ile Leu Pro Gly Ser Gly Ser Thr Asn Tyr Asn Glu Lys Phe  
50 55 60

Lys Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr  
65 70 75 80

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

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr Trp Gly Gln Gly Thr  
100 105 110

Thr Leu Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro  
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly  
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn  
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln  
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser  
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser  
195 200 205

18JIN2622346-Rothe-F

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys  
210 215

<210> 12  
<211> 219  
<212> PRT  
<213> Homo sapiens

<400> 12

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

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

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr  
65 70 75 80

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

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr Trp Gly Gln Gly Thr  
100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro  
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly  
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn  
145 150 155 160

18JIN2622346-Rothe-F

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln  
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser  
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser  
195 200 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys  
210 215

<210> 13  
<211> 219  
<212> PRT  
<213> Homo sapiens

<400> 13

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

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

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr  
65 70 75 80

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

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr Trp Gly Gln Gly Thr  
100 105 110

18JIN2622346-Rothe-F

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro  
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly  
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn  
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln  
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser  
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser  
195 200 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys  
210 215

<210> 14  
<211> 219  
<212> PRT  
<213> Homo sapiens

<400> 14

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

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

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

18JIN2622346-Rothe-F

Gly Glu Ile Leu Pro Gly Ser Gly Ser Thr Asn Tyr Ala Gln Lys Phe  
 50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr  
 65 70 75 80

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

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr Trp Gly Gln Gly Thr  
 100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro  
 115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly  
 130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn  
 145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln  
 165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser  
 180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser  
 195 200 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys  
 210 215

<210> 15  
 <211> 219  
 <212> PRT  
 <213> Homo sapiens

18JIN2622346-Rothe-F

<400> 15

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

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

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

Gly Glu Ile Leu Pro Gly Ser Gly Ser Thr Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr  
65 70 75 80

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

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr Trp Gly Gln Gly Thr  
100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro  
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly  
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn  
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln  
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser  
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser  
195 200 205

18JIN2622346-Rothe-F

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys  
210 215

<210> 16  
<211> 219  
<212> PRT  
<213> Homo sapiens

<400> 16

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

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

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

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

Ser His Ile Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu  
115 120 125

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

18JIN2622346-Rothe-F

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln  
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser  
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu  
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser  
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
210 215

<210> 17  
<211> 219  
<212> PRT  
<213> Homo sapiens

<400> 17

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val Tyr Ser  
20 25 30

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

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

Ser His Ile Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

18JIN2622346-Rothe-F

100

105

110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu  
115 120 125

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

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln  
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser  
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu  
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser  
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
210 215

<210> 18

<211> 219

<212> PRT

<213> Homo sapiens

<400> 18

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val Tyr Ser  
20 25 30

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

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

18JIN2622346-Rothe-F

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 Val Gly Val Tyr Tyr Cys Phe Gln Gly  
85 90 95

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu  
115 120 125

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

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln  
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser  
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu  
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser  
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
210 215

<210> 19

<211> 21

<212> PRT

<213> Homo sapiens

<400> 19

Tyr Arg Gln Ser Met Asn Asn Phe Gln Gly Leu Arg Ser Phe Gly Cys  
1 5 10 15

18JIN2622346-Rothe-F

Arg Phe Gly Thr Cys  
20

<210> 20  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 20

Ala Pro Arg Ser Lys Ile Ser Pro Gln Gly Tyr  
1 5 10

<210> 21  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 21

Cys Thr Val Gln Lys Leu Ala His Gln Ile Tyr Gln Phe Thr Asp Lys  
1 5 10 15

Asp Lys Asp Asn Val Ala  
20

<210> 22  
<211> 13  
<212> PRT  
<213> Homo sapiens

<400> 22

Ala His Gln Ile Tyr Gln Phe Thr Asp Lys Asp Lys Asp  
1 5 10

<210> 23  
<211> 50  
<212> PRT  
<213> Homo sapiens

<400> 23

Tyr Arg Gln Ser Met Asn Gln Gly Ser Arg Ser Thr Gly Cys Arg Phe  
1 5 10 15

18JIN2622346-Rothe-F

Gly Thr Cys Thr Met Gln Lys Leu Ala His Gln Ile Tyr Gln Phe Thr  
 20 25 30

Asp Lys Asp Lys Asp Gly Met Ala Pro Arg Asn Lys Ile Ser Pro Gln  
 35 40 45

Gly Tyr  
 50

<210> 24  
 <211> 12  
 <212> PRT  
 <213> Homo sapiens

<400> 24

Cys Thr Val Gln Lys Leu Ala His Gln Ile Tyr Gln  
 1 5 10

<210> 25  
 <211> 19  
 <212> PRT  
 <213> Mouse

<400> 25

Tyr Arg Gln Ser Met Asn Gln Gly Ser Arg Ser Asn Gly Cys Arg Phe  
 1 5 10 15

Gly Thr Cys

<210> 26  
 <211> 448  
 <212> PRT  
 <213> Humanized mouse

<400> 1

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

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

18JIN2622346-Rothe-F

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr  
 65 70 75 80

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

Thr Glu Gly Tyr Glu Tyr Asp Gly Phe Asp Tyr Trp Gly Gln Gly Thr  
 100 105 110

Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro  
 115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly  
 130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn  
 145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln  
 165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser  
 180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser  
 195 200 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr  
 210 215 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser  
 225 230 235 240

18JIN2622346-Rothe-F

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg  
245 250 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro  
260 265 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala  
275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val  
290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr  
305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr  
325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu  
340 345 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys  
355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser  
370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp  
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser  
405 410 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala  
420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
435 440 445

18JIN2622346-Rothe-F

<210> 27  
 <211> 219  
 <212> PRT  
 <213> Humanized mouse

<400> 2

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

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val Tyr Ser  
 20 25 30

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

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

Ser His Ile Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu  
 115 120 125

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

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln  
 145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser  
 165 170 175

18JIN2622346-Rothe-F

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Tyr | Ser | Leu | Ser | Ser | Thr | Leu | Thr | Leu | Ser | Lys | Ala | Asp | Tyr | Glu |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Lys | His | Lys | Val | Tyr | Ala | Cys | Glu | Val | Thr | His | Gln | Gly | Leu | Ser | Ser |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Pro | Val | Thr | Lys | Ser | Phe | Asn | Arg | Gly | Glu | Cys |
| 210 |     |     |     |     |     | 215 |     |     |     |     |