

eolf-seql

SEQUENCE LISTING

<110> F. Hoffmann-La Roche AG

<120> ANTI-PD1 ANTIBODIES AND METHODS OF USE

<130> P33103-WO

<150> EP15188061.4

<151> 2015-10-02

<160> 77

<170> PatentIn version 3.5

<210> 1

<211> 7

<212> PRT

<213> Mus Musculus

<400> 1

Gly Phe Ser Phe Ser Ser Tyr  
1 5

<210> 2

<211> 3

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Gly Gly Arg  
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<211> 9

<212> PRT

<213> Mus Musculus

<400> 3

Thr Gly Arg Val Tyr Phe Ala Leu Asp  
1 5

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<210> 4  
 <211> 11  
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<400> 4

Ser Glu Ser Val Asp Thr Ser Asp Asn Ser Phe  
 1 5 10

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Arg Ser Ser  
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<210> 6  
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<400> 6

Asn Tyr Asp Val Pro Trp  
 1 5

<210> 7  
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 <213> Mus Musculus

<400> 7

Glu Val Ile Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly  
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr  
 20 25 30

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Thr Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Asp Trp Val  
35 40 45

Ala Thr Ile Ser Gly Gly Gly Arg Asp Ile Tyr Tyr Pro Asp Ser Val  
50 55 60

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

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

Val Leu Leu Thr Gly Arg Val Tyr Phe Ala Leu Asp Ser Trp Gly Gln  
100 105 110

Gly Thr Ser Val Thr Val Ser Ser  
115 120

<210> 8  
<211> 111  
<212> PRT  
<213> Mus Musculus

<400> 8

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

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

Asp Asn Ser Phe Ile His Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro  
35 40 45

Lys Leu Leu Ile Tyr Arg Ser Ser Thr Leu Glu Ser Gly Val Pro Ala  
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp

| eolf-seql |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| 65        |     |     |     | 70  |     |     |     | 75  |     |     |     | 80  |     |     |     |  |
| Pro       | Val | Glu | Ala | Asp | Asp | Val | Ala | Thr | Tyr | Tyr | Cys | Gln | Gln | Asn | Tyr |  |
|           |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |
| Asp       | Val | Pro | Trp | Thr | Phe | Gly | Gly | Gly | Thr | Lys | Leu | Glu | Ile | Lys |     |  |
|           |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |  |

eolf-seql

<400> 12

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

<210> 13

<211> 3

<212> PRT

<213> Mus Musculus

<400> 13

Lys Val Ser  
1

<210> 14

<211> 6

<212> PRT

<213> Mus Musculus

<400> 14

Gly Ser His Phe Pro Leu  
1 5

<210> 15

<211> 120

<212> PRT

<213> Mus Musculus

<400> 15

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

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp  
20 25 30

Tyr Ala Trp Asn Trp Ile Arg Gln Phe Pro Gly Asp Lys Leu Glu Trp  
35 40 45

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

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

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

Ala Arg Trp His Gly Ser Ala Pro Trp Tyr Phe Asp Tyr Trp Gly Arg  
100 105 110

Gly Thr Thr Leu Thr Val Ser Ser  
115 120

<210> 16  
<211> 112  
<212> PRT  
<213> Mus Musculus

<400> 16

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

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

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

Pro Asn Leu Leu Ile Tyr Lys Val Ser Arg 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

eolf-seql

85

90

95

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

<210> 17  
<211> 8  
<212> PRT  
<213> Mus Musculus

<400> 17

Gly Tyr Ser Ile Thr Ser Asp Tyr  
1 5

<210> 18  
<211> 3  
<212> PRT  
<213> Mus Musculus

<400> 18

Tyr Thr Gly  
1

<210> 19  
<211> 9  
<212> PRT  
<213> Mus Musculus

<400> 19

Met Asp Tyr Tyr Gly Ser Thr Leu Asp  
1 5

<210> 20  
<211> 11  
<212> PRT  
<213> Mus Musculus

<400> 20

Ser Glu Ser Val Asp Arg Tyr Gly Asn Ser Phe

1 5 eolf-seql  
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<210> 21  
<211> 3  
<212> PRT  
<213> Mus Musculus

<400> 21

Arg Ala Ser  
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<210> 22  
<211> 6  
<212> PRT  
<213> Mus Musculus

<400> 22

Asn Asn Glu Asp Pro Tyr  
1 5

<210> 23  
<211> 120  
<212> PRT  
<213> Mus Musculus

<400> 23

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

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp  
20 25 30

Tyr Ala Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp  
35 40 45

Met Gly Tyr Ile Thr Tyr Thr Gly Arg Thr Ser Tyr Asn Pro Ser Leu  
50 55 60

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

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

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

Gly Thr Thr Leu Thr Val Ser Ser  
115 120

<210> 24  
<211> 111  
<212> PRT  
<213> Mus Musculus

<400> 24

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

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

Gly Asn Ser Phe Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro  
35 40 45

Lys Val Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Phe Pro Ala  
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp  
65 70 75 80

Pro Val Glu Ala Asp Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Asn Asn  
85 90 95

Glu Asp Pro Tyr Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys

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100

105

110

<210> 25  
 <211> 7  
 <212> PRT  
 <213> Mus Musculus

<400> 25

Gly Tyr Thr Phe Thr Asp Tyr  
 1 5

<210> 26  
 <211> 3  
 <212> PRT  
 <213> Mus Musculus

<400> 26

Tyr Ser Gly  
 1

<210> 27  
 <211> 7  
 <212> PRT  
 <213> Mus Musculus

<400> 27

Gly Ile Thr Thr Gly Phe Ala  
 1 5

<210> 28  
 <211> 11  
 <212> PRT  
 <213> Mus Musculus

<400> 28

Ser Lys Gly Val Ser Thr Ser Ser Tyr Ser Phe  
 1 5 10

<210> 29

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<211> 3  
 <212> PRT  
 <213> Mus Musculus

<400> 29

Tyr Ala Ser  
 1

<210> 30  
 <211> 6  
 <212> PRT  
 <213> Mus Musculus

<400> 30

Ser Arg Glu Phe Pro Trp  
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<210> 31  
 <211> 118  
 <212> PRT  
 <213> Mus Musculus

<400> 31

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

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

Ala Met His Trp Val Lys Gln Ser His Ala Arg Thr Leu Glu Trp Ile  
 35 40 45

Gly Val Ile Ser Thr Tyr Ser Gly Asp Thr Asn Tyr Asn Gln Lys Phe  
 50 55 60

Lys Asp Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr  
 65 70 75 80

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

Ala Arg Leu Gly Ile Thr Thr Gly Phe Ala Tyr Trp Gly Gln Gly Thr  
100 105 110

Leu Val Thr Val Ser Ala  
115

<210> 32  
<211> 111  
<212> PRT  
<213> Mus Musculus

<400> 32

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

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

Ser Tyr Ser Phe Met His Trp Tyr Gln Gln Lys Pro Arg Gln Pro Pro  
35 40 45

Lys Leu Leu Ile Lys Tyr Ala Ser Tyr Leu Glu Ser Gly Val Pro Ala  
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
65 70 75 80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys His His Ser Arg  
85 90 95

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

<210> 33

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<211> 7  
 <212> PRT  
 <213> Mus Musculus

<400> 33

Gly Phe Thr Phe Ser Asn Tyr  
 1 5

<210> 34  
 <211> 3  
 <212> PRT  
 <213> Mus Musculus

<400> 34

Gly Gly Arg  
 1

<210> 35  
 <211> 5  
 <212> PRT  
 <213> Mus Musculus

<400> 35

Tyr Tyr Gly Ile Asp  
 1 5

<210> 36  
 <211> 7  
 <212> PRT  
 <213> Mus Musculus

<400> 36

Ser Gln Asp Val Thr Thr Ala  
 1 5

<210> 37  
 <211> 3  
 <212> PRT  
 <213> Mus Musculus

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<400> 37

Trp Ala Ser  
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<210> 38

<211> 6

<212> PRT

<213> Mus Musculus

<400> 38

His Tyr Ser Ile Pro Trp  
1 5

<210> 39

<211> 116

<212> PRT

<213> Mus Musculus

<400> 39

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

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr  
20 25 30

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

Ala Thr Ile Ser Gly Gly Gly Arg Asp Thr Tyr Tyr Pro Asp Ser Val  
50 55 60

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

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

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Ala Ser Tyr Tyr Tyr Gly Ile Asp Tyr Trp Gly Gln Gly Thr Ser Val  
 100 105 110

Thr Val Ser Ser  
 115

<210> 40  
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 <212> PRT  
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 <400> 40

Asp Ile Val Met Thr Gln Pro His Lys Phe Met Ser Thr Ser Val Gly  
 1 5 10 15

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

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

Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly  
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Val Gln Ala  
 65 70 75 80

Glu Asp Leu Ala Leu Tyr Tyr Cys Gln Gln His Tyr Ser Ile Pro Trp  
 85 90 95

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

<210> 41  
 <211> 7  
 <212> PRT  
 <213> Mus Musculus

eolf-seql

<400> 41

Gly Tyr Thr Phe Thr Ser Thr  
1 5

<210> 42

<211> 3

<212> PRT

<213> Mus Musculus

<400> 42

Ser Asp Ser  
1

<210> 43

<211> 3

<212> PRT

<213> Mus Musculus

<400> 43

Pro Phe Asp  
1

<210> 44

<211> 7

<212> PRT

<213> Mus Musculus

<400> 44

Ser Gln Asp Val Ser Thr Ala  
1 5

<210> 45

<211> 3

<212> PRT

<213> Mus Musculus

<400> 45

Ser Ala Ser  
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# eolf-seql

<210> 46  
<211> 6  
<212> PRT  
<213> Mus Musculus

<400> 46

His Tyr Ser His Pro Phe  
1 5

<210> 47  
<211> 114  
<212> PRT  
<213> Mus Musculus

<400> 47

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

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

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

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

Lys Gly Lys Ala Thr Leu Thr Val Asp Thr Ser Ser Thr 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 Arg Ser Pro Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val  
100 105 110

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Ser Ser

<210> 48  
 <211> 107  
 <212> PRT  
 <213> Mus Musculus

<400> 48

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly  
 1 5 10 15

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

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

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly  
 50 55 60

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

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser His Pro Phe  
 85 90 95

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

<210> 49  
 <211> 8  
 <212> PRT  
 <213> Mus Musculus

<400> 49

Gly Tyr Ser Ile Thr Ser Gly Tyr  
 1 5

eolf-seql

<210> 50  
<211> 3  
<212> PRT  
<213> Mus Musculus

<400> 50

Ser Ser Gly  
1

<210> 51  
<211> 6  
<212> PRT  
<213> Mus Musculus

<400> 51

Arg Asn Trp Tyr Phe Asp  
1 5

<210> 52  
<211> 13  
<212> PRT  
<213> Mus Musculus

<400> 52

Ser Gln Ser Leu Leu Asn Ser Gly Thr Gln Lys Asn Tyr  
1 5 10

<210> 53  
<211> 3  
<212> PRT  
<213> Mus Musculus

<400> 53

Trp Ala Ser  
1

<210> 54  
<211> 6

eolf-seql

<212> PRT

<213> Mus Musculus

<400> 54

Asp Tyr Thr Phe Pro Leu  
1 5

<210> 55

<211> 117

<212> PRT

<213> Mus Musculus

<400> 55

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

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Gly  
20 25 30

Tyr Ser Trp His Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp  
35 40 45

Met Gly Phe Ile His Ser Ser Gly Asp Thr Asn Tyr Asn Pro Ser Leu  
50 55 60

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

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

Ala Thr Tyr Arg Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr  
100 105 110

Val Thr Val Ser Ser  
115

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<210> 56  
 <211> 113  
 <212> PRT  
 <213> Mus Musculus

<400> 56

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

Glu Lys Val Thr Met Arg Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser  
 20 25 30

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

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val  
 50 55 60

Pro Asn Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
 65 70 75 80

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

Asp Tyr Thr Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu  
 100 105 110

Lys

<210> 57  
 <211> 120  
 <212> PRT  
 <213> Artificial

<220>  
 <223> humanized variant -heavy chain variable domain VH of PD1-0103\_01

<400> 57

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

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

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

Ala Thr Ile Ser Gly Gly Gly Arg Asp Ile Tyr Tyr Pro Asp Ser Val  
50 55 60

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

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

Val Leu Leu Thr Gly Arg Val Tyr Phe Ala Leu Asp Ser Trp Gly Gln  
100 105 110

Gly Thr Leu Val Thr Val Ser Ser  
115 120

<210> 58  
<211> 111  
<212> PRT  
<213> Artificial

<220>  
<223> humanized variant -light chain variable domain VL of PD1-0103\_01

<400> 58

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

Glu Arg Ala Thr Ile Asn Cys Lys Ala Ser Glu Ser Val Asp Thr Ser

eolf-seql

20

25

30

Asp Asn Ser Phe Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro  
35 40 45

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

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser  
65 70 75 80

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

Asp Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
100 105 110

<210> 59

<211> 111

<212> PRT

<213> Artificial

<220>

<223> humanized variant -light chain variable domain VL of PD1-0103\_02

<400> 59

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 Ala Ser Glu Ser Val Asp Thr Ser  
20 25 30

Asp Asn Ser Phe Ile His Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro  
35 40 45

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

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

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Asn Tyr  
85 90 95

Asp Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
100 105 110

<210> 60

<211> 111

<212> PRT

<213> Artificial

<220>

<223> humanized variant -light chain variable domain VL of PD1-0103\_03

<400> 60

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Thr Ser  
20 25 30

Asp Asn Ser Phe Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro  
35 40 45

Arg Leu Leu Ile Tyr Arg Ser Ser Thr Leu Glu Ser Gly Ile Pro Ala  
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser  
65 70 75 80

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asn Tyr  
85 90 95

Asp Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

eolf-seql

100

105

110

<210> 61  
<211> 111  
<212> PRT  
<213> Artificial

<220>  
<223> humanized variant -light chain variable domain VL of PD1-0103\_04

<400> 61

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Glu Ser Val Asp Thr Ser  
20 25 30

Asp Asn Ser Phe Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro  
35 40 45

Arg Leu Leu Ile Tyr Arg Ser Ser Thr Leu Glu Ser Gly Ile Pro Ala  
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser  
65 70 75 80

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asn Tyr  
85 90 95

Asp Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
100 105 110

<210> 62  
<211> 107  
<212> PRT  
<213> Homo Sapiens

<400> 62

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Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu  
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe  
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln  
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser  
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu  
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser  
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
100 105

<210> 63  
<211> 105  
<212> PRT  
<213> Homo Sapiens

<400> 63

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

Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe  
20 25 30

Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val  
35 40 45

Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys

eolf-seql

50

55

60

Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser  
65 70 75 80

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu  
85 90 95

Lys Thr Val Ala Pro Thr Glu Cys Ser  
100 105

<210> 64  
<211> 330  
<212> PRT  
<213> Homo Sapiens

<400> 64

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

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser  
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser  
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr  
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys  
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys  
100 105 110

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Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro  
 115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys  
 130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp  
 145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu  
 165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu  
 180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn  
 195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly  
 210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu  
 225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr  
 245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn  
 260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe  
 275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn  
 290 295 300

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Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr  
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
325 330

<210> 65  
<211> 330  
<212> PRT  
<213> homo sapiens

<400> 65

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

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser  
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser  
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr  
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys  
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys  
100 105 110

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro  
115 120 125

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Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys  
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp  
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu  
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu  
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn  
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly  
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu  
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr  
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn  
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe  
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn  
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr  
305 310 315 320

eolf-seql

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
 325 330

<210> 66  
 <211> 330  
 <212> PRT  
 <213> homo sapiens

<400> 66

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

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

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser  
 35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser  
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr  
 65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys  
 85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys  
 100 105 110

Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro  
 115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys  
 130 135 140

eolf-seql

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp  
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu  
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu  
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn  
195 200 205

Lys Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly  
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu  
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr  
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn  
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe  
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn  
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr  
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
325 330

eolf-seql

<210> 67  
 <211> 327  
 <212> PRT  
 <213> Homo Sapiens

<400> 67

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg  
 1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr  
 20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser  
 35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser  
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr  
 65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys  
 85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro  
 100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys  
 115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val  
 130 135 140

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

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe

eolf-seql

165

170

175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp  
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu  
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg  
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys  
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp  
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys  
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser  
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser  
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser  
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys  
325

<210> 68

<211> 268

<212> PRT

<213> Homo Sapiens

eolf-seql

<400> 68

Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr  
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe  
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr  
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu  
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu  
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn  
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala  
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg  
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly  
130 135 140

Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly Leu Leu Gly Ser  
145 150 155 160

Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys Ser Arg Ala Ala  
165 170 175

Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro Leu Lys Glu Asp  
180 185 190

eolf-seql

Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly Glu Leu Asp Phe  
195 200 205

Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro Cys Val Pro Glu  
210 215 220

Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly Met Gly Thr Ser  
225 230 235 240

Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg Ser Ala Gln Pro  
245 250 255

Leu Arg Pro Glu Asp Gly His Cys Ser Trp Pro Leu  
260 265

<210> 69  
<211> 150  
<212> PRT  
<213> Homo Sapiens

<400> 69

Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr  
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe  
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr  
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu  
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu  
65 70 75 80

eolf-seql

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn  
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala  
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg  
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly  
130 135 140

Gln Phe Gln Thr Leu Val  
145 150

<210> 70  
<211> 288  
<212> PRT  
<213> homo sapiens

<400> 70

Met Gln Ile Pro Gln Ala Pro Trp Pro Val Val Trp Ala Val Leu Gln  
1 5 10 15

Leu Gly Trp Arg Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp  
20 25 30

Asn Pro Pro Thr Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp  
35 40 45

Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val  
50 55 60

Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala  
65 70 75 80

eolf-seql

Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg  
85 90 95

Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg  
100 105 110

Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu  
115 120 125

Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val  
130 135 140

Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro  
145 150 155 160

Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Val Gly Val Val Gly Gly  
165 170 175

Leu Leu Gly Ser Leu Val Leu Leu Val Trp Val Leu Ala Val Ile Cys  
180 185 190

Ser Arg Ala Ala Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly Gln Pro  
195 200 205

Leu Lys Glu Asp Pro Ser Ala Val Pro Val Phe Ser Val Asp Tyr Gly  
210 215 220

Glu Leu Asp Phe Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro Val Pro  
225 230 235 240

Cys Val Pro Glu Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro Ser Gly  
245 250 255

Met Gly Thr Ser Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly Pro Arg  
260 265 270

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|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Ala | Gln | Pro | Leu | Arg | Pro | Glu | Asp | Gly | His | Cys | Ser | Trp | Pro | Leu |
|     | 275 |     |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |

<210> 71  
 <211> 4  
 <212> PRT  
 <213> Artificial

<220>  
 <223> Minimal HVR1 of PD1-0103 and PD1-0103 humanized variant  
 PD1-0103-0312, PD1-0103-0313, PD1-0103-0314 , and PD1-0103-0315

<400> 71

Ser Ser Tyr Thr  
 1

<210> 72  
 <211> 8  
 <212> PRT  
 <213> Artificial

<220>  
 <223> Minimal HVR2 of PD1-0103 and PD1-0103 humanized variant  
 PD1-0103-0312, PD1-0103-0313, PD1-0103-0314 , and PD1-0103-0315

<400> 72

Ser Gly Gly Gly Arg Asp Ile Tyr  
 1 5

<210> 73  
 <211> 5  
 <212> PRT  
 <213> Artificial

<220>  
 <223> Minimal HVR3 of PD1-0103 and PD1-0103 humanized variant  
 PD1-0103-0312, PD1-0103-0313, PD1-0103-0314 , and PD1-0103-0315

<400> 73

Gly Arg Val Tyr Phe  
 1 5

eolf-seql

<210> 74  
<211> 6  
<212> PRT  
<213> Artificial

<220>  
<223> Minimal LVR1 of PD1-0103 and PD1-0103 humanized variant  
PD1-0103-0312, PD1-0103-0313, PD1-0103-0314 , and PD1-0103-0315

<400> 74

Thr Ser Asp Asn Ser Phe  
1 5

<210> 75  
<211> 7  
<212> PRT  
<213> Artificial

<220>  
<223> Minimal LVR2 of PD1-0103 and PD1-0103 humanized variant  
PD1-0103-0312, PD1-0103-0313, PD1-0103-0314 , and PD1-0103-0315

<400> 75

Arg Ser Ser Thr Leu Glu Ser  
1 5

<210> 76  
<211> 6  
<212> PRT  
<213> Artificial

<220>  
<223> Minimal LVR3 of PD1-0103 and PD1-0103 humanized variant  
PD1-0103-0312, PD1-0103-0313, PD1-0103-0314 , and PD1-0103-0315

<400> 76

Asn Tyr Asp Val Pro Trp  
1 5

<210> 77  
<211> 3

eolf-seql

<212> PRT

<213> Artificial

<220>

<223> fragment of FR-H3 comprising the amino acid sequence RDN at positions of 71, 72, 73 according to Kabat numbering

<400> 77

Arg Asp Asn

1