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Beckmann, Dr. Roland

<120> DUAL TARGETING

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<140> PCT/EP 2012/002279
<141> 2012-05-29

<150> EP 11004373.4
<151> 2011-05-27

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<170> PatentIn version 3.3

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


Ser Gly Ser Gly Xaa Xaa Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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35 40 45

Tyr Ala Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Xaa Xaa Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Asn Asp Asn Val
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65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Thr Val Ser Ser
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Ala Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
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Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Xaa Tyr Xaa Xaa Xaa Xaa
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Xaa Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Thr Val Ser Ser
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Ala Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Xaa Trp Ile
        35                  40                  45


Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Xaa Tyr Xaa Xaa Xaa Xaa
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Xaa 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
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35 40 45

Xaa Ala Ala Ser Xaa Leu Xaa Xaa Xaa Xaa Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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35 40 45

Xaa Ala Ala Ser Xaa Leu Xaa Xaa Xaa Xaa Pro Ser Arg Phe Ser Gly
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Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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Ala Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Asn Asp Asn Val
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Leu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Xaa Thr Leu Tyr
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Ala Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

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

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Ala Arg Asp Ser Gly Tyr Phe Asp Xaa Trp Gly Gln Gly Thr Leu Val
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Thr Val Ser Ser
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Ala Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

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

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

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

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

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

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

Gly Thr Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Asn Asp Asn Val
    50                  55                  60

Leu 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
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Val Thr Val Ser Ser
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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
            20                  25                  30

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

Ile Xaa Gly Asn Asn Xaa Arg Xaa Xaa Xaa Xaa Pro Asp Arg Phe Ser
    50                  55                  60
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Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
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Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
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Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Thr Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Asn Asp Asn Val
50 55 60

Leu 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

Ala Xaa Thr Xaa Xaa Gly Xaa Phe Asp Xaa Trp Gly Gln Gly Thr Leu
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35 40 45

Tyr Ala Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

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

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
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35 40 45

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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35 40 45

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

Ser Gly Ser Gly Lys Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
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35 40 45

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Trp Tyr Asn His Asp Ile
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
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35 40 45

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Asn Asp Asn Val
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Leu 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

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

Thr Val Ser Ser
115

<210> 23
<211> 116
<212> PRT
<213> Artificial

<220>
<223> synthetic VH domain

<400> 23

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

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

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

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Trp Tyr Asn His Asp Ile
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

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

Thr Val Ser Ser
115

<210> 24
<211> 108
<212> PRT
<213> Artificial

<220>

<223> synthetic Vkappa domain

<400> 24

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Leu Trp His Ile Ser Ser Tyr
20 25 30

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

Tyr Ala Ala Ser Ser Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 25
<211> 108
<212> PRT
<213> Artificial

<220>
<223> synthetic Vkappa domain

<400> 25

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

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

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

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 26
<211> 108
<212> PRT
<213> Artificial

<220>
<223> synthetic Vkappa domain

<400> 26

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Leu Trp His Ile Ser Ser Tyr
20 25 30

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

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 27
<211> 116
<212> PRT
<213> Artificial

<220>
<223> synthetic VH domain

<400> 27

Glu Val Gln Leu Val 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 Thr Phe Ser Ser Tyr
20 25 30

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

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Val Tyr Asn Tyr Asn Val
50 55 60

Leu 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

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

Thr Val Ser Ser
        115
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<210> 28
<211> 116
<212> PRT
<213> Artificial

<220>
<223> synthetic VH domain

<400> 28

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

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

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

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

Leu 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

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

Thr Val Ser Ser
        115
```

<210> 29
<211> 116
<212> PRT
<213> Artificial

<220>
<223> synthetic VH domain

<400> 29

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

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

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

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Val Tyr Asn Tyr Asn Val
    50                  55                  60

Leu 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

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

Thr Val Ser Ser
        115


<210>  30
<211>  108
<212>  PRT
<213>  Artificial

<220>
<223>  synthetic Vkappa domain

<400>  30

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Leu Trp His Ile Ser Ser Tyr
            20                  25                  30

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

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
            100                 105
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<210> 31
<211> 116
<212> PRT
<213> Artificial

<220>
<223> synthetic VH domain

<400> 31

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

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

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

Gly Gln Ile Ser Gly Ser Gly Gly Ser Thr Val Tyr Asn Tyr Asn Val
50 55 60

Leu 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

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

Thr Val Ser Ser
115