

SEQUENCE LISTING

<110> Ablynx N.V.

<120> Binding molecules with multiple binding sites, compositions comprising the same and uses thereof

<130> 125 623

<160> 33

<170> PatentIn version 3.4

<210> 1

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<212> PRT

<213> -Artificial

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Ser	Leu	Thr	Ile	Ser	Cys	Ala	Ala	Ser	Gly	Ile	Thr	Phe	Ser
			20					25					30

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Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Ala	Gly	Gly
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Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Val	Asp	Ala	Ser
			20					25					30

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

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

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Asp Ser Ile Val Ser
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Asn Ser Ala Met Gly
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<400> 6

Ser Gly Thr Met Gly
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Trp Tyr Arg Arg Ala Arg Gly Lys Gln Arg Glu Trp Val Ala
1 5 10

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Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Trp Val Ala
1 5 10

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Trp Phe Arg Arg Ala Pro Gly Lys Glu Arg Glu Phe Val Ala
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Gly Ile Ser Asn Gly Gly Thr Thr Lys Tyr Ala Glu Ser Val Leu Gly
1 5 10 15

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Arg Ile Thr Gly Gly Gly Leu Ile Ala Tyr Thr Asp Ser Val Lys Gly
1 5 10 15

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Ser Ile Pro Trp Ser Gly Gly Arg Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Asp

<210> 13
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Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Met Val Tyr Leu Gln
1 5 10 15

Met Asn Gly Leu Asn Pro Glu Asp Thr Ala Val Tyr Leu Cys Lys Val
 20 25 30

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Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser Thr Val Tyr Leu Gln
 1 5 10 15

Met Asn Ser Leu Glu Pro Glu Asp Thr Ala Val Tyr Tyr Cys Asn Thr
 20 25 30

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Arg Phe Thr Ile Ser Arg Asp Asn Ala Gln Asn Thr Val Phe Leu Gln
 1 5 10 15

Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Phe
 20 25 30

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Arg Gln Tyr
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Ile Asn Ser Arg Asp Gly
 1 5

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Lys Glu Arg Ser Thr Gly Trp Asp Phe Ala Ser
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Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 1 5 10

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Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 1 5 10

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Trp Gly Gln Gly Ile Gln Val Thr Val Ser Ser
 1 5 10

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

Ser Leu Thr Ile Ser Cys Ala Ala Ser Gly Ile Thr Phe Ser Asp Ser
 20 25 30

Ile Val Ser Trp Tyr Arg Arg Ala Arg Gly Lys Gln Arg Glu Trp Val
 35 40 45

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

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

Gln Met Asn Gly Leu Asn Pro Glu Asp Thr Ala Val Tyr Leu Cys Lys
 85 90 95

Val Arg Gln Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 100 105 110

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Val Asp Ala Ser Asn Ser
 20 25 30

Ala Met Gly Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Trp Val
 35 40 45

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

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

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

Thr Ile Asn Ser Arg Asp Gly Trp Gly Gln Gly Thr Gln Val Thr Val
 100 105 110

Ser Ser

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

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

Thr Met Gly Trp Phe Arg Arg Ala Pro Gly Lys Glu Arg Glu Phe Val
35 40 45

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

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

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

Ala Phe Lys Glu Arg Ser Thr Gly Trp Asp Phe Ala Ser Trp Gly Gln
100 105 110

Gly Ile Gln Val Thr Val Ser Ser
115 120

<210> 25
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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 Leu Asp Tyr Tyr
20 25 30

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

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

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

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

Ala Ala Ser Gln Ala Pro Ile Thr Ile Ala Thr Met Met Lys Pro Phe
 100 105 110

Tyr Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 115 120 125

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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 Leu Asp Tyr Tyr
 20 25 30

Ala Lys Cys Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Trp Val
 35 40 45

Ser Cys Ile Ser Ser Ser Asp Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

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

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

Ala Ala Arg His Gly Gly Pro Leu Thr Val Glu Tyr Phe Phe Asp Tyr

100 105 110
 Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 115 120

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 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 Asp Tyr Tyr
 20 25 30

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

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

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

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

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

 Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 115 120

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

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

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

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

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

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

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

Val Ser Ser
 115

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

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

Val Ser Asn Tyr Ala Met Gly Trp Gly Arg Gln Ala Pro Gly Thr Gln
 35 40 45

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

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

Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val
 85 90 95

Tyr Tyr Cys Phe Glu His Gln Val Ala Gly Leu Thr Trp Gly Gln Gly
 100 105 110

Thr Gln Val Thr Val Ser Ser
 115

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

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

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

Ser Thr Ile Asn Ser Gly Gly Gly Ile Thr Tyr Arg Gly Ser Val Lys
 50 55 60

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

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

Asn Gly Gly Ser Ser Tyr Arg Arg Gly Gln Gly Thr Gln Val Thr Val
 100 105 110

Ser Ser

<210> 31
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Thr Gly Gly

1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Asp Tyr Tyr
 20 25 30
 Gly Ile Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Gly Val
 35 40 45
 Ser Phe Ile Ser Gly Ser Asp Gly Ser Thr Tyr Tyr Ala Glu Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Lys Ala Lys Asn Thr Val Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Ala Asp Pro Trp Gly Pro Pro Ser Ile Ala Thr Met Thr Ser Tyr
 100 105 110
 Glu Tyr Lys His Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
 115 120 125
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 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 Thr Tyr
 20 25 30
 Thr Met Ile Trp Leu Arg Arg Ala Pro Gly Lys Gly Phe Glu Trp Val
 35 40 45
 Ser Thr Ile Asp Lys Asp Gly Asn Thr Asn Tyr Val Asp Ser Val Lys
 50 55 60
 Gly Arg Phe Ala Val Ser Arg Asp Asn Thr Lys Asn Thr Leu Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Met Tyr Tyr Cys Thr
85 90 95

Lys His Gly Ser Ser Ala Arg Gly Gln Gly Thr Arg Val Thr Val Ser
100 105 110

Ser

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<223> Xaa can be any naturally occurring amino acid

<400> 33

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

Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Xaa Ala Leu Lys Ile Xaa
20 25 30

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

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

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

Gln Met Asn Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys Arg

85

90

95

Glu Trp Asn Ser Gly Tyr Pro Pro Val Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Gln Val Thr Val Ser Ser
115