

## SEQUENCE LISTING

<110> Complix NV

<120> AlphaBodies for HIV Entry Inhibition

<130> 135623

<160> 29

<170> PatentIn version 3.4

<210> 1

<211> 856

<212> PRT

<213> Human immunodeficiency virus type 1 HXB2

<400> 1

Met Arg Val Lys Glu Lys Tyr Gln His Leu Trp Arg Trp Gly Trp Arg  
1 5 10 15

Trp Gly Thr Met Leu Leu Gly Met Leu Met Ile Cys Ser Ala Thr Glu  
20 25 30

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

Thr Thr Thr Leu Phe Cys Ala Ser Asp Ala Lys Ala Tyr Asp Thr Glu  
 50 55 60

Val His Asn Val Trp Ala Thr His Ala Cys Val Pro Thr Asp Pro Asn  
 65 70 75 80

Pro Gln Glu Val Val Leu Val Asn Val Thr Glu Asn Phe Asn Met Trp  
 85 90 95

Lys Asn Asp Met Val Glu Gln Met His Glu Asp Ile Ile Ser Leu Trp  
 100 105 110

Asp Gln Ser Leu Lys Pro Cys Val Lys Leu Thr Pro Leu Cys Val Ser  
 115 120 125

Leu Lys Cys Thr Asp Leu Lys Asn Asp Thr Asn Thr Asn Ser Ser Ser  
 130 135 140

Gly Arg Met Ile Met Glu Lys Gly Glu Ile Lys Asn Cys Ser Phe Asn  
 145 150 155 160

Ile Ser Thr Ser Ile Arg Gly Lys Val Gln Lys Glu Tyr Ala Phe Phe  
 165 170 175

Tyr Lys Leu Asp Ile Ile Pro Ile Asp Asn Asp Thr Thr Ser Tyr Lys  
                   180                                  185                                  190

Leu Thr Ser Cys Asn Thr Ser Val Ile Thr Gln Ala Cys Pro Lys Val  
                   195                                  200                                  205

Ser Phe Glu Pro Ile Pro Ile His Tyr Cys Ala Pro Ala Gly Phe Ala  
                   210                                  215                                  220

Ile Leu Lys Cys Asn Asn Lys Thr Phe Asn Gly Thr Gly Pro Cys Thr  
  225                                  230                                  235                                  240

Asn Val Ser Thr Val Gln Cys Thr His Gly Ile Arg Pro Val Val Ser  
                                   245                                  250                                  255

Thr Gln Leu Leu Leu Asn Gly Ser Leu Ala Glu Glu Glu Val Val Ile  
                   260                                  265                                  270

Arg Ser Val Asn Phe Thr Asp Asn Ala Lys Thr Ile Ile Val Gln Leu  
                   275                                  280                                  285

Asn Thr Ser Val Glu Ile Asn Cys Thr Arg Pro Asn Asn Asn Thr Arg  
                   290                                  295                                  300

Lys Arg Ile Arg Ile Gln Arg Gly Pro Gly Arg Ala Phe Val Thr Ile  
 305 310 315 320

Gly Lys Ile Gly Asn Met Arg Gln Ala His Cys Asn Ile Ser Arg Ala  
 325 330 335

Lys Trp Asn Asn Thr Leu Lys Gln Ile Ala Ser Lys Leu Arg Glu Gln  
 340 345 350

Phe Gly Asn Asn Lys Thr Ile Ile Phe Lys Gln Ser Ser Gly Gly Asp  
 355 360 365

Pro Glu Ile Val Thr His Ser Phe Asn Cys Gly Gly Glu Phe Phe Tyr  
 370 375 380

Cys Asn Ser Thr Gln Leu Phe Asn Ser Thr Trp Phe Asn Ser Thr Trp  
 385 390 395 400

Ser Thr Glu Gly Ser Asn Asn Thr Glu Gly Ser Asp Thr Ile Thr Leu  
 405 410 415

Pro Cys Arg Ile Lys Gln Ile Ile Asn Met Trp Gln Lys Val Gly Lys  
 420 425 430

Ala Met Tyr Ala Pro Pro Ile Ser Gly Gln Ile Arg Cys Ser Ser Asn  
 435 440 445

Ile Thr Gly Leu Leu Leu Thr Arg Asp Gly Gly Asn Ser Asn Asn Glu  
 450 455 460

Ser Glu Ile Phe Arg Pro Gly Gly Gly Asp Met Arg Asp Asn Trp Arg  
 465 470 475 480

Ser Glu Leu Tyr Lys Tyr Lys Val Val Lys Ile Glu Pro Leu Gly Val  
 485 490 495

Ala Pro Thr Lys Ala Lys Arg Arg Val Val Gln Arg Glu Lys Arg Ala  
 500 505 510

Val Gly Ile Gly Ala Leu Phe Leu Gly Phe Leu Gly Ala Ala Gly Ser  
 515 520 525

Thr Met Gly Ala Ala Ser Met Thr Leu Thr Val Gln Ala Arg Gln Leu  
 530 535 540

Leu Ser Gly Ile Val Gln Gln Gln Asn Asn Leu Leu Arg Ala Ile Glu  
 545 550 555 560

Ala Gln Gln His Leu Leu Gln Leu Thr Val Trp Gly Ile Lys Gln Leu  
565 570 575

Gln Ala Arg Ile Leu Ala Val Glu Arg Tyr Leu Lys Asp Gln Gln Leu  
580 585 590

Leu Gly Ile Trp Gly Cys Ser Gly Lys Leu Ile Cys Thr Thr Ala Val  
595 600 605

Pro Trp Asn Ala Ser Trp Ser Asn Lys Ser Leu Glu Gln Ile Trp Asn  
610 615 620

His Thr Thr Trp Met Glu Trp Asp Arg Glu Ile Asn Asn Tyr Thr Ser  
625 630 635 640

Leu Ile His Ser Leu Ile Glu Glu Ser Gln Asn Gln Gln Glu Lys Asn  
645 650 655

Glu Gln Glu Leu Leu Glu Leu Asp Lys Trp Ala Ser Leu Trp Asn Trp  
660 665 670

Phe Asn Ile Thr Asn Trp Leu Trp Tyr Ile Lys Leu Phe Ile Met Ile  
675 680 685

Val Gly Gly Leu Val Gly Leu Arg Ile Val Phe Ala Val Leu Ser Ile  
 690 695 700

Val Asn Arg Val Arg Gln Gly Tyr Ser Pro Leu Ser Phe Gln Thr His  
 705 710 715 720

Leu Pro Thr Pro Arg Gly Pro Asp Arg Pro Glu Gly Ile Glu Glu Glu  
 725 730 735

Gly Gly Glu Arg Asp Arg Asp Arg Ser Ile Arg Leu Val Asn Gly Ser  
 740 745 750

Leu Ala Leu Ile Trp Asp Asp Leu Arg Ser Leu Cys Leu Phe Ser Tyr  
 755 760 765

His Arg Leu Arg Asp Leu Leu Leu Ile Val Thr Arg Ile Val Glu Leu  
 770 775 780

Leu Gly Arg Arg Gly Trp Glu Ala Leu Lys Tyr Trp Trp Asn Leu Leu  
 785 790 795 800

Gln Tyr Trp Ser Gln Glu Leu Lys Asn Ser Ala Val Ser Leu Leu Asn  
 805 810 815

Ala Thr Ala Ile Ala Val Ala Glu Gly Thr Asp Arg Val Ile Glu Val  
                   820                  825                  830

Val Gln Gly Ala Cys Arg Ala Ile Arg His Ile Pro Arg Arg Ile Arg  
                   835                  840                  845

Gln Gly Leu Glu Arg Ile Leu Leu  
                   850                  855

<210> 2

<211> 117

<212> PRT

<213> Artificial

<220>

<223> Alphabody scAB013

<400> 2

Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln  
   1                  5                  10                  15

Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr Gly Gly Ser Gly  
                   20                  25                  30

Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Met Ser Ile Glu  
                   35                  40                  45



Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln Ile Ala Ala Ile  
50 55 60

Gln Lys Gln Ile Tyr Arg Met Thr Gly Gly Ser Gly Gly Gly Ser Gly  
65 70 75 80

Gly Gly Ser Gly Gly Gly Ser Gly Met Ser Ile Glu Glu Ile Gln Lys  
85 90 95

Gln Ile Ala Ala Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln Ile  
100 105 110

Tyr Arg Met Thr Pro  
115

<210> 3

<211> 97

<212> PRT

<213> Artificial

<220>

<223> scAB013\_N1

<400> 3

10

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

Ile Ala Ala Gln Gln His Leu Ile Tyr Leu Met Thr Gly Gly Ser Ser  
20 25 30

Gly Gly Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln  
35 40 45

Lys Gln Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr Gly Gly  
50 55 60

Ser Ser Gly Gly Met Ser Leu Ser Ala Ile Val Lys Gln Gln Asn Ala  
65 70 75 80

Ile Leu Lys Gln Ile Gln Ala Ile Gln Lys Gln Leu Gln Arg Met Val  
85 90 95

Ala

<210> 4

<211> 97

<212> PRT

<213> Artificial

&lt;220&gt;

&lt;223&gt; scAB013\_N2

&lt;400&gt; 4

Gln Gln Ile Ala Asn Leu Gln Lys Ala Ile Ala Ala Gln Gln His Leu  
 1 5 10 15

Ile Ala Leu Ile Gln Trp Gly Ile Tyr Arg Met Thr Gly Gly Ser Ser  
 20 25 30

Gly Gly Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln  
 35 40 45

Lys Gln Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr Gly Gly  
 50 55 60

Ser Ser Gly Gly Met Ser Gln Asn Ala Ile Leu Lys Gln Ile Gln Ala  
 65 70 75 80

Ile Gln Lys Gln Leu Gln Ala Ile Val Lys Gln Ile Lys Ala Met Gln  
 85 90 95

Ala

<210> 5  
<211> 97  
<212> PRT  
<213> Artificial

<220>  
<223> scAB013\_N3

<400> 5

Ala Ala Ile Ala Ala Gln Gln His Leu Ile Ala Leu Ile Gln Trp Gly  
1 5 10 15

Ile Ala Gln Leu Gln Ala Arg Ile Tyr Ala Met Thr Gly Gly Ser Ser  
20 25 30

Gly Gly Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln  
35 40 45

Lys Gln Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr Gly Gly  
50 55 60

Ser Ser Gly Gly Met Ser Ile Gln Ala Ile Gln Lys Gln Leu Gln Ala  
65 70 75 80

Ile Val Lys Gln Ile Lys Ala Ile Gln Lys Gln Ile Leu Ala Met Glu  
                     85                    90                    95

Ala

<210> 6

<211> 99

<212> PRT

<213> Artificial

<220>

<223> scAB013\_C1

<400> 6

Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln  
  1                    5                    10                    15

Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr Gly Gly Ser Ser  
                     20                    25                    30

Gly Gly Gly Gly Ser Ser Gly Gly Thr Trp Gln Met Trp Glu Ile Gln  
                     35                    40                    45

Ile Gln Ile Tyr Thr Ile Gln Ile Gln Ile Leu Ile Ile Gln Ala Gln  
                     50                    55                    60

2

2

•

5

•

4

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

Ile Gln Ile Leu Ile Ile Gln Ala Gln Ile Gln Gln Ile Gln Asn Gln  
           50                                  55                                  60

Ile Glu Leu Met Thr Leu Met Ser Ile Glu Glu Ile Gln Lys Gln Ile  
  65                                  70                                  75                                  80

Ala Ala Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg  
                                   85                                  90                                  95

Met Thr Pro

<210> 8

<211> 6

<212> PRT

<213> Artificial

<220>

<223> Linker sequence

<400> 8

Gly Gly Ser Ser Gly Gly

1

5

<210> 9  
 <211> 40  
 <212> PRT  
 <213> Human immunodeficiency virus type 1 HXB2

<400> 9

Gln Leu Leu Ser Gly Ile Val Gln Gln Gln Asn Asn Leu Leu Arg Ala  
 1 5 10 15

Ile Glu Ala Gln Gln His Leu Leu Gln Leu Thr Val Trp Gly Ile Lys  
 20 25 30

Gln Leu Gln Ala Arg Ile Leu Ala  
 35 40

<210> 10  
 <211> 28  
 <212> PRT  
 <213> Artificial

<220>  
 <223> Amino acid sequence of Alphabody helix

<400> 10

Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln



17

1 5 10 15

Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr  
20 25

<210> 11

<211> 38

<212> PRT

<213> Human immunodeficiency virus type 1 HXB2

<400> 11

His Thr Thr Trp Met Glu Trp Asp Arg Glu Ile Asn Asn Tyr Thr Ser  
1 5 10 15

Leu Ile His Ser Leu Ile Glu Glu Ser Gln Asn Gln Gln Glu Lys Asn  
20 25 30

Glu Gln Glu Leu Leu Glu  
35

<210> 12

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Alphabody sequence

<400> 12

Met Leu Ile Glu Gly Ile Gln Lys Gln Ile Ala Asn Ile Gln Lys Ala  
1 5 10 15

Ile Ala Ala Ile Gln Lys Leu Ile Tyr Leu Met Thr  
20 25

<210> 13

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Alphabody sequence

<400> 13

Met Gln Ile Glu Asn Ile Gln Lys Ala Ile Ala Ala Ile Gln Lys Leu  
1 5 10 15

Ile Ala Leu Ile Gln Lys Gly Ile Tyr Gln Met Thr  
20 25

<210> 14

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Alphabody sequence

<400> 14

Met	Ala	Ile	Glu	Ala	Ile	Gln	Lys	Leu	Ile	Ala	Leu	Ile	Gln	Lys	Gly
1				5				10					15		

Ile	Ala	Gln	Ile	Gln	Lys	Arg	Ile	Tyr	Ala	Met	Thr
			20					25			

<210> 15

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Alphabody sequence

<400> 15

Met	Ser	Ile	Ser	Glu	Ile	Val	Lys	Gln	Ile	Asn	Ala	Ile	Leu	Lys	Gln
1				5				10					15		

Ile	Glu	Ala	Ile	Gln	Lys	Gln	Ile	Gln	Arg	Met	Val
				20				25			

<210> 16

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Alphabody sequence

<400> 16

Met	Ser	Ile	Asn	Glu	Ile	Leu	Lys	Gln	Ile	Glu	Ala	Ile	Gln	Lys	Gln
1				5					10					15	

Ile	Gln	Ala	Ile	Val	Lys	Gln	Ile	Lys	Arg	Met	Gln
			20					25			

<210> 17

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Alphabody sequence

<400> 17

Met	Ser	Ile	Glu	Glu	Ile	Gln	Lys	Gln	Ile	Gln	Ala	Ile	Val	Lys	Gln
1					5					10				15	

Ile Lys Ala Ile Gln Lys Gln Ile Leu Arg Met Thr  
                   20                                  25

<210> 18

<211> 43

<212> PRT

<213> Human immunodeficiency virus type 1 HBX2

<400> 18

Gln Leu Leu Ser Gly Ile Val Gln Gln Gln Asn Asn Leu Leu Arg Ala  
   1                          5                                  10                                  15

Ile Glu Ala Gln Gln His Leu Leu Gln Leu Thr Val Trp Gly Ile Lys  
                   20                                  25                                  30

Gln Leu Gln Ala Arg Ile Leu Ala Val Glu Arg  
                   35                                  40

<210> 19

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of structurally optimized Alphabody A-helix

<400> 19

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

Ile	Ala	Ala	Gln	Gln	His	Leu	Ile	Tyr	Leu	Met	Thr
			20					25			

<210> 20

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of structurally optimized Alphabody A-helix

<400> 20

Gln	Gln	Ile	Ala	Asn	Leu	Gln	Lys	Ala	Ile	Ala	Ala	Gln	Gln	His	Leu
1				5					10					15	

Ile	Ala	Leu	Ile	Gln	Trp	Gly	Ile	Tyr	Arg	Met	Thr
				20				25			

<210> 21

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of structurally optimized Alphabody A-helix

<400> 21

Ala	Ala	Ile	Ala	Ala	Gln	Gln	His	Leu	Ile	Ala	Leu	Ile	Gln	Trp	Gly
1				5					10					15	

Ile	Ala	Gln	Leu	Gln	Ala	Arg	Ile	Tyr	Ala	Met	Thr
			20					25			

<210> 22

<211> 29

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of structurally optimized Alphabody C-helix

<400> 22

Met	Ser	Leu	Ser	Ala	Ile	Val	Lys	Gln	Gln	Asn	Ala	Ile	Leu	Lys	Gln
1				5					10					15	

Ile Gln Ala Ile Gln Lys Gln Leu Gln Arg Met Val Ala

20

25

&lt;210&gt; 23

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;

&lt;223&gt; Amino acid sequence of structurally optimized Alphabody C-helix

&lt;400&gt; 23

Met Ser Gln Asn Ala Ile Leu Lys Gln Ile Gln Ala Ile Gln Lys Gln

1

5

10

15

Leu Gln Ala Ile Val Lys Gln Ile Lys Ala Met Gln Ala

20

25

&lt;210&gt; 24

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Artificial

&lt;220&gt;



<223> Amino acid sequence of structurally optimized Alphabody C-helix

<400> 24

Met	Ser	Ile	Gln	Ala	Ile	Gln	Lys	Gln	Leu	Gln	Ala	Ile	Val	Lys	Gln
1				5					10					15	

Ile	Lys	Ala	Ile	Gln	Lys	Gln	Ile	Leu	Ala	Met	Glu	Ala
			20					25				

<210> 25

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of Alphabody B-helix with grafted HR2 residues

<400> 25

Trp	Ser	Ile	Trp	Asp	Ile	Gln	Ile	Gln	Ile	Tyr	Thr	Ile	Gln	Ile	Gln
1				5					10					15	

Ile	Leu	Ile	Ile	Gln	Ser	Gln	Ile	Gln	Gln	Met	Thr
				20					25		

<210> 26

<211> 28

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of Alphabody B-helix with grafted HR2 residues

<400> 26

Ile	Ser	Ile	Tyr	Thr	Ile	Gln	Ile	Gln	Ile	Leu	Ile	Ile	Gln	Ser	Gln
1				5					10					15	

Ile	Gln	Gln	Ile	Gln	Asn	Gln	Ile	Glu	Leu	Met	Thr
			20				25				

<210> 27

<211> 30

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of structurally optimized Alphabody B-helix

<400> 27

Thr	Trp	Gln	Met	Trp	Glu	Ile	Gln	Ile	Gln	Ile	Tyr	Thr	Ile	Gln	Ile
1				5					10					15	

Gln Ile Leu Ile Ile Gln Ala Gln Ile Gln Gln Trp Lys Gln  
                   20                  25                  30

<210> 28

<211> 30

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of structurally optimized Alphabody B-helix

<400> 28

Ser Met Gln Met Tyr Thr Ile Gln Ile Gln Ile Leu Ile Ile Gln Ala  
   1                  5                  10                  15

Gln Ile Gln Gln Ile Gln Asn Gln Ile Glu Leu Met Thr Leu  
                   20                  25                  30

<210> 29

<211> 29

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of the non-mutated Alphabody C-helix

&lt;400&gt; 29

Met Ser Ile Glu Glu Ile Gln Lys Gln Ile Ala Ala Ile Gln Lys Gln  
1 5 10 15

Ile Ala Ala Ile Gln Lys Gln Ile Tyr Arg Met Thr Pro  
20 25