

SEQUENCE LISTING

<110> Vivalis

<120> In vitro method to determine whether a drug candidate active against a target protein is active against a variant of said protein

<130> D26388

<150> EP08300146.1

<151> 2008-03-14

<160> 68

<170> PatentIn version 3.3

<210> 1

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<212> DNA

<213> Hepatitis C Virus

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<221> misc_feature

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 <400> 46
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Arg Gln Lys Lys Val Thr Phe Asp Arg Met Gln Val Leu Asp Asp His
50 55 60

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

Ala Arg Leu Leu Ser Ile Glu Glu Ala Cys Lys Leu Thr Pro Pro His
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Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Ser Leu
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Ser Ser Arg Ala Val Asn His Ile Arg Ser Val Trp Glu Asp Leu Leu
115 120 125

Glu Asp Thr Glu Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu
130 135 140

Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu
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Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu
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Tyr Asp Val Val Ser Thr Leu Pro Gln Ala Val Met Gly Pro Ser Tyr
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Gly Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Thr
195 200 205

Trp Lys Ser Lys Lys Cys Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys
210 215 220

Phe Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Thr Glu Glu Ser Ile
225 230 235 240

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260 265 270

Gln Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr
275 280 285

Ser Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Thr Ala Ala Cys
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Arg Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp
305 310 315 320

Leu Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser
325 330 335

Leu Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly
340 345 350

Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser
355 360 365

Ser Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr

370

375

380

Leu Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr
 385 390 395 400

Val Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr
 405 410 415

Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser
 420 425 430

Ile Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile
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Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile
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Glu Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro
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Gly Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro
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Pro Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Lys Leu
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Leu Ser Gln Gly Gly Arg Ala Ala Thr Cys Gly Lys Tyr Leu Phe Asn
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Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser
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Gln Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Asn Gly Gly Asp
 545 550 555 560

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<223> genotype 1b NS3 full length protein

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35 40 45

Val Cys Trp Thr Val Tyr His Gly Ala Gly Ser Lys Thr Leu Ala Gly
50 55 60

Pro Lys Gly Pro Ile Thr Gln Met Tyr Thr Asn Val Asp Gln Asp Leu
65 70 75 80

Val Gly Trp Pro Ala Pro Pro Gly Ala Arg Ser Met Thr Pro Cys Thr
85 90 95

Cys Gly Ser Ser Asp Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile
100 105 110

Pro Val Arg Arg Arg Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg
115 120 125

Pro Val Ser Tyr Leu Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro
130 135 140

Ser Gly His Val Val Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly
145 150 155 160

Val Ala Lys Ala Val Asp Phe Ile Pro Val Glu Ser Met Glu Thr Thr
165 170 175

Met Arg Ser Pro Val Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro
180 185 190

Gln Thr Phe Gln Val Ala His Leu His Ala Pro Thr Gly Ser Gly Lys
195 200 205

Ser Thr Lys Val Pro Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val Leu
210 215 220

Val Leu Asn Pro Ser Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met
225 230 235 240

Ser Lys Ala His Gly Ile Glu Pro Asn Ile Arg Thr Gly Val Arg Thr
245 250 255

Ile Thr Thr Gly Gly Pro Ile Thr Tyr Ser Thr Tyr Gly Lys Phe Leu
260 265 270

Ala Asp Gly Gly Cys Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp
275 280 285

Glu Cys His Ser Thr Asp Trp Thr Thr Ile Leu Gly Ile Gly Thr Val
290 295 300

Leu Asp Gln Ala Glu Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr
305 310 315 320

Ala Thr Pro Pro Gly Ser Ile Thr Val Pro His Pro Asn Ile Glu Glu
325 330 335

Val Ala Leu Ser Asn Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile
340 345 350

Pro Ile Glu Ala Ile Lys Gly Gly Arg His Leu Ile Phe Cys His Ser
355 360 365

Lys Lys Lys Cys Asp Glu Leu Ala Ala Lys Leu Thr Gly Leu Gly Leu
370 375 380

Asn Ala Val Ala Tyr Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr
385 390 395 400

Ser Gly Asp Val Val Val Val Ala Thr Asp Ala Leu Met Thr Gly Phe
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Thr Gly Asp Phe Asp Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln
420 425 430

Thr Val Asp Phe Ser Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr Thr
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Cys Ala Trp Tyr Glu Leu Thr Pro Ala Glu Thr Thr Val Arg Leu Arg
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Phe Trp Glu Ser Val Phe Thr Gly Leu Thr His Ile Asp Ala His Phe
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Leu Ser Gln Thr Lys Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala
 545 550 555 560

Tyr Gln Ala Thr Val Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp
 565 570 575

Asp Gln Met Trp Lys Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly
 580 585 590

Pro Thr Pro Leu Leu Tyr Arg Leu Gly Ala Val Gln Asn Glu Ile Thr
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Leu Thr His Pro Ile Thr Lys Phe Val Met Ala Cys Met Ser Ala Asp
 610 615 620

Leu Glu Val Val Thr
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<220>
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 <223> Nucleic acid encoding the Protein N (A.N. D00736, REGION:
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cgtcaagata taaatggaaa ggaaatgaaa ttcgaagtat taacattatc aagcttgaca 360
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gcagtaatta ggagggcaaa caatgtctta aaaaacgaaa taaaacgcta caagggcctc 600
ataccaaagg atatagctaa cagttttttat gaagtgtttg aaaaacaccc tcatcttata 660
gatgtttttg tgcactttgg cattgcacaa tcatccacaa gagggggtag tagagttgaa 720
ggaatctttg caggattatt tatgaatgcc tatggttcag ggcaagtaat gctaagatgg 780
ggagttctag ccaaactctgt aaaaaatatac atgctaggac atgctagtgt ccaggcagaa 840
atggaacaag ttgtggaagt ttatgagtat gcacagaagt tgggaggaga agctggattc 900
taccatatac tgaacaatcc aaaagcatca ttgctgtcat taactcaatt tcctaacttc 960
tcaagtgtgg tcctaggcaa tgcagcaggt ctaggcataa tgggagagta tagaggtaca 1020
ccaagaaacc aagatctata tgatgcggcc aaagcatatg cagagcaact caaagaaaat 1080
ggagtaataa actacagtgt attagactta acagcagaag aattggaagc cataaagcat 1140
caactcaacc ccaaagaaga tgatgtagag ctttaa 1176

```

```

<210> 54
<211> 391
<212> PRT
<213> Respiratory syncytial virus

```

```

<220>
<221> misc_feature
<223> Protein N (A.N. D00736, REGION: 1085..2260)

```

```
<400> 54
```

```

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

```

```

Leu Leu Ser Ser Ser Lys Tyr Thr Ile Gln Arg Ser Thr Gly Asp Asn
20           25           30

```

```

Ile Asp Thr Pro Asn Tyr Asp Val Gln Lys His Leu Asn Lys Leu Cys
35           40           45

```

```
Gly Met Leu Leu Ile Thr Glu Asp Ala Asn His Lys Phe Thr Gly Leu
```

50

55

60

Ile Gly Met Leu Tyr Ala Met Ser Arg Leu Gly Arg Glu Asp Thr Ile
65 70 75 80

Lys Ile Leu Lys Asp Ala Gly Tyr His Val Lys Ala Asn Gly Val Asp
85 90 95

Ile Thr Thr Tyr Arg Gln Asp Ile Asn Gly Lys Glu Met Lys Phe Glu
100 105 110

Val Leu Thr Leu Ser Ser Leu Thr Ser Glu Ile Gln Val Asn Ile Glu
115 120 125

Ile Glu Ser Arg Lys Ser Tyr Lys Lys Leu Leu Lys Glu Met Gly Glu
130 135 140

Val Ala Pro Glu Tyr Arg His Asp Ser Pro Asp Cys Gly Met Ile Ile
145 150 155 160

Leu Cys Ile Ala Ala Leu Val Ile Thr Lys Leu Ala Ala Gly Asp Arg
165 170 175

Ser Gly Leu Thr Ala Val Ile Arg Arg Ala Asn Asn Val Leu Lys Asn
180 185 190

Glu Ile Lys Arg Tyr Lys Gly Leu Ile Pro Lys Asp Ile Ala Asn Ser
195 200 205

Phe Tyr Glu Val Phe Glu Lys His Pro His Leu Ile Asp Val Phe Val
210 215 220

His Phe Gly Ile Ala Gln Ser Ser Thr Arg Gly Gly Ser Arg Val Glu
225 230 235 240

Gly Ile Phe Ala Gly Leu Phe Met Asn Ala Tyr Gly Ser Gly Gln Val
245 250 255

Met Leu Arg Trp Gly Val Leu Ala Lys Ser Val Lys Asn Ile Met Leu
260 265 270

Gly His Ala Ser Val Gln Ala Glu Met Glu Gln Val Val Glu Val Tyr
275 280 285

Glu Tyr Ala Gln Lys Leu Gly Gly Glu Ala Gly Phe Tyr His Ile Leu
290 295 300

Asn Asn Pro Lys Ala Ser Leu Leu Ser Leu Thr Gln Phe Pro Asn Phe
305 310 315 320

Ser Ser Val Val Leu Gly Asn Ala Ala Gly Leu Gly Ile Met Gly Glu
325 330 335

Tyr Arg Gly Thr Pro Arg Asn Gln Asp Leu Tyr Asp Ala Ala Lys Ala
340 345 350

Tyr Ala Glu Gln Leu Lys Glu Asn Gly Val Ile Asn Tyr Ser Val Leu
355 360 365

Asp Leu Thr Ala Glu Glu Leu Glu Ala Ile Lys His Gln Leu Asn Pro
370 375 380

Lys Glu Asp Asp Val Glu Leu
385 390

<210> 55
<211> 1350
<212> DNA
<213> Influenza virus A

<220>
<221> misc_feature
<223> Nucleic acid encoding for Neuraminidase (A.N. AAT72506; VERSION
AAT72506.1 ; GI:50261907; Accession AY646425.1)

<400> 55
atgaatccaa atcagaagat aataaccatc ggatcaatct gtatggtaat tggaatagtt 60
agcttgatgt taaaaattgg gaacataatc tcaatatggg ccagtcattc aattcagaca 120
gggaatcaac accaagctga accaatcagc aataccaatt ttcttgctga gaaagctgtg 180
gcttcagtaa cattagcggg caattcatct ctttgcccca ttagcggatg ggctgtacac 240
agtaaggaca acggtataag gatcgggtcc aagggggatg tgtttgttat aagagagccg 300
ttcatctcat gctcccactt ggaatgcaga actttctttt tgactcaggg agccttgctg 360
aatgacaagc actccaatgg gaccgtcaaa gacagaagcc ctacagagc attgatgagt 420
tgtcctgtgg gtgaggctcc ctccccatat aactcaaggt ttgagtctgt tgcttggtcg 480
gcaagtgctt gccatgatgg caccagttgg ttgacaattg gaatttctgg ccagacaat 540
ggggctgtgg ctgtattgaa atacaacggc ataataacag acactatcaa gagttggagg 600
aacaacatac tgagaactca agagtctgaa tgtgcatgtg taaatggctc ttgctttact 660
gtaatgactg acggaccaag taatgggcag gcctcatata agatcttcaa aatggaaaaa 720

```

gggaaagtag ttaaatacgt cgaattggat gccctaatt atcactatga ggagtgtcc      780
tggtatcctg atgctggcga aatcacatgt gtgtgcaggg ataattggca tggctcaa      840
cggccatggg tatctttcaa tcaaaatttg gagtatcaaa taggatatat atgcagtgg      900
gttttcggag acaatccacg cccaatgat ggaacaggca gttgtggtcc ggtgtccct      960
aacggggcat atggggtaaa agggttttca tttaaatacg gcaatggtgt ttggatcggg    1020
agaacaaaa gcattaattc caggagcggc ttgaaatga tttgggatcc aaatgggtgg      1080
actggaacgg acagtagctt ctcggtgaaa caagatatcg tagcgataac tgattggtca      1140
ggatatagcg ggagttttgt ccagcatcca gaactgacag gattagattg cataagacct      1200
tgtttctggg ttgagctaata cagagggcgg ccaaagaga gcacaatttg gactagtga      1260
agcagcatat cttttgtgg tgtaaatagt gacactgtgg gttggtcttg gccagacgg      1320
gctgagttgc cattcaccat tgacaagtag                                     1350

```

```

<210> 56
<211> 449
<212> PRT
<213> Influenza virus A

```

```

<220>
<221> misc_feature
<223> Neuraminidase (A.N. AAT72506; VERSION AAT72506.1; GI:50261907;
Accession AY646425.1)

```

```
<400> 56
```

```

Met Asn Pro Asn Gln Lys Ile Ile Thr Ile Gly Ser Ile Cys Met Val
1           5           10           15

```

```

Ile Gly Ile Val Ser Leu Met Leu Gln Ile Gly Asn Ile Ile Ser Ile
          20           25           30

```

```

Trp Ala Ser His Ser Ile Gln Thr Gly Asn Gln His Gln Ala Glu Pro
          35           40           45

```

```

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

```

```

Leu Ala Gly Asn Ser Ser Leu Cys Pro Ile Ser Gly Trp Ala Val His
65           70           75           80

```

```

Ser Lys Asp Asn Gly Ile Arg Ile Gly Ser Lys Gly Asp Val Phe Val
          85           90           95

```

Ile Arg Glu Pro Phe Ile Ser Cys Ser His Leu Glu Cys Arg Thr Phe
100 105 110

Phe Leu Thr Gln Gly Ala Leu Leu Asn Asp Lys His Ser Asn Gly Thr
115 120 125

Val Lys Asp Arg Ser Pro His Arg Ala Leu Met Ser Cys Pro Val Gly
130 135 140

Glu Ala Pro Ser Pro Tyr Asn Ser Arg Phe Glu Ser Val Ala Trp Ser
145 150 155 160

Ala Ser Ala Cys His Asp Gly Thr Ser Trp Leu Thr Ile Gly Ile Ser
165 170 175

Gly Pro Asp Asn Gly Ala Val Ala Val Leu Lys Tyr Asn Gly Ile Ile
180 185 190

Thr Asp Thr Ile Lys Ser Trp Arg Asn Asn Ile Leu Arg Thr Gln Glu
195 200 205

Ser Glu Cys Ala Cys Val Asn Gly Ser Cys Phe Thr Val Met Thr Asp
210 215 220

Gly Pro Ser Asn Gly Gln Ala Ser Tyr Lys Ile Phe Lys Met Glu Lys
225 230 235 240

Gly Lys Val Val Lys Ser Val Glu Leu Asp Ala Pro Asn Tyr His Tyr
245 250 255

Glu Glu Cys Ser Cys Tyr Pro Asp Ala Gly Glu Ile Thr Cys Val Cys
260 265 270

Arg Asp Asn Trp His Gly Ser Asn Arg Pro Trp Val Ser Phe Asn Gln
275 280 285

Asn Leu Glu Tyr Gln Ile Gly Tyr Ile Cys Ser Gly Val Phe Gly Asp
290 295 300

Asn Pro Arg Pro Asn Asp Gly Thr Gly Ser Cys Gly Pro Val Ser Pro
305 310 315 320

Asn Gly Ala Tyr Gly Val Lys Gly Phe Ser Phe Lys Tyr Gly Asn Gly
325 330 335

Val Trp Ile Gly Arg Thr Lys Ser Ile Asn Ser Arg Ser Gly Phe Glu

340

345

350

Met Ile Trp Asp Pro Asn Gly Trp Thr Gly Thr Asp Ser Ser Phe Ser
 355 360 365

Val Lys Gln Asp Ile Val Ala Ile Thr Asp Trp Ser Gly Tyr Ser Gly
 370 375 380

Ser Phe Val Gln His Pro Glu Leu Thr Gly Leu Asp Cys Ile Arg Pro
 385 390 395 400

Cys Phe Trp Val Glu Leu Ile Arg Gly Arg Pro Lys Glu Ser Thr Ile
 405 410 415

Trp Thr Ser Gly Ser Ser Ile Ser Phe Cys Gly Val Asn Ser Asp Thr
 420 425 430

Val Gly Trp Ser Trp Pro Asp Gly Ala Glu Leu Pro Phe Thr Ile Asp
 435 440 445

Lys

<210> 57
 <211> 297
 <212> DNA
 <213> Human immunodeficiency virus 1

<220>
 <221> misc_feature
 <223> Nucleic acid encoding for HIV-1 Protease (A.N. CAA09614; VERSION
 CAA09614.1; GI:4375887; embl accession AJ011406.1)

<400> 57
 cctcasatca ctctttggca acgacccatc gtcacaataa agataggggg gcaactaaaa 60
 gaagctctat tagatacagg agcagatgat acagtattag aagacgtgga ttgcccagga 120
 agatggaaac caaaaatgat agtgggaatt ggaggttttg tcaaagtaag acagtatgaa 180
 gaggtacca tagaaatctg tggacataaa gttataggta cagtattaat aggacctaca 240
 cctgccaatg taattggaag aaatctgtta actcagcttg gctgcacttt aaatttt 297

<210> 58
 <211> 99
 <212> PRT
 <213> Human immunodeficiency virus 1

<220>

<221> misc_feature
<223> HIV-1 Protease (A.N. CAA09614; VERSION CAA09614.1; GI:4375887;
embl accession AJ011406.1)

<220>
<221> misc_feature
<222> (2)..(2)
<223> Xaa = non determined

<400> 58

Pro Xaa Ile Thr Leu Trp Gln Arg Pro Ile Val Thr Ile Lys Ile Gly
1 5 10 15

Gly Gln Leu Lys Glu Ala Leu Leu Asp Thr Gly Ala Asp Asp Thr Val
20 25 30

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

Gly Ile Gly Gly Phe Val Lys Val Arg Gln Tyr Glu Glu Val Pro Ile
50 55 60

Glu Ile Cys Gly His Lys Val Ile Gly Thr Val Leu Ile Gly Pro Thr
65 70 75 80

Pro Ala Asn Val Ile Gly Arg Asn Leu Leu Thr Gln Leu Gly Cys Thr
85 90 95

Leu Asn Phe

<210> 59
<211> 15
<212> PRT
<213> Artificial

<220>
<223> NS5B Peptide sensor N21C272

<400> 59

Asp Gly Cys Ala Arg Cys Val Ala Ser Val Gln Leu Tyr Gly Asp
1 5 10 15

<210> 60
<211> 15
<212> PRT
<213> Artificial

<220>
<223> NS3 Protease Peptide sensor V7-62

<400> 60

Trp Arg Pro Tyr Tyr Thr Val Leu Cys Ala Leu Ala Ser Trp His
1 5 10 15

<210> 61

<211> 15

<212> PRT

<213> Artificial

<220>

<223> NS3 full length peptide sensor H5-34

<400> 61

Pro Ser Asn His Arg Gln Ser Thr Arg Ser Thr Pro Trp Leu Trp
1 5 10 15

<210> 62

<211> 14

<212> PRT

<213> Artificial

<220>

<223> NS5B peptide sensor N21 I4

<400> 62

Tyr Cys Cys Pro Trp Asn Lys Leu Arg Leu Val Phe Gln Ser
1 5 10

<210> 63

<211> 15

<212> PRT

<213> Artificial

<220>

<223> NS5B peptide sensor T1E7

<400> 63

Thr His Leu Val Leu Cys Asp Ala Arg Thr Cys Leu Asn Tyr Val
1 5 10 15

<210> 64

<211> 15

<212> PRT

<213> Artificial

<220>

<223> NS3 full length peptide sensor VF9A11

<400> 64

Gly Thr Gln Lys Glu Ala Val Ile Tyr Pro Cys Tyr Val Pro Trp
1 5 10 15

<210> 65
<211> 8
<212> PRT
<213> Artificial

<220>
<223> NS3 full length peptide sensor VFII-N4

<400> 65

Val Asn Ala Trp Ala Trp Gly Trp
1 5

<210> 66
<211> 15
<212> PRT
<213> Artificial

<220>
<223> NS3 full length peptide sensor VFII-N13

<400> 66

Thr Leu Pro Ile Gly Thr Lys Ala Asp Phe Leu Trp Leu Pro Phe
1 5 10 15

<210> 67
<211> 15
<212> PRT
<213> Artificial

<220>
<223> NS3 full length peptide sensor T4C11

<400> 67

Leu Leu Gly Pro Tyr Pro Asn Leu Thr Thr Leu Cys Pro Pro Trp
1 5 10 15

<210> 68
<211> 15
<212> PRT
<213> Artificial

<220>
<223> NS3 full length peptide sensor T3G5

<400> 68

Leu Leu His Leu Leu Ala His His Leu Arg His Ile Ala Arg Ala
1 5 10 15