

eol f - ot hd- 000001. t xt
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<110> Gl axoSmi thKl i ne Bi ol ogi cal s S. A.

<120> Vacci nes for Mal ari a

<130> VB62777

<150> US61/ 016522

<151> 2007- 12- 24

<150> US61/ 016525

<151> 2007- 12- 24

<160> 11

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<210> 1

<211> 771

<212> DNA

<213> Arti f i ci al Sequence

<220>

<223> Pv- CS nucl eoti de sequence

<400> 1

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aaaaaagcgg aaccaaaaaa tccaagggaa aat aaat t aa aacagcccgg ggat cgcgcg      240
gat ggt caag cggcgggt aa tggggcgggg ggt caaccag cgggggat cg cgcggt ggt      300
cagccagcgg gggat cgcg ggct ggt cag ccagcggggg at ggt gcggc t ggccaacca      360
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aacgcggg cg gtaat gcgg cgccaaggt cagaacaacg aaggggct aa tgcaccaaac      600
gaaaaat ct g tcaaagaat a tctcgat aaa gt ccgcgt a cagt agggac agaat ggacg      660
ccat gct ct g taacat gt gg tgt cggggt a cgcgt gcgcc gccgt gt caa tgcggct aac      720
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<210> 2

<211> 257

<212> PRT

<213> Arti f i ci al Sequence

<220>

<223> Ami no aci d sequence of Pv- CS pr otei n

<400> 2

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Gly Val Asn Phe Asn Asn Val Asp Ala Ser Ser Leu Gly Ala Ala His

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Val Gly Gln Ser Ala Ser Arg Gly Arg Gly Leu Gly Glu Asn Pro Asp
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 Pro Lys Asn Pro Arg Glu Asn Lys Leu Lys Gln Pro Gly Asp Arg Ala
 65 70 75 80
 Asp Gly Gln Ala Ala Gly Asn Gly Ala Gly Gly Gln Pro Ala Gly Asp
 85 90 95
 Arg Ala Ala Gly Gln Pro Ala Gly Asp Arg Ala Ala Gly Gln Pro Ala
 100 105 110
 Gly Asp Gly Ala Ala Gly Gln Pro Ala Gly Asp Arg Ala Asp Gly Gln
 115 120 125
 Pro Ala Gly Asp Arg Ala Asp Gly Gln Pro Ala Gly Asp Arg Ala Ala
 130 135 140
 Gly Gln Ala Ala Gly Asn Gly Ala Gly Gly Gln Ala Ala Ala Asn Gly
 145 150 155 160
 Ala Gly Asn Gln Pro Gly Gly Gly Asn Ala Ala Asn Lys Lys Ala Glu
 165 170 175
 Asp Ala Gly Gly Asn Ala Gly Gly Asn Ala Gly Gly Gln Gly Gln Asn
 180 185 190
 Asn Glu Gly Ala Asn Ala Pro Asn Glu Lys Ser Val Lys Glu Tyr Leu
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 Asp Lys Val Arg Ala Thr Val Gly Thr Glu Trp Thr Pro Cys Ser Val
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<210> 3
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 <212> DNA
 <213> Artificial Sequence

<220>

<223> CSV hybrid gene

<400> 3

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cagcctgctg gt gat agagc t gct ggacaa cct gct ggag acggt gccgc cggt caacct 360
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gct ggt aacc aaccaggt gg t ggt aacgct gccacaaga aagct gaaga cgct ggt ggt 540
aat gct ggag gt aat gcagg t ggt cagggt caaaacaacg aaggt gct aa cgct ccaaac 600
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ccat gtt ct g t t act t gt gg t gt cggt gtt agagt t agaa gaagagt t aa cgccgct aac 720
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<211> 1485

<212> DNA

<213> Artificial Sequence

<220>

<223> CSV- S fusion nucleotide sequence

<400> 4

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aagaagaagg acggt aagaa ggccgaacca aagaaccaa gagaaaacaa gt t gaaacaa 240
ccaggt gaca gagccgacgg acaagcagct ggt aat ggt g ct ggaggt ca accagct ggt 300
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gccgccggt c aacct gct gg t gat agagca gacggacaac cagct ggt ga ccgt gct gac 420
ggacagccag ccggcgat ag ggct gcaggt caagccgct g gt aacggt gc cggt ggt caa 480
gct gct gct a acggt gct gg t aaccaacca ggt ggt ggt a acgct gccaa caagaaagct 540
gaagacgct g gt ggt aat gc t ggaggt aat gcaggt ggt c aggggt caaaa caacgaaggt 600
gct aacgct c caaacgaaa gt ct gt t aag gaat act t ag at aaggt t ag agct act gt c 660
ggg act gaat ggact ccat g t t ct gt t act t gt ggt gt cg gt gt t agagt t agaagaaga 720
gt t aacgccg ct aacaagaa gccagaagac t t gact ct aa acgact t gga aact gacgt t 780
t gt act cccg ggcct gt gac gaacat ggag aacat cacat caggat t cct aggaccct g 840
ct cgt gt t ac aggcgggggt t t t t ct t gt t g acaagaat cc t cacaat acc gcagagt ct a 900

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 tcagctatat ggatgatgtg gtattggggg ccaagtctgt acagcatcgt gaggcccttt 1440
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<210> 5
 <211> 494
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence for hybrid fusion protein CSV-S
 <400> 5

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Leu Gly Ala Ala His Val Gly Gln Ser Ala Ser Arg Gly Arg Gly Leu
 35 40 45

Gly Gu Asn Pro Asp Asp Gu Gu Gly Asp Ala Lys Lys Lys Lys Asp
 50 55 60

Gly Lys Lys Ala Gu Pro Lys Asn Pro Arg Gu Asn Lys Leu Lys Gln
 65 70 75 80

Pro Gly Asp Arg Ala Asp Gly Gln Ala Ala Gly Asn Gly Ala Gly Gly
 85 90 95

Gln Pro Ala Gly Asp Arg Ala Ala Gly Gln Pro Ala Gly Asp Arg Ala
 100 105 110

Ala Gly Gln Pro Ala Gly Asp Gly Ala Ala Gly Gln Pro Ala Gly Asp
 115 120 125

Arg Ala Asp Gly Gln Pro Ala Gly Asp Arg Ala Asp Gly Gln Pro Ala
 130 135 140

Gly Asp Arg Ala Ala Gly Gln Ala Ala Gly Asn Gly Ala Gly Gly Gln
 145 150 155 160

Al a Al a Al a Asn Gly Al a Gly Asn Gn Pro Gly Gly Gly Asn Al a Al a
 165 170 175
 Asn Lys Lys Al a Gu Asp Al a Gly Gly Asn Al a Gly Gly Asn Al a Gly
 180 185 190
 Gly Gn Gly Gn Asn Asn Gu Gly Al a Asn Al a Pro Asn Gu Lys Ser
 195 200 205
 Val Lys Gu Tyr Leu Asp Lys Val Arg Al a Thr Val Gly Thr Gu Trp
 210 215 220
 Thr Pro Cys Ser Val Thr Cys Gly Val Gly Val Arg Val Arg Arg Arg
 225 230 235 240
 Val Asn Al a Al a Asn Lys Lys Pro Gu Asp Leu Thr Leu Asn Asp Leu
 245 250 255
 Gu Thr Asp Val Cys Thr Pro Gly Pro Val Thr Asn Met Gu Asn Ile
 260 265 270
 Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gn Al a Gly Phe Phe
 275 280 285
 Leu Leu Thr Arg Ile Leu Thr Ile Pro Gn Ser Leu Asp Ser Trp Trp
 290 295 300
 Thr Ser Leu Asn Phe Leu Gly Gly Ser Pro Val Cys Leu Gly Gn Asn
 305 310 315 320
 Ser Gn Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile
 325 330 335
 Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu
 340 345 350
 Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr
 355 360 365
 Gn Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly Ser Thr Thr Thr
 370 375 380
 Asn Thr Gly Pro Cys Lys Thr Cys Thr Thr Pro Al a Gn Gly Asn Ser
 385 390 395 400
 Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Thr Asp Gly Asn Cys Thr
 405 410 415
 Cys Ile Pro Ile Pro Ser Ser Trp Al a Phe Al a Lys Tyr Leu Trp Gu
 420 425 430

Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val
435 440 445

Gln Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu Ser Ala Ile Trp
450 455 460

Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Ser Ile Val Ser Pro Phe
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Ile Pro Leu Leu Pro Ile Phe Phe Oys Leu Trp Val Tyr Ile
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<210> 6
<211> 3509
<212> DNA
<213> Artificial Sequence

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acttgatgca aattcccaa gctaataca t gcaagacac gtacggc caa gaagacat at 180
ttgacctctt aactggttca gacgcgactg cctcatcagt aagaccctt gaaaagaact 240
tacctgaaaa aaacgaat at atactagcgt tgaatgttag cgtcaacaac aagaagttta 300
atgacgcgga ggccaaggca aaaagattcc ttgattacgt aaggggagtta gaatcatttt 360
gaataaaaaa cacgcttttt cagttcgagt ttatcattat caatactgcc atttcaaaga 420
atcgtaat aattaatagt agtgattttc ctactttat ttagtcaaaa attagccttt 480
taattctgct gtaaccctga catgccaaa atagggggcg ggttacacag aat at aac 540
atcgtagggtg tctgggtgaa cagtttatcc ctggcatcca cttaat at aa tggagctcgc 600
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aaccatcagt tcataggctc attctcttag cgcaactaca gagaacaggg gcacaaacag 720
gcaaaaaacg ggcacaacct caatggagt g atgcaacctg cctggagt aa atgatgacac 780
aaggcaattg acccagcat gtatctatct cattttctta caccttctat tacttctgc 840
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tccaaatgca aacccaat g caaacccaaa t gcaaacc caatgcaaat c ct aat aaaaa 1320

eol f - ot hd- 000001. t xt

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aaat gct aat gccacaat g ct gt aaaaaa t aat aat aac gaagaacca gt gat aagca	1440
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gagt gt gt t t aat gt cgt aa at agt cgacc t gt gacgaac at ggagaaca t cacat cagg	1680
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cgaat t ccaa gct gaaacaa t t caaagggt t t t caaat caa t caagaact t gt ct ct gt gg	2400
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<210> 7
<211> 427
<212> PRT
<213> Artificial Sequence

<220>
<223> Predicted translation product of the RTS-HBsAg hybrid protein
<400> 7

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Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala
35 40 45

Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala
50 55 60

Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala
65 70 75 80

Asn Pro Asn Lys Asn Asn Gln Gly Asn Gly Gln Gly His Asn Met Pro
85 90 95

Asn Asp Pro Asn Asp Pro Asn Arg Asn Val Asp Glu Asn Ala Asn Ala
100 105 110

Asn Asn Ala Val Lys Asn Asn Asn Asn Glu Glu Pro Ser Asp Lys His
115 120 125

Ile Glu Gln Tyr Leu Lys Lys Ile Lys Asn Ser Ile Ser Thr Glu Trp
130 135 140

Ser Pro Cys Ser Val Thr Cys Gly Asn Gly Ile Gln Val Arg Ile Lys
145 150 155 160

Pro Gly Ser Ala Asn Lys Pro Lys Asp Glu Leu Asp Tyr Glu Asn Asp
165 170 175

Ile Glu Lys Lys Ile Cys Lys Met Glu Lys Cys Ser Ser Val Phe Asn
180 185 190

Val Val Asn Ser Arg Pro Val Thr Asn Met Glu Asn Ile Thr Ser Gly
195 200 205

Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr
210 215 220

Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu
225 230 235 240

Asn Phe Leu Gly Gly Ser Pro Val Cys Leu Gly Gln Asn Ser Gln Ser
245 250 255

Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly
260 265 270

Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu
275 280 285

Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met
290 295 300

Leu Pro Val Cys Pro Leu Ile Pro Gly Ser Thr Thr Thr Asn Thr Gly
305 310 315 320

Pro Cys Lys Thr Cys Thr Thr Pro Ala Gln Gly Asn Ser Met Phe Pro
325 330 335

Ser Cys Cys Cys Thr Lys Pro Thr Asp Gly Asn Cys Thr Cys Ile Pro
340 345 350

Ile Pro Ser Ser Trp Ala Phe Ala Lys Tyr Leu Trp Glu Trp Ala Ser
355 360 365

Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe
370 375 380

Val Gly Leu Ser Pro Thr Val Trp Leu Ser Ala Ile Trp Met Met Trp
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405 410 415

Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile
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<210> 8
<211> 1485
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide sequence CSV-S fusion gene (cloned into pHL-D2 integrative Pichia pastoris expression vector)

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aacggtgtta atttcaacaa cgtcgatgct tcttcttttag gtgccgctca tgttggtcaa 120
Page 9

eol f - ot hd- 000001. t xt

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gacagagct g ccggt cagcc t gct ggt gat agagct gct g gacaacct gc t ggagacggt      360
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ggt act gaat ggact ccat g t t ct gt t act t gt ggt gt cg gt gt t agagt t agaagaaga      720
gt t aacgccg ct aacaagaa gccagaagac t t gact ct aa acgact t gga aact gacgt t      780
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ct cgt gt t ac aggcgggggt t t t t ct t gt t g acaagaat cc t cacaat acc gcagagt ct a      900
gact cgt ggt ggact t ct ct caat t t t ct a gggggat cac ccgt gt gt ct t ggccaaaat      960
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<210> 9

<211> 494

<212> PRT

<213> Artificial Sequence

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<223> Amino-Acid sequence CSV-S fusion protein expressed in Pichia pastoris

<400> 9

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20 25 30

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 P r o G l y A s p A r g A l a A s p G l y G l n A l a A l a G l y A s n G l y A l a G l y G l y
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 G l n P r o A l a G l y A s p A r g A l a A l a G l y G l n P r o A l a G l y A s p A r g A l a
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 A l a G l y G l n P r o A l a G l y A s p G l y A l a A l a G l y G l n P r o A l a G l y A s p
 115 120 125
 A r g A l a A s p G l y G l n P r o A l a G l y A s p A r g A l a A s p G l y G l n P r o A l a
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 G l y A s p A r g A l a A l a G l y G l n A l a A l a G l y A s n G l y A l a G l y G l y G l n
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 A l a A l a A l a A s n G l y A l a G l y A s n G l n P r o G l y G l y G l y A s n A l a A l a
 165 170 175
 A s n L y s L y s A l a G l u A s p A l a G l y G l y A s n A l a G l y G l y A s n A l a G l y
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 G l y G l n G l y G l n A s n A s n G l u G l y A l a A s n A l a P r o A s n G l u L y s S e r
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 V a l L y s G l u T y r L e u A s p L y s V a l A r g A l a T h r V a l G l y T h r G l u T r p
 210 215 220
 T h r P r o C y s S e r V a l T h r C y s G l y V a l G l y V a l A r g V a l A r g A r g A r g
 225 230 235 240
 V a l A s n A l a A l a A s n L y s L y s P r o G l u A s p L e u T h r L e u A s n A s p L e u
 245 250 255
 G l u T h r A s p V a l C y s T h r P r o G l y P r o V a l T h r A s n M e t G l u A s n I l e
 260 265 270
 T h r S e r G l y P h e L e u G l y P r o L e u L e u V a l L e u G l n A l a G l y P h e P h e
 275 280 285
 L e u L e u T h r A r g I l e L e u T h r I l e P r o G l n S e r L e u A s p S e r T r p T r p
 290 295 300
 T h r S e r L e u A s n P h e L e u G l y G l y S e r P r o V a l C y s L e u G l y G l n A s n
 305 310 315 320

Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile
325 330 335

Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu
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Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr
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Gln Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly Ser Thr Thr Thr
370 375 380

Asn Thr Gly Pro Cys Lys Thr Cys Thr Thr Pro Ala Gln Gly Asn Ser
385 390 395 400

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

Leu Gly Glu Asn Ser Glu Ser Pro Thr Ser Asn His Ser Pro Thr Ser
 50 55 60

Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe
 65 70 75 80

Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val
 85 90 95

Leu Leu Asp Tyr Glu Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly
 100 105 110

Ser Thr Thr Thr Asn Thr Gly Pro Cys Lys Thr Cys Thr Thr Pro Ala
 115 120 125

Glu Gly Asn Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Thr Asp
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Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Lys
 145 150 155 160

Tyr Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu
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Val Pro Phe Val Glu Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu
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195 200 205

Val Ser Pro Phe Ile Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val
210 215 220

Tyr Ile
225