

# SEQUENCE LISTING

5 <110> MERCK SERONO S.A.  
 HELMAN, DANIEL  
 BAR-SHIMON, MEIRAV  
 TOISTER-ACHITUV, MIRA  
  
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 <151> 2011-12-27  
  
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 Gly Gln Asp Gly Ser Tyr Leu Ala Glu Phe Leu Leu Glu Lys Gly Tyr  
 25 35 40 45  
  
 Glu Val His Gly Ile Val Arg Arg Ser Ser Ser Phe Asn Thr Gly Arg  
 50 55 60  
  
 Ile Glu His Leu Tyr Lys Asn Pro Gln Ala His Ile Glu Gly Asn Met  
 30 65 70 75 80  
  
 Lys Leu His Tyr Gly Asp Leu Thr Asp Ser Thr Cys Leu Val Lys Ile  
 35 85 90 95  
  
 Ile Asn Glu Val Lys Pro Thr Glu Ile Tyr Asn Leu Gly Ala Gln Ser  
 40 100 105 110  
  
 His Val Lys Ile Ser Phe Asp Leu Ala Glu Tyr Thr Ala Asp Val Asp  
 115 120 125  
  
 Gly Val Gly Thr Leu Arg Leu Leu Asp Ala Ile Lys Thr Cys Gly Leu  
 45 130 135 140  
  
 Ile Asn Ser Val Lys Phe Tyr Gln Ala Ser Thr Ser Glu Leu Tyr Gly  
 50 145 150 155 160  
  
 Lys Val Gln Glu Ile Pro Gln Lys Glu Thr Thr Pro Phe Tyr Pro Arg  
 55 165 170 175  
  
 Ser Pro Tyr Gly Ala Ala Lys Leu Tyr Ala Tyr Trp Ile Val Val Asn  
 180 185 190  
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Phe Arg Glu Ala Tyr Asn Leu Phe Ala Val Asn Gly Ile Leu Phe Asn  
 195 200 205

5 His Glu Ser Pro Arg Arg Gly Ala Asn Phe Val Thr Arg Lys Ile Ser  
 210 215 220

10 Arg Ser Val Ala Lys Ile Tyr Leu Gly Gln Leu Glu Cys Phe Ser Leu  
 225 230 235 240

15 Gly Asn Leu Asp Ala Lys Arg Asp Trp Gly His Ala Lys Asp Tyr Val  
 245 250 255

20 Glu Asp Phe Leu Gln Gly Asp Cys Ser Lys Ala Gln Gln Lys Leu Asn  
 260 265 270

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

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

60 Gly Thr Leu Arg Leu Leu Asp Ala Ile Lys Thr Cys Gly Leu Ile Asn  
 65 70 75 80

|    |                                                                 |     |     |     |
|----|-----------------------------------------------------------------|-----|-----|-----|
|    | Ser Val Lys Phe Tyr Gln Ala Ser Thr Ser Glu Leu Tyr Gly Lys Val | 85  | 90  | 95  |
| 5  | Gln Glu Ile Pro Gln Lys Glu Thr Thr Pro Phe Tyr Pro Arg Ser Pro | 100 | 105 | 110 |
| 10 | Tyr Gly Ala Ala Lys Leu Tyr Ala Tyr Trp Ile Val Val Asn Phe Arg | 115 | 120 | 125 |
| 15 | Glu Ala Tyr Asn Leu Phe Ala Val Asn Gly Ile Leu Phe Asn His Glu | 130 | 135 | 140 |
| 20 | Ser Pro Arg Arg Gly Ala Asn Phe Val Thr Arg Lys Ile Ser Arg Ser | 145 | 150 | 155 |
|    | Val Ala Lys Ile Tyr Leu Gly Gln Leu Glu Cys Phe Ser Leu Gly Asn | 165 | 170 | 175 |
| 25 | Leu Asp Ala Lys Arg Asp Trp Gly His Ala Lys Asp Tyr Val Glu Ala | 180 | 185 | 190 |
| 30 | Met Trp Leu Met Leu Gln Asn Asp Glu Pro Glu Asp Phe Val Ile Ala | 195 | 200 | 205 |
| 35 | Thr Gly Glu Val His Ser Val Arg Glu Phe Val Glu Lys Ser Phe Met | 210 | 215 | 220 |
| 40 | His Ile Gly Lys Thr Ile Val Trp Glu Gly Lys Asn Glu Asn Glu Val | 225 | 230 | 235 |
|    | Gly Arg Cys Lys Glu Thr Gly Lys Ile His Val Thr Val Asp Leu Lys | 245 | 250 | 255 |
| 45 | Tyr Tyr Arg Pro Thr Glu Val Asp Phe Leu Gln Gly Asp Cys Ser Lys | 260 | 265 | 270 |
| 50 | Ala Gln Gln Lys Leu Asn Trp Lys Pro Arg Val Ala Phe Asp Glu Leu | 275 | 280 | 285 |
| 55 | Val Arg Glu Met Val Gln Ala Asp Val Glu Leu Met Arg Thr Asn Pro | 290 | 295 | 300 |
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 Gly Gln Asp Gly Ser Tyr Leu Ala Glu Phe Leu Leu Glu Lys Gly Tyr  
 35 40 45  
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 Glu Val His Gly Ile Val Arg Arg Ser Ser Ser Phe Asn Thr Gly Arg  
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 30 Ile Glu His Leu Tyr Lys Asn Pro Gln Ala His Ile Glu Gly Asn Met  
 65 70 75 80  
 35 Lys Leu His Tyr Gly Asp Leu Thr Asp Ser Thr Cys Leu Val Lys Ile  
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 40 Ile Asn Glu Val Lys Pro Thr Glu Ile Tyr Asn Leu Gly Ala Gln Ser  
 100 105 110  
 His Val Lys Ile Ser Phe Asp Leu Ala Glu Tyr Thr Ala Asp Val Asp  
 115 120 125  
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 130 135 140  
 50 Ile Asn Ser Val Lys Phe Tyr Gln Ala Ser Thr Ser Glu Leu Tyr Gly  
 145 150 155 160  
 55 Lys Val Gln Glu Ile Pro Gln Lys Glu Thr Thr Pro Phe Tyr Pro Arg  
 165 170 175  
 Ser Pro Tyr Gly Ala Ala Lys Leu Tyr Ala Tyr Trp Ile Val Val Asn  
 180 185 190  
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Phe Arg Glu Ala Tyr Asn Leu Phe Ala Val Asn Gly Ile Leu Phe Asn  
 195 200 205

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His Glu Ser Pro Arg Arg Gly Ala Asn Phe Val Thr Arg Lys Ile Ser  
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Arg Ser Val Ala Lys Ile Tyr Leu Gly Gln Leu Glu Cys Phe Ser Leu  
 225 230 235 240

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Gly Asn Leu Asp Ala Lys Arg Asp Trp Gly His Ala Lys Asp Tyr Val  
 245 250 255

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Glu Ala Met Trp Leu Met Leu Gln Asn Asp Glu Pro Glu Asp Phe Val  
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Ile Ala Thr Gly Glu Val His Ser Val Arg Glu Phe Val Glu Lys Ser  
 275 280 285

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Phe Met His Ile Gly Lys Thr Ile Val Trp Glu Gly Lys Asn Glu Asn  
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Glu Val Gly Arg Cys Lys Glu Thr Gly Lys Ile His Val Thr Val Asp  
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Leu Lys Tyr Tyr Arg Pro Thr Glu Val Asp Phe Leu Gln Gly Asp Cys  
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Ser Lys Ala Gln Gln Lys Leu Asn Trp Lys Pro Arg Val Ala Phe Asp  
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Glu Leu Val Arg Glu Met Val Gln Ala Asp Val Glu Leu Met Arg Thr  
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Asn Pro Asn Ala  
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 aatacaggtc gaattgaaca tttatataag aatccacagg ctcatattga aggaaacatg  
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 aagttgcact atgggtgacct caccgacagc acctgcctag taaaaatcat caatgaagtc  
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 20 420  
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 25 540  
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 gcggtgaacg gcattctctt caatcatgag agtcctagaa gaggagctaa ttttgttact  
 30 660  
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 35 720  
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 780  
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 gaattcctgc tggagaaagg atacgagatt tcctttgact tagcagagta cactgcagat  
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 15 cagaaagaga ccaccccttt ctatccaagg tcgccctatg gagcagccaa actttatgcc  
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 aaatcattca tgcacattgg aaagaccatt gtgtgggaag gaaagaatga aaatgaagtg  
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 5 120  
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 aatacaggtc gaattgaaca tttatataag aatccacagg ctcatattga aggaaacatg  
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 aagttgcact atggtgacct caccgacagc acctgcctag taaaaatcat caatgaagtc  
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 15 360  
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 20 420  
 acttgtggcc ttataaatc tgtgaagttc taccaggcct caactagtga actgtatgga  
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Asn Asp His Pro Asp His Ser Ser Arg Glu Leu Ser Lys Ile Leu Ala  
35 40 45

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Lys Leu Glu Arg Leu Lys Gln Gln Asn Glu Asp Leu Arg Arg Met Ala  
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Glu Ser Leu Arg Ile Pro Glu Gly Pro Ile Asp Gln Gly Thr Ala Thr  
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Gly Arg Val Arg Val Leu Glu Glu Gln Leu Val Lys Ala Lys Glu Gln  
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Ile Glu Asn Tyr Lys Lys Gln Ala Arg Asn Asp Leu Gly Lys Asp His  
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Glu Ile Leu Arg Arg Arg Ile Glu Asn Gly Ala Lys Glu Leu Trp Phe  
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Phe Leu Gln Ser Glu Leu Lys Lys Leu Lys Lys Leu Glu Gly Asn Glu  
130 135 140

Leu Gln Arg His Ala Asp Glu Ile Leu Leu Asp Leu Gly His His Glu  
145 150 155 160

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Arg Ser Ile Met Thr Asp Leu Tyr Tyr Leu Ser Gln Thr Asp Gly Ala  
165 170 175

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Gly Glu Trp Arg Glu Lys Glu Ala Lys Asp Leu Thr Glu Leu Val Gln  
180 185 190

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Arg Arg Ile Thr Tyr Leu Gln Asn Pro Lys Asp Cys Ser Lys Ala Arg  
195 200 205

Lys Leu Val Cys Asn Ile Asn Lys Gly Cys Gly Tyr Gly Cys Gln Leu  
210 215 220

60

|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
|    | His | His | Val | Val | Tyr | Cys | Phe | Met | Ile | Ala | Tyr | Gly | Thr | Gln | Arg | Thr |  |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| 5  | Leu | Ile | Leu | Glu | Ser | Gln | Asn | Trp | Arg | Tyr | Ala | Thr | Gly | Gly | Trp | Glu |  |
|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| 10 | Thr | Val | Phe | Arg | Pro | Val | Ser | Glu | Thr | Cys | Thr | Asp | Arg | Ser | Gly | Leu |  |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |  |
| 15 | Ser | Thr | Gly | His | Trp | Ser | Gly | Glu | Val | Lys | Asp | Lys | Asn | Val | Gln | Val |  |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| 20 | Val | Glu | Leu | Pro | Ile | Val | Asp | Ser | Leu | His | Pro | Arg | Pro | Pro | Tyr | Leu |  |
|    |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |
| 25 | Pro | Leu | Ala | Val | Pro | Glu | Asp | Leu | Ala | Asp | Arg | Leu | Leu | Arg | Val | His |  |
|    | 305 |     |     |     |     | 310 |     |     |     | 315 |     |     |     |     | 320 |     |  |
| 30 | Gly | Asp | Pro | Ala | Val | Trp | Trp | Val | Ser | Gln | Phe | Val | Lys | Tyr | Leu | Ile |  |
|    |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |  |
| 35 | Arg | Pro | Gln | Pro | Trp | Leu | Glu | Arg | Glu | Ile | Glu | Glu | Thr | Thr | Lys | Lys |  |
|    |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |  |
| 40 | Leu | Gly | Phe | Lys | His | Pro | Val | Ile | Gly | Val | His | Val | Arg | Arg | Thr | Asp |  |
|    |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |  |
| 45 | Lys | Val | Gly | Thr | Glu | Ala | Ala | Phe | His | Pro | Ile | Glu | Glu | Tyr | Met | Val |  |
|    |     | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |  |
| 50 | His | Val | Glu | Glu | His | Phe | Gln | Leu | Leu | Glu | Arg | Arg | Met | Lys | Val | Asp |  |
|    | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |  |
| 55 | Lys | Lys | Arg | Val | Tyr | Leu | Ala | Thr | Asp | Asp | Pro | Ser | Leu | Leu | Lys | Glu |  |
|    |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     | 415 |     |  |
| 60 | Ala | Lys | Thr | Lys | Tyr | Ser | Asn | Tyr | Glu | Phe | Ile | Ser | Asp | Asn | Ser | Ile |  |
|    |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |  |
| 65 | Ser | Trp | Ser | Ala | Gly | Leu | His | Asn | Arg | Tyr | Thr | Glu | Asn | Ser | Leu | Arg |  |
|    |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |  |
| 70 | Gly | Val | Ile | Leu | Asp | Ile | His | Phe | Leu | Ser | Gln | Ala | Asp | Phe | Leu | Val |  |
|    |     | 450 |     |     |     |     | 455 |     |     |     |     | 460 |     |     |     |     |  |

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|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
|    | Val | Leu | His | Ser | Ala | Phe | Glu | Val | Gly | Thr | Arg | Lys | Val | Val | Ser | Cys |  |
|    |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |
| 5  | Leu | Ser | Thr | Cys | Ile | Phe | Pro | Asp | Lys | Thr | Thr | Tyr | Pro | Ile | Asp | Glu |  |
|    |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |
| 10 | Thr | Met | Ile | His | Asn | Gly | Pro | Pro | His | Ser | Ser | Asn | Phe | Gly | Tyr | Ser |  |
|    |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |
| 15 | Tyr | Ala | Lys | Arg | Met | Ile | Asp | Val | Gln | Asn | Arg | Ala | Tyr | Phe | Gln | Gln |  |
|    | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |
| 20 | His | Gly | Cys | Thr | Phe | Thr | Ala | Val | Ile | Pro | Thr | Asn | Val | Phe | Gly | Pro |  |
|    |     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |  |
| 25 | His | Asp | Asn | Phe | Asn | Ile | Glu | Asp | Gly | His | Val | Leu | Pro | Gly | Leu | Ile |  |
|    |     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |
| 30 | His | Lys | Val | His | Leu | Ala | Lys | Ser | Asn | Gly | Ser | Ala | Leu | Thr | Val | Trp |  |
|    |     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |
| 35 | Gly | Thr | Gly | Lys | Pro | Arg | Arg | Gln | Phe | Ile | Tyr | Ser | Leu | Asp | Leu | Ala |  |
|    |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |
| 40 | Arg | Leu | Phe | Ile | Trp | Val | Leu | Arg | Glu | Tyr | Asn | Glu | Val | Glu | Pro | Ile |  |
|    | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
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|    |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| 50 | Glu | Ala | Val | Val | Glu | Ala | Met | Asp | Phe | Cys | Gly | Glu | Val | Thr | Phe | Asp |  |
|    |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |  |
| 55 | Ser | Thr | Lys | Ser | Asp | Gly | Gln | Tyr | Lys | Lys | Thr | Ala | Ser | Asn | Gly | Lys |  |
|    |     |     | 275 |     |     |     |     | 280 |     |     |     |     |     | 285 |     |     |  |
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