

SEQUENCE LISTING

<110> Regeneron Pharmaceuticals, Inc
Heslin, David
Ally, Roxanne
Siao, Chia-Jen
Lai, Ka-Man Venus
Valenzuela, David M.
Guo, Chunguang
LaCroix-Fralish, Michael
Macdonald, Lynn
Sharma, Aarti
Kajimura, Daisuke
Droguett, Gustavo
Freundewey, David

<120> NON-HUMAN ANIMALS HAVING A HEXANUCLEOTIDE REPEAT EXPANSION IN A
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<151> 2016-09-30

<150> 62452795

<151> 2017-01-31

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<170> PatentIn version 3.5

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<213> Artificial Sequence

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<213> Artificial Sequence

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<223> 8026 insert nucleic acid without homology arms and after excision of neo

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 <212> DNA
 <213> Artificial Sequence

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<220>
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 without homology arms

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<210> 8
 <211> 3821
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> 8026 targeting nucleic acid with homology arms and neo cassette

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<210> 9

<211> 4387

<212> DNA

<213> Artificial Sequence

<220>

<223> 8026 insert nucleic acid with homology arms, hexanucleotide repeat(s) and neo cassette

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 <212> DNA
 <213> Homo sapiens

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<210> 11

<211> 222

<212> PRT

<213> Homo sapiens

<400> 11

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35 40 45

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

His Thr Leu Asn Gly Glu Ile Leu Arg Asn Ala Glu Ser Gly Ala Ile
65 70 75 80

Asp Val Lys Phe Phe Val Leu Ser Glu Lys Gly Val Ile Ile Val Ser
85 90 95

Leu Ile Phe Asp Gly Asn Trp Asn Gly Asp Arg Ser Thr Tyr Gly Leu
100 105 110

Ser Ile Ile Leu Pro Gln Thr Glu Leu Ser Phe Tyr Leu Pro Leu His
115 120 125

Arg Val Cys Val Asp Arg Leu Thr His Ile Ile Arg Lys Gly Arg Ile
130 135 140

Trp Met His Lys Glu Arg Gln Glu Asn Val Gln Lys Ile Ile Leu Glu
145 150 155 160

Gly Thr Glu Arg Met Glu Asp Gln Gly Gln Ser Ile Ile Pro Met Leu
165 170 175

Thr Gly Glu Val Ile Pro Val Met Glu Leu Leu Ser Ser Met Lys Ser
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His Ser Val Pro Glu Glu Ile Asp Ile Ala Asp Thr Val Leu Asn Asp
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<212> DNA
<213> Homo sapiens

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 <211> 481
 <212> PRT
 <213> Homo sapiens

<400> 13

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Ile	Ala	Leu	Ser	Gly	Lys	Ser	Pro	Leu	Leu	Ala	Ala	Thr	Phe	Ala	Tyr
			20				25						30		

Trp Asp Asn Ile Leu Gly Pro Arg Val Arg His Ile Trp Ala Pro Lys
35 40 45

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

His Thr Leu Asn Gly Glu Ile Leu Arg Asn Ala Glu Ser Gly Ala Ile
65 70 75 80

Asp Val Lys Phe Phe Val Leu Ser Glu Lys Gly Val Ile Ile Val Ser
85 90 95

Leu Ile Phe Asp Gly Asn Trp Asn Gly Asp Arg Ser Thr Tyr Gly Leu
100 105 110

Ser Ile Ile Leu Pro Gln Thr Glu Leu Ser Phe Tyr Leu Pro Leu His
115 120 125

Arg Val Cys Val Asp Arg Leu Thr His Ile Ile Arg Lys Gly Arg Ile
130 135 140

Trp Met His Lys Glu Arg Gln Glu Asn Val Gln Lys Ile Ile Leu Glu
145 150 155 160

Gly Thr Glu Arg Met Glu Asp Gln Gly Gln Ser Ile Ile Pro Met Leu
165 170 175

Thr Gly Glu Val Ile Pro Val Met Glu Leu Leu Ser Ser Met Lys Ser
180 185 190

His Ser Val Pro Glu Glu Ile Asp Ile Ala Asp Thr Val Leu Asn Asp
195 200 205

Asp Asp Ile Gly Asp Ser Cys His Glu Gly Phe Leu Leu Asn Ala Ile
210 215 220

Ser Ser His Leu Gln Thr Cys Gly Cys Ser Val Val Val Gly Ser Ser
225 230 235 240

Ala Glu Lys Val Asn Lys Ile Val Arg Thr Leu Cys Leu Phe Leu Thr
245 250 255

Pro Ala Glu Arg Lys Cys Ser Arg Leu Cys Glu Ala Glu Ser Ser Phe
260 265 270

Lys Tyr Glu Ser Gly Leu Phe Val Gln Gly Leu Leu Lys Asp Ser Thr
275 280 285

Gly Ser Phe Val Leu Pro Phe Arg Gln Val Met Tyr Ala Pro Tyr Pro
290 295 300

Thr Thr His Ile Asp Val Asp Val Asn Thr Val Lys Gln Met Pro Pro
305 310 315 320

Cys His Glu His Ile Tyr Asn Gln Arg Arg Tyr Met Arg Ser Glu Leu
325 330 335

Thr Ala Phe Trp Arg Ala Thr Ser Glu Glu Asp Met Ala Gln Asp Thr
340 345 350

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

Asp Val Leu His Arg Asp Thr Leu Val Lys Ala Phe Leu Asp Gln Val
370 375 380

Phe Gln Leu Lys Pro Gly Leu Ser Leu Arg Ser Thr Phe Leu Ala Gln
385 390 395 400

Phe Leu Leu Val Leu His Arg Lys Ala Leu Thr Leu Ile Lys Tyr Ile
405 410 415

Glu Asp Asp Thr Gln Lys Gly Lys Lys Pro Phe Lys Ser Leu Arg Asn
420 425 430

Leu Lys Ile Asp Leu Asp Leu Thr Ala Glu Gly Asp Leu Asn Ile Ile
 435 440 445

Met Ala Leu Ala Glu Lys Ile Lys Pro Gly Leu His Ser Phe Ile Phe
 450 455 460

Gly Arg Pro Phe Tyr Thr Ser Val Gln Glu Arg Asp Val Leu Met Thr
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Phe

<210> 14
 <211> 3356
 <212> DNA
 <213> Homo sapiens

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<210> 15
 <211> 481
 <212> PRT
 <213> Homo sapiens

<400> 15

Met	Ser	Thr	Leu	Cys	Pro	Pro	Pro	Ser	Pro	Ala	Val	Ala	Lys	Thr	Glu
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Ile	Ala	Leu	Ser	Gly	Lys	Ser	Pro	Leu	Leu	Ala	Ala	Thr	Phe	Ala	Tyr
		20					25						30		

Trp Asp Asn Ile Leu Gly Pro Arg Val Arg His Ile Trp Ala Pro Lys
35 40 45

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

His Thr Leu Asn Gly Glu Ile Leu Arg Asn Ala Glu Ser Gly Ala Ile
65 70 75 80

Asp Val Lys Phe Phe Val Leu Ser Glu Lys Gly Val Ile Ile Val Ser
85 90 95

Leu Ile Phe Asp Gly Asn Trp Asn Gly Asp Arg Ser Thr Tyr Gly Leu
100 105 110

Ser Ile Ile Leu Pro Gln Thr Glu Leu Ser Phe Tyr Leu Pro Leu His
115 120 125

Arg Val Cys Val Asp Arg Leu Thr His Ile Ile Arg Lys Gly Arg Ile
130 135 140

Trp Met His Lys Glu Arg Gln Glu Asn Val Gln Lys Ile Ile Leu Glu
145 150 155 160

Gly Thr Glu Arg Met Glu Asp Gln Gly Gln Ser Ile Ile Pro Met Leu
165 170 175

Thr Gly Glu Val Ile Pro Val Met Glu Leu Leu Ser Ser Met Lys Ser
180 185 190

His Ser Val Pro Glu Glu Ile Asp Ile Ala Asp Thr Val Leu Asn Asp
195 200 205

Asp Asp Ile Gly Asp Ser Cys His Glu Gly Phe Leu Leu Asn Ala Ile
210 215 220

Ser Ser His Leu Gln Thr Cys Gly Cys Ser Val Val Val Gly Ser Ser
225 230 235 240

Ala Glu Lys Val Asn Lys Ile Val Arg Thr Leu Cys Leu Phe Leu Thr
245 250 255

Pro Ala Glu Arg Lys Cys Ser Arg Leu Cys Glu Ala Glu Ser Ser Phe
260 265 270

Lys Tyr Glu Ser Gly Leu Phe Val Gln Gly Leu Leu Lys Asp Ser Thr
275 280 285

Gly Ser Phe Val Leu Pro Phe Arg Gln Val Met Tyr Ala Pro Tyr Pro
290 295 300

Thr Thr His Ile Asp Val Asp Val Asn Thr Val Lys Gln Met Pro Pro
305 310 315 320

Cys His Glu His Ile Tyr Asn Gln Arg Arg Tyr Met Arg Ser Glu Leu
325 330 335

Thr Ala Phe Trp Arg Ala Thr Ser Glu Glu Asp Met Ala Gln Asp Thr
340 345 350

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

Asp Val Leu His Arg Asp Thr Leu Val Lys Ala Phe Leu Asp Gln Val
370 375 380

Phe Gln Leu Lys Pro Gly Leu Ser Leu Arg Ser Thr Phe Leu Ala Gln
385 390 395 400

Phe Leu Leu Val Leu His Arg Lys Ala Leu Thr Leu Ile Lys Tyr Ile
405 410 415

Glu Asp Asp Thr Gln Lys Gly Lys Lys Pro Phe Lys Ser Leu Arg Asn
420 425 430

Leu Lys Ile Asp Leu Asp Leu Thr Ala Glu Gly Asp Leu Asn Ile Ile
 435 440 445

Met Ala Leu Ala Glu Lys Ile Lys Pro Gly Leu His Ser Phe Ile Phe
 450 455 460

Gly Arg Pro Phe Tyr Thr Ser Val Gln Glu Arg Asp Val Leu Met Thr
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Phe

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 <212> DNA
 <213> Mus musculus

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 <211> 481
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 <213> Mus musculus

<400> 17

Met	Ser	Thr	Ile	Cys	Pro	Pro	Pro	Ser	Pro	Ala	Val	Ala	Lys	Thr	Glu
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		20					25					30			

Trp	Asp	Asn	Ile	Leu	Gly	Pro	Arg	Val	Arg	His	Ile	Trp	Ala	Pro	Lys
		35					40				45				

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

His Thr Leu Asn Gly Glu Ile Leu Arg Asn Ala Glu Ser Gly Ala Ile
65 70 75 80

Asp Val Lys Phe Phe Val Leu Ser Glu Lys Gly Val Ile Ile Val Ser
85 90 95

Leu Ile Phe Asp Gly Asn Trp Asn Gly Asp Arg Ser Thr Tyr Gly Leu
100 105 110

Ser Ile Ile Leu Pro Gln Thr Glu Leu Ser Phe Tyr Leu Pro Leu His
115 120 125

Arg Val Cys Val Asp Arg Leu Thr His Ile Ile Arg Lys Gly Arg Ile
130 135 140

Trp Met His Lys Glu Arg Gln Glu Asn Val Gln Lys Ile Val Leu Glu
145 150 155 160

Gly Thr Glu Arg Met Glu Asp Gln Gly Gln Ser Ile Ile Pro Met Leu
165 170 175

Thr Gly Glu Val Ile Pro Val Met Glu Leu Leu Ala Ser Met Lys Ser
180 185 190

His Ser Val Pro Glu Asp Ile Asp Ile Ala Asp Thr Val Leu Asn Asp
195 200 205

Asp Asp Ile Gly Asp Ser Cys His Glu Gly Phe Leu Leu Asn Ala Ile
210 215 220

Ser Ser His Leu Gln Thr Cys Gly Cys Ser Val Val Val Gly Ser Ser
225 230 235 240

Ala Glu Lys Val Asn Lys Ile Val Arg Thr Leu Cys Leu Phe Leu Thr
245 250 255

Pro Ala Glu Arg Lys Cys Ser Arg Leu Cys Glu Ala Glu Ser Ser Phe
260 265 270

Lys Tyr Glu Ser Gly Leu Phe Val Gln Gly Leu Leu Lys Asp Ala Thr
275 280 285

Gly Ser Phe Val Leu Pro Phe Arg Gln Val Met Tyr Ala Pro Tyr Pro
290 295 300

Thr Thr His Ile Asp Val Asp Val Asn Thr Val Lys Gln Met Pro Pro
305 310 315 320

Cys His Glu His Ile Tyr Asn Gln Arg Arg Tyr Met Arg Ser Glu Leu
325 330 335

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340 345 350

Ile Ile Tyr Thr Asp Glu Ser Phe Thr Pro Asp Leu Asn Ile Phe Gln
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Asp Val Leu His Arg Asp Thr Leu Val Lys Ala Phe Leu Asp Gln Val
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Phe His Leu Lys Pro Gly Leu Ser Leu Arg Ser Thr Phe Leu Ala Gln
385 390 395 400

Phe Leu Leu Ile Leu His Arg Lys Ala Leu Thr Leu Ile Lys Tyr Ile
405 410 415

Glu Asp Asp Thr Gln Lys Gly Lys Lys Pro Phe Lys Ser Leu Arg Asn
420 425 430

Leu Lys Ile Asp Leu Asp Leu Thr Ala Glu Gly Asp Leu Asn Ile Ile
435 440 445

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 <213> Rattus norvegicus

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 <212> PRT
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<400> 19

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35 40 45

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

His Thr Leu Asn Gly Glu Ile Leu Arg Asn Ala Glu Ser Gly Ala Ile
65 70 75 80

Asp Val Lys Phe Phe Val Leu Ser Glu Lys Gly Val Ile Ile Val Ser
85 90 95

Leu Ile Phe Asp Gly Asn Trp Asn Gly Asp Arg Ser Thr Tyr Gly Leu
100 105 110

Ser Ile Ile Leu Pro Gln Thr Glu Leu Ser Phe Tyr Leu Pro Leu His
115 120 125

Arg Val Cys Val Asp Arg Leu Thr His Ile Ile Arg Lys Gly Arg Ile
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Trp Met His Lys Glu Arg Gln Glu Asn Val Gln Lys Ile Val Leu Glu
145 150 155 160

Gly Thr Glu Arg Met Glu Asp Gln Gly Gln Ser Ile Ile Pro Met Leu
165 170 175

Thr Gly Glu Val Ile Pro Val Met Glu Leu Leu Ala Ser Met Arg Ser
180 185 190

His Ser Val Pro Glu Asp Leu Asp Ile Ala Asp Thr Val Leu Asn Asp
195 200 205

Asp Asp Ile Gly Asp Ser Cys His Glu Gly Phe Leu Leu Asn Ala Ile
210 215 220

Ser Ser His Leu Gln Thr Cys Gly Cys Ser Val Val Val Gly Ser Ser
225 230 235 240

Ala Glu Lys Val Asn Lys Ile Val Arg Thr Leu Cys Leu Phe Leu Thr
245 250 255

Pro Ala Glu Arg Lys Cys Ser Arg Leu Cys Glu Ala Glu Ser Ser Phe
260 265 270

Lys Tyr Glu Ser Gly Leu Phe Val Gln Gly Leu Leu Lys Asp Ala Thr
275 280 285

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305 310 315 320

Cys His Glu His Ile Tyr Asn Gln Arg Arg Tyr Met Arg Ser Glu Leu
325 330 335

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340 345 350

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370 375 380

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385 390 395 400

Phe Leu Leu Ile Leu His Arg Lys Ala Leu Thr Leu Ile Lys Tyr Ile
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Glu Asp Asp Thr Gln Lys Gly Lys Lys Pro Phe Lys Ser Leu Arg Asn
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435 440 445

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Phe

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<212> DNA
<213> Mus musculus

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<212> DNA
<213> Artificial Sequence

<220>
<223> floxed neo cassette of 8026 plus lox sites

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<212> DNA
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<220>
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<212> DNA
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<211> 1052
<212> DNA
<213> Mus musculus

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ccagtgtatt ctactcttgt ccccggtata aatttgattg ttccgaacta cataaattgt	360
agaaggatth tttagatgca catatcattt tctgtgatac cttccacaca cccctcccc	420
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aagaggcgcg ggtagaagcg ggggctctcc tcagagctcg acgcattttt actttccctc	180
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ggggcggggc ctagcaagag caggtgtggg tttaggag 158

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<212> DNA
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cttgtctgaa aagggagtga ttattgtttc attaatcttt gatggaaact ggaatgggga	360
tcgcagcaca tatggactat caattatact tccacagaca gaacttagtt tctacctccc	420
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gcataag	487

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<400> 38

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<210> 43
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<223> Synthetic

<400> 62

ggagacagct cgggtactga 20

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<211> 82

<212> DNA

<213> Artificial Sequence

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aaaagtgga ccgagtcggt gc 82

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<400> 71
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<210> 72
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<400> 72

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21

<210> 73

<211> 20

<212> DNA

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<400> 75

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