

SEQUENCE LISTING

<110> Regeneron Pharmaceuticals, Inc.
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 Strowig, Till
 Yancopoulos, George D.
 de Zoete, Marcel

<120> GENETICALLY MODIFIED NON-HUMAN ANIMALS AND METHODS OF USE THEREOF

<130> REGN-016WO

<150> US62/146938

<151> 2015-04-13

<150> US62/148667

<151> 2015-04-16

<150> US62/287842

<151> 2016-01-27

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<213> Mus musculus

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Ser Glu Pro Asp Thr Glu Ile Gln Ser Gly Gly Gly Thr Glu Val Tyr
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Gly Val Ala Cys Ala Leu Leu Val Val Leu Leu Met Ala Ala Leu Tyr
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355

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Ala Ser Ile Glu Thr Gly Lys Val Pro Arg Pro Glu Asp Thr Leu Thr
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<211> 3845

<212> DNA

<213> Mus musculus

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Arg Ala Pro Glu Pro Asn Asn His Thr Glu Tyr Ala Ser Ile Glu Thr
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<210> 27
<211> 527
<212> PRT
<213> Mus musculus

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<400> 27
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Met Ser Leu Gln Met Val Thr Val Gly His Asn Ile Ala Leu Ile Gln
1           5           10           15

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```

Pro Gly Phe Ser Leu Met Asn Phe Asp Gly Gln Val Phe Phe Phe Gly
          20           25           30

```

```

Gln Lys Gly Trp Pro Lys Arg Ser Cys Pro Thr Gly Val Phe His Phe
          35           40           45

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```

Asp Ile Lys Gln Asn His Leu Lys Leu Lys Pro Ala Ile Phe Ser Lys
50           55           60

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```

Asp Ser Cys Tyr Leu Pro Pro Leu Arg Tyr Pro Ala Thr Cys Ser Tyr
65           70           75           80

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```

Lys Gly Ser Ile Asp Ser Asp Lys His Gln Tyr Ile Ile His Gly Gly
          85           90           95

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```

Lys Thr Pro Asn Asn Glu Leu Ser Asp Lys Ile Tyr Ile Met Ser Val
          100           105           110

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Ala Cys Lys Asn Asn Lys Lys Val Thr Phe Arg Cys Thr Glu Lys Asp
          115           120           125

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Leu Val Gly Asp Val Pro Glu Pro Arg Tyr Gly His Ser Ile Asp Val
 130 135 140

Val Tyr Ser Arg Gly Lys Ser Met Gly Val Leu Phe Gly Gly Arg Ser
 145 150 155 160

Tyr Met Pro Ser Thr Gln Arg Thr Thr Glu Lys Trp Asn Ser Val Ala
 165 170 175

Asp Cys Leu Pro His Val Phe Leu Ile Asp Phe Glu Phe Gly Cys Ala
 180 185 190

Thr Ser Tyr Ile Leu Pro Glu Leu Gln Asp Gly Leu Ser Phe His Val
 195 200 205

Ser Ile Ala Arg Asn Asp Thr Val Tyr Ile Leu Gly Gly His Ser Leu
 210 215 220

Ala Ser Asn Ile Arg Pro Ala Asn Leu Tyr Arg Ile Arg Val Asp Leu
 225 230 235 240

Pro Leu Gly Thr Pro Ala Val Asn Cys Thr Val Leu Pro Gly Gly Ile
 245 250 255

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

Ile Val Gly Gly Tyr Gln Leu Glu Asn Gln Lys Arg Met Val Cys Ser
 275 280 285

Leu Val Ser Leu Gly Asp Asn Thr Ile Glu Ile Ser Glu Met Glu Thr
 290 295 300

Pro Asp Trp Thr Ser Asp Ile Lys His Ser Lys Ile Trp Phe Gly Ser
 305 310 315 320

Asn Met Gly Asn Gly Thr Ile Phe Leu Gly Ile Pro Gly Asp Asn Lys
 325 330 335

Gln Ala Met Ser Glu Ala Phe Tyr Phe Tyr Thr Leu Arg Cys Ser Glu
 340 345 350

Glu Asp Leu Ser Glu Asp Gln Lys Ile Val Ser Asn Ser Gln Thr Ser
 355 360 365

Thr Glu Asp Pro Gly Asp Ser Thr Pro Phe Glu Asp Ser Glu Glu Phe
 370 375 380

Cys Phe Ser Ala Glu Ala Thr Ser Phe Asp Gly Asp Asp Glu Phe Asp
 385 390 395 400

Thr Tyr Asn Glu Asp Asp Glu Asp Asp Glu Ser Val Thr Gly Tyr Trp
 405 410 415

Ile Thr Cys Cys Pro Thr Cys Asp Val Asp Ile Asn Thr Trp Val Pro
 420 425 430

Phe Tyr Ser Thr Glu Leu Asn Lys Pro Ala Met Ile Tyr Cys Ser His
 435 440 445

Gly Asp Gly His Trp Val His Ala Gln Cys Met Asp Leu Glu Glu Arg
 450 455 460

Thr Leu Ile His Leu Ser Glu Gly Ser Asn Lys Tyr Tyr Cys Asn Glu
 465 470 475 480

His Val Gln Ile Ala Arg Ala Leu Gln Thr Pro Lys Arg Asn Pro Pro
 485 490 495

Leu Gln Lys Pro Pro Met Lys Ser Leu His Lys Lys Gly Ser Gly Lys
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Val Leu Thr Pro Ala Lys Lys Ser Phe Leu Arg Arg Leu Phe Asp
 515 520 525

<210> 28
 <211> 1612
 <212> DNA
 <213> Mus musculus

<400> 28
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gcaccaccac acccagcatg gtccttctct tttataggat tctccctccc tttttctacc     1560
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<210> 29
<211> 369
<212> PRT
<213> Mus musculus

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<400> 29

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Met Leu Lys Leu Leu Leu Ser Pro Arg Ser Phe Leu Val Leu Gln Leu
1           5           10          15

```

```

Leu Leu Leu Arg Ala Gly Trp Ser Ser Lys Val Leu Met Ser Ser Ala
20           25           30

```

```

Asn Glu Asp Ile Lys Ala Asp Leu Ile Leu Thr Ser Thr Ala Pro Glu
35           40           45

```

```

His Leu Ser Ala Pro Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val
50           55           60

```

```

Phe Asn Ile Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro
65           70           75          80

```

```

Gln Ala Thr Asn Leu Thr Leu His Tyr Arg Tyr Lys Val Ser Asp Asn
85           90           95

```

Asn	Thr	Phe	Gln	Glu	Cys	Ser	His	Tyr	Leu	Phe	Ser	Lys	Glu	Ile	Thr		
			100					105					110				
Ser	Gly	Cys	Gln	Ile	Gln	Lys	Glu	Asp	Ile	Gln	Leu	Tyr	Gln	Thr	Phe		
		115					120					125					
Val	Val	Gln	Leu	Gln	Asp	Pro	Gln	Lys	Pro	Gln	Arg	Arg	Ala	Val	Gln		
	130					135					140						
Lys	Leu	Asn	Leu	Gln	Asn	Leu	Val	Ile	Pro	Arg	Ala	Pro	Glu	Asn	Leu		
145					150					155					160		
Thr	Leu	Ser	Asn	Leu	Ser	Glu	Ser	Gln	Leu	Glu	Leu	Arg	Trp	Lys	Ser		
			165						170					175			
Arg	His	Ile	Lys	Glu	Arg	Cys	Leu	Gln	Tyr	Leu	Val	Gln	Tyr	Arg	Ser		
			180					185						190			
Asn	Arg	Asp	Arg	Ser	Trp	Thr	Glu	Leu	Ile	Val	Asn	His	Glu	Pro	Arg		
		195					200					205					
Phe	Ser	Leu	Pro	Ser	Val	Asp	Glu	Leu	Lys	Arg	Tyr	Thr	Phe	Arg	Val		
	210					215					220						
Arg	Ser	Arg	Tyr	Asn	Pro	Ile	Cys	Gly	Ser	Ser	Gln	Gln	Trp	Ser	Lys		
225					230					235					240		
Trp	Ser	Gln	Pro	Val	His	Trp	Gly	Ser	His	Thr	Val	Glu	Glu	Asn	Pro		
				245					250					255			
Ser	Leu	Phe	Ala	Leu	Glu	Ala	Val	Leu	Ile	Pro	Val	Gly	Thr	Met	Gly		
			260					265					270				
Leu	Ile	Ile	Thr	Leu	Ile	Phe	Val	Tyr	Cys	Trp	Leu	Glu	Arg	Met	Pro		
		275					280					285					
Pro	Ile	Pro	Pro	Ile	Lys	Asn	Leu	Glu	Asp	Leu	Val	Thr	Glu	Tyr	Gln		
	290					295					300						
Gly	Asn	Phe	Ser	Ala	Trp	Ser	Gly	Val	Ser	Lys	Gly	Leu	Thr	Glu	Ser		
305					310					315					320		
Leu	Gln	Pro	Asp	Tyr	Ser	Glu	Arg	Phe	Cys	His	Val	Ser	Glu	Ile	Pro		
				325					330					335			
Pro	Lys	Gly	Gly	Ala	Leu	Gly	Glu	Gly	Pro	Gly	Gly	Ser	Pro	Cys	Ser		
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Leu His Ser Pro Tyr Trp Pro Pro Pro Cys Tyr Ser Leu Lys Pro Glu
 355 360 365

Ala

<210> 30
 <211> 2012
 <212> DNA
 <213> Homo sapiens

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<210> 31
<211> 160
<212> PRT
<213> Homo sapiens

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<400> 31

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Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr
1           5           10           15

```

```

Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu Ala Gly Ile His
          20           25           30

```

```

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
          35           40           45

```

```

Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
          50           55           60

```

```

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
65           70           75           80

```

```

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
          85           90           95

```

```

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
          100          105          110

```

```

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
          115          120          125

```

```

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
          130          135          140

```

```

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
145           150           155           160

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<210> 32
 <211> 2333
 <212> DNA
 <213> Homo sapiens

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<400> 33

Pro Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys
20 25 30

Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr
35 40 45

Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe
50 55 60

Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile
65 70 75 80

His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser
85 90 95

Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu
100 105 110

Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val
115 120 125

Gln Met Phe Ile Asn Thr Ser
130 135

<210> 34
 <211> 1297
 <212> DNA
 <213> Mus musculus

<400> 34
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<210> 35
 <211> 160
 <212> PRT
 <213> Mus musculus

<400> 35

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20 25 30

Val Phe Ile Leu Gly Cys Val Ser Val Gly Leu Pro Lys Thr Glu Ala
35 40 45

Asn Trp Ile Asp Val Arg Tyr Asp Leu Glu Lys Ile Glu Ser Leu Ile
50 55 60

Gln Ser Ile His Ile Asp Thr Thr Leu Tyr Thr Asp Ser Asp Phe His
65 70 75 80

Pro Ser Cys Lys Val Thr Ala Met Asn Cys Phe Leu Leu Glu Leu Gln
85 90 95

Val Ile Leu His Glu Tyr Ser Asn Met Thr Leu Asn Glu Thr Val Arg
100 105 110

Asn Val Leu Tyr Leu Ala Asn Ser Thr Leu Ser Ser Asn Lys Asn Val
115 120 125

Ala Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Thr Phe
130 135 140

Thr Glu Phe Leu Gln Ser Phe Ile Arg Ile Val Gln Met Phe Ile Asn
145 150 155 160

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<211> 1287
<212> DNA
<213> Mus musculus

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