SEQUENCE LISTING

<110> Celgene Corporation
Acceleron Pharma Inc.

<120> TREATMENT OF BETA-THALASSEMIA USING
ACTRII LIGAND TRAPS

<130> 12827-952-228

<140> TBA
<141> On even date herewith

<150> 62/161,136
<151> 2015-05-13

<150> 62/173,836
<151> 2015-06-10

<150> 62/243,457
<151> 2015-10-19

<160> 50

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 513
<212> PRT
<213> Homo sapiens

<220>
<223> human ActRIIA precursor polypeptide

<400> 1

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Met Gly Ala Ala Ala Lys Leu Ala Phe Ala Val Phe Leu Ile Ser Cys
 1               5                  10                  15
Ser Ser Gly Ala Ile Leu Gly Arg Ser Glu Thr Gln Glu Cys Leu Phe
            20                  25                  30
Phe Asn Ala Asn Trp Glu Lys Asp Arg Thr Asn Gln Thr Gly Val Glu
        35                  40                  45
Pro Cys Tyr Gly Asp Lys Asp Lys Arg Arg His Cys Phe Ala Thr Trp
    50                  55                  60
Lys Asn Ile Ser Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu
65                  70                  75                  80
Asp Asp Ile Asn Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp
                85                  90                  95
```

```
Ser Pro Glu Val Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu
            100                 105                 110
Lys Phe Ser Tyr Phe Pro Glu Met Glu Val Thr Gln Pro Thr Ser Asn
        115                 120                 125
Pro Val Thr Pro Lys Pro Pro Tyr Tyr Asn Ile Leu Leu Tyr Ser Leu
    130                 135                 140
Val Pro Leu Met Leu Ile Ala Gly Ile Val Ile Cys Ala Phe Trp Val
145                 150                 155                 160
Tyr Arg His His Lys Met Ala Tyr Pro Pro Val Leu Val Pro Thr Gln
                165                 170                 175
Asp Pro Gly Pro Pro Pro Pro Ser Pro Leu Leu Gly Leu Lys Pro Leu
            180                 185                 190
Gln Leu Leu Glu Val Lys Ala Arg Gly Arg Phe Gly Cys Val Trp Lys
        195                 200                 205
Ala Gln Leu Leu Asn Glu Tyr Val Ala Val Lys Ile Phe Pro Ile Gln
    210                 215                 220
Asp Lys Gln Ser Trp Gln Asn Glu Tyr Glu Val Tyr Ser Leu Pro Gly
225                 230                 235                 240
Met Lys His Glu Asn Ile Leu Gln Phe Ile Gly Ala Glu Lys Arg Gly
                245                 250                 255
Thr Ser Val Asp Val Asp Leu Trp Leu Ile Thr Ala Phe His Glu Lys
            260                 265                 270
Gly Ser Leu Ser Asp Phe Leu Lys Ala Asn Val Val Ser Trp Asn Glu
        275                 280                 285
Leu Cys His Ile Ala Glu Thr Met Ala Arg Gly Leu Ala Tyr Leu His
    290                 295                 300
Glu Asp Ile Pro Gly Leu Lys Asp Gly His Lys Pro Ala Ile Ser His
305                 310                 315                 320
Arg Asp Ile Lys Ser Lys Asn Val Leu Leu Lys Asn Asn Leu Thr Ala
                325                 330                 335
Cys Ile Ala Asp Phe Gly Leu Ala Leu Lys Phe Glu Ala Gly Lys Ser
            340                 345                 350
Ala Gly Asp Thr His Gly Gln Val Gly Thr Arg Arg Tyr Met Ala Pro
        355                 360                 365
Glu Val Leu Glu Gly Ala Ile Asn Phe Gln Arg Asp Ala Phe Leu Arg
    370                 375                 380
Ile Asp Met Tyr Ala Met Gly Leu Val Leu Trp Glu Leu Ala Ser Arg
385                 390                 395                 400
Cys Thr Ala Ala Asp Gly Pro Val Asp Glu Tyr Met Leu Pro Phe Glu
                405                 410                 415
Glu Glu Ile Gly Gln His Pro Ser Leu Glu Asp Met Gln Glu Val Val
            420                 425                 430
Val His Lys Lys Lys Arg Pro Val Leu Arg Asp Tyr Trp Gln Lys His
        435                 440                 445
Ala Gly Met Ala Met Leu Cys Glu Thr Ile Glu Glu Cys Trp Asp His
    450                 455                 460
Asp Ala Glu Ala Arg Leu Ser Ala Gly Cys Val Gly Glu Arg Ile Thr
465                 470                 475                 480
```

```
Gln Met Gln Arg Leu Thr Asn Ile Ile Thr Thr Glu Asp Ile Val Thr
                485                 490                 495
Val Val Thr Met Val Thr Asn Val Asp Phe Pro Pro Lys Glu Ser Ser
            500                 505                 510
Leu
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<210> 2
<211> 115
<212> PRT
<213> Homo sapiens

<220>
<223> human ActRIIA soluble (extracellular), processed polypeptide sequence

<400> 2

```
Ile Leu Gly Arg Ser Glu Thr Gln Glu Cys Leu Phe Phe Asn Ala Asn
 1               5                  10                  15
Trp Glu Lys Asp Arg Thr Asn Gln Thr Gly Val Glu Pro Cys Tyr Gly
            20                  25                  30
Asp Lys Asp Lys Arg Arg His Cys Phe Ala Thr Trp Lys Asn Ile Ser
        35                  40                  45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
    50                  55                  60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu Lys Phe Ser Tyr
                85                  90                  95
Phe Pro Glu Met Glu Val Thr Gln Pro Thr Ser Asn Pro Val Thr Pro
            100                 105                 110
Lys Pro Pro
        115
```

<210> 3
<211> 100
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIA soluble (extracellular), processed polypeptide sequence with the C-terminal 15 amino acids deleted

<400> 3

```
Ile Leu Gly Arg Ser Glu Thr Gln Glu Cys Leu Phe Phe Asn Ala Asn
 1               5                  10                  15
```

```
Trp Glu Lys Asp Arg Thr Asn Gln Thr Gly Val Glu Pro Cys Tyr Gly
            20                  25                  30
Asp Lys Asp Lys Arg Arg His Cys Phe Ala Thr Trp Lys Asn Ile Ser
        35                  40                  45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
    50                  55                  60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu Lys Phe Ser Tyr
                85                  90                  95
Phe Pro Glu Met
            100
```

<210> 4
<211> 1542
<212> DNA
<213> Homo sapiens

<220>
<223> nucleic acid sequence of human ActRIIA precursor protein

<400> 4

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atgggagctg ctgcaaagtt ggcgtttgcc gtctttctta tctcctgttc ttcaggtgct 60
atacttggta gatcagaaac tcaggagtgt cttttcttta atgctaattg ggaaaaagac 120
agaaccaatc aaactggtgt tgaaccgtgt tatggtgaca aagataaacg gcggcattgt 180
tttgctacct ggaagaatat ttctggttcc attgaaatag tgaaacaagg ttgttggctg 240
gatgatatca actgctatga caggactgat tgtgtagaaa aaaaagacag ccctgaagta 300
tatttttgtt gctgtgaggg caatatgtgt aatgaaaagt tttcttattt tccagagatg 360
gaagtcacac agcccacttc aaatccagtt acacctaagc caccctatta caacatcctg 420
ctctattcct tggtgccact tatgttaatt gcggggattg tcatttgtgc attttgggtg 480
tacaggcatc acaagatggc ctaccctcct gtacttgttc caactcaaga cccaggacca 540
cccccacctt ctccattact agggttgaaa ccactgcagt tattagaagt gaaagcaagg 600
ggaagatttg gttgtgtctg gaaagcccag ttgcttaacg aatatgtggc tgtcaaaata 660
tttccaatac aggacaaaca gtcatggcaa aatgaatacg aagtctacag tttgcctgga 720
atgaagcatg agaacatatt acagttcatt ggtgcagaaa aacgaggcac cagtgttgat 780
gtggatcttt ggctgatcac agcatttcat gaaaagggtt cactatcaga ctttcttaag 840
gctaatgtgg tctcttggaa tgaactgtgt catattgcag aaaccatggc tagaggattg 900
gcatatttac atgaggatat acctggccta aaagatggcc acaaacctgc catatctcac 960
agggacatca aaagtaaaaa tgtgctgttg aaaaacaacc tgacagcttg cattgctgac 1020
tttgggttgg ccttaaaatt tgaggctggc aagtctgcag gcgataccca tggacaggtt 1080
ggtacccgga ggtacatggc tccagaggta ttagagggtg ctataaactt cgaaagggat 1140
gcatttttga ggatagatat gtatgccatg ggattagtcc tatgggaact ggcttctcgc 1200
tgtactgctg cagatggacc tgtagatgaa tacatgttgc catttgagga ggaaattggc 1260
cagcatccat ctcttgaaga catgcaggaa gttgttgtgc ataaaaaaaa gaggcctgtt 1320
ttaagagatt attggcagaa acatgctgga atggcaatgc tctgtgaaac cattgaagaa 1380
tgttgggatc acgacgcaga agccaggtta tcagctggat gtgtaggtga aagaattacc 1440
cagatgcaga gactaacaaa tattattacc acagaggaca ttgtaacagt ggtcacaatg 1500
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gtgacaaatg ttgactttcc tcccaaagaa tctagtctat ga 1542

<210> 5
<211> 345
<212> DNA
<213> Homo sapiens

<220>
<223> human ActRIIA soluble (extracellular) polypeptide

<400> 5
atacttggta gatcagaaac tcaggagtgt cttttcttta atgctaattg ggaaaaagac 60
agaaccaatc aaactggtgt tgaaccgtgt tatggtgaca aagataaacg gcggcattgt 120
tttgctacct ggaagaatat ttctggttcc attgaaatag tgaaacaagg ttgttggctg 180
gatgatatca actgctatga caggactgat tgtgtagaaa aaaaagacag ccctgaagta 240
tatttttgtt gctgtgaggg caatatgtgt aatgaaaagt tttcttattt tccagagatg 300
gaagtcacac agcccacttc aaatccagtt acacctaagc caccc 345

<210> 6
<211> 228
<212> PRT
<213> Artificial Sequence

<220>
<223> fusion protein comprising a soluble extracellular domain of
ActRIIA fused to an Fc domain

<220>
<221> VARIANT
<222> 44
<223> Xaa = Asp or Ala

<220>
<221> VARIANT
<222> 102
<223> Xaa = Lys or Ala

<220>
<221> VARIANT
<222> 215
<223> Xaa = Asn or Ala

<400> 6
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 1   5   10   15
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
            20   25   30
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Xaa Val Ser His Glu

```
        35                  40                  45
Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    50                  55                  60
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
65                  70                  75                  80
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                85                  90                  95
Glu Tyr Lys Cys Lys Xaa Val Ser Asn Lys Ala Leu Pro Val Pro Ile
            100                 105                 110
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    130                 135                 140
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175
Val Leu Asp Ser Asp Gly Pro Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205
His Glu Ala Leu His Asn Xaa His Tyr Thr Gln Lys Ser Leu Ser Leu
    210                 215                 220
Ser Pro Gly Lys
225
```

<210> 7
<211> 344
<212> PRT
<213> Artificial Sequence

<220>
<223> Extracellular domain of human ActRIIA fused to a human
Fc domain

<400> 7

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Ile Leu Gly Arg Ser Glu Thr Gln Glu Cys Leu Phe Phe Asn Ala Asn
 1               5                  10                  15
Trp Glu Lys Asp Arg Thr Asn Gln Thr Gly Val Glu Pro Cys Tyr Gly
            20                  25                  30
Asp Lys Asp Lys Arg Arg His Cys Phe Ala Thr Trp Lys Asn Ile Ser
        35                  40                  45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
    50                  55                  60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu Lys Phe Ser Tyr
```

```
                85                  90                  95
Phe Pro Glu Met Glu Val Thr Gln Pro Thr Ser Asn Pro Val Thr Pro
            100                 105                 110
Lys Pro Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala
        115                 120                 125
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
    130                 135                 140
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
145                 150                 155                 160
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
                165                 170                 175
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
            180                 185                 190
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
        195                 200                 205
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
    210                 215                 220
Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
225                 230                 235                 240
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
                245                 250                 255
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
            260                 265                 270
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
        275                 280                 285
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
    290                 295                 300
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
305                 310                 315                 320
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
                325                 330                 335
Ser Leu Ser Leu Ser Pro Gly Lys
            340
```

<210> 8
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Leader sequence of Honey bee mellitin (HBML)

<400> 8

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Met Lys Phe Leu Val Asn Val Ala Leu Val Phe Met Val Val Tyr Ile
 1               5                  10                  15
Ser Tyr Ile Tyr Ala
            20
```

<210> 9
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Leader sequence of Tissue Plasminogen Activator (TPA)

<400> 9
Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
 1   5   10   15
Ala Val Phe Val Ser Pro
            20

<210> 10
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Native ActRIIA leader

<400> 10
Met Gly Ala Ala Ala Lys Leu Ala Phe Ala Val Phe Leu Ile Ser Cys
 1   5   10   15
Ser Ser Gly Ala
            20

<210> 11
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> ActRIIA-hFc and mActRIIA-Fc N-terminal sequence

<400> 11
Ile Leu Gly Arg Ser Glu Thr Gln Glu
 1   5

<210> 12
<211> 329
<212> PRT

<213> Artificial Sequence

<220>
<223> ActRIIA-Fc Protein with deletion of the C-terminal 15 amino acids of the extracellular domain of ActRIIA

<400> 12

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Ile Leu Gly Arg Ser Glu Thr Gln Glu Cys Leu Phe Phe Asn Ala Asn
 1               5                  10                  15
Trp Glu Lys Asp Arg Thr Asn Gln Thr Gly Val Glu Pro Cys Tyr Gly
            20                  25                  30
Asp Lys Asp Lys Arg Arg His Cys Phe Ala Thr Trp Lys Asn Ile Ser
        35                  40                  45
Gly Ser Ile Glu Ile Val Lys Gln Gly Cys Trp Leu Asp Asp Ile Asn
    50                  55                  60
Cys Tyr Asp Arg Thr Asp Cys Val Glu Lys Lys Asp Ser Pro Glu Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Met Cys Asn Glu Lys Phe Ser Tyr
                85                  90                  95
Phe Pro Glu Met Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro
            100                 105                 110
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        115                 120                 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    130                 135                 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145                 150                 155                 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                165                 170                 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            180                 185                 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        195                 200                 205
Ala Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    210                 215                 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225                 230                 235                 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
                245                 250                 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            260                 265                 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        275                 280                 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    290                 295                 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305                 310                 315                 320
Lys Ser Leu Ser Leu Ser Pro Gly Lys
```

325

<210> 13
<211> 369
<212> PRT
<213> Artificial Sequence

<220>
<223> Unprocessed ActRIIA-hFc with TPA leader sequence

<400> 13

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Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
 1               5                  10                  15
Ala Val Phe Val Ser Pro Gly Ala Ala Ile Leu Gly Arg Ser Glu Thr
            20                  25                  30
Gln Glu Cys Leu Phe Phe Asn Ala Asn Trp Glu Lys Asp Arg Thr Asn
        35                  40                  45
Gln Thr Gly Val Glu Pro Cys Tyr Gly Asp Lys Asp Lys Arg Arg His
    50                  55                  60
Cys Phe Ala Thr Trp Lys Asn Ile Ser Gly Ser Ile Glu Ile Val Lys
65                  70                  75                  80
Gln Gly Cys Trp Leu Asp Asp Ile Asn Cys Tyr Asp Arg Thr Asp Cys
                85                  90                  95
Val Glu Lys Lys Asp Ser Pro Glu Val Tyr Phe Cys Cys Cys Glu Gly
            100                 105                 110
Asn Met Cys Asn Glu Lys Phe Ser Tyr Phe Pro Glu Met Glu Val Thr
        115                 120                 125
Gln Pro Thr Ser Asn Pro Val Thr Pro Lys Pro Pro Thr Gly Gly Gly
    130                 135                 140
Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
145                 150                 155                 160
Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                165                 170                 175
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
            180                 185                 190
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        195                 200                 205
Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
    210                 215                 220
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
225                 230                 235                 240
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Val Pro Ile Glu Lys
                245                 250                 255
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
            260                 265                 270
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
        275                 280                 285
```

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
290 295 300
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
305 310 315 320
Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
325 330 335
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
340 345 350
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
355 360 365
Lys

<210> 14
<211> 1113
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid sequence encoding Unprocessed ActRIIA-hFc
with TPA leader sequence

<400> 14
atggatgcaa tgaagagagg gctctgctgt gtgctgctgc tgtgtggagc agtcttcgtt 60
tcgcccggcg ccgctatact tggtagatca gaaactcagg agtgtctttt tttaatgcta 120
attgggaaaa agacagaacc aatcaaactg gtgttgaacc gtgttatggt gacaaagata 180
aacggcggca ttgttttgct acctggaaga atatttctgg ttccattgaa tagtgaaaca 240
aggttgttgg ctggatgata tcaactgcta tgacaggact gattgtgtag aaaaaaaaga 300
cagccctgaa gtatatttct gttgctgtga gggcaatatg tgtaatgaaa agttttctta 360
ttttccggag atggaagtca cacagcccac ttcaaatcca gttacaccta agccacccac 420
cggtggtgga actcacacat gcccaccgtg cccagcacct gaactcctgg ggggaccgtc 480
agtcttcctc ttcccccaa aacccaagga caccctcatg atctcccgga cccctgaggt 540
cacatgcgtg gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt 600
ggacggcgtg gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac 660
gtaccgtgtg gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta 720
caagtgcaag gtctccaaca aagccctccc agtccccatc gagaaaacca tctccaaagc 780
caaagggcag ccccgagaac cacaggtgta caccctgccc ccatcccggg aggagatgac 840
caagaaccag gtcagcctga cctgcctggt caaaggcttc tatcccagcg acatcgccgt 900
ggagtgggag agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga 960
ctccgacggc tccttcttcc tctatagcaa gctcaccgtg gacaagagca ggtggcagca 1020
ggggaacgtc ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa 1080
gagcctctcc ctgtctccgg taaatgagaa ttc 1113

<210> 15
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular processed polypeptide with
the N-terminal 6 aa of the EC domain deleted and the C-terminal 4 aa
of the EC domain deleted (aa 25-130 of SEQ ID NO:28) and with an L79D
mutation

<400> 15
Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg
1 5 10 15
Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg
20 25 30
Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser Gly Thr Ile Glu Leu
35 40 45
Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln
50 55 60
Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys
65 70 75 80
Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly
85 90 95
Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro
100 105

<210> 16
<211> 512
<212> PRT
<213> Homo sapiens

<220>
<223> human ActRIIB precursor protein sequence (A64)

<400> 16
Met Thr Ala Pro Trp Val Ala Leu Ala Leu Leu Trp Gly Ser Leu Trp
1 5 10 15
Pro Gly Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr
20 25 30
Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg
35 40 45
Cys Glu Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala
50 55 60
Asn Ser Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp
65 70 75 80
Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn
85 90 95
Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg
100 105 110
Phe Thr His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro

```
        115                 120                 125
Pro Pro Thr Ala Pro Thr Leu Leu Thr Val Leu Ala Tyr Ser Leu Leu
    130                 135                 140
Pro Ile Gly Gly Leu Ser Leu Ile Val Leu Leu Ala Phe Trp Met Tyr
145                 150                 155                 160
Arg His Arg Lys Pro Pro Tyr Gly His Val Asp Ile His Glu Asp Pro
                165                 170                 175
Gly Pro Pro Pro Pro Ser Pro Leu Val Gly Leu Lys Pro Leu Gln Leu
            180                 185                 190
Leu Glu Ile Lys Ala Arg Gly Arg Phe Gly Cys Val Trp Lys Ala Gln
        195                 200                 205
Leu Met Asn Asp Phe Val Ala Val Lys Ile Phe Pro Leu Gln Asp Lys
    210                 215                 220
Gln Ser Trp Gln Ser Glu Arg Glu Ile Phe Ser Thr Pro Gly Met Lys
225                 230                 235                 240
His Glu Asn Leu Leu Gln Phe Ile Ala Ala Glu Lys Arg Gly Ser Asn
                245                 250                 255
Leu Glu Val Glu Leu Trp Leu Ile Thr Ala Phe His Asp Lys Gly Ser
            260                 265                 270
Leu Thr Asp Tyr Leu Lys Gly Asn Ile Ile Thr Trp Asn Glu Leu Cys
        275                 280                 285
His Val Ala Glu Thr Met Ser Arg Gly Leu Ser Tyr Leu His Glu Asp
    290                 295                 300
Val Pro Trp Cys Arg Gly Glu Gly His Lys Pro Ser Ile Ala His Arg
305                 310                 315                 320
Asp Phe Lys Ser Lys Asn Val Leu Leu Lys Ser Asp Leu Thr Ala Val
                325                 330                 335
Leu Ala Asp Phe Gly Leu Ala Val Arg Phe Glu Pro Gly Lys Pro Pro
            340                 345                 350
Gly Asp Thr His Gly Gln Val Gly Thr Arg Arg Tyr Met Ala Pro Glu
        355                 360                 365
Val Leu Glu Gly Ala Ile Asn Phe Gln Arg Asp Ala Phe Leu Arg Ile
    370                 375                 380
Asp Met Tyr Ala Met Gly Leu Val Leu Trp Glu Leu Val Ser Arg Cys
385                 390                 395                 400
Lys Ala Ala Asp Gly Pro Val Asp Glu Tyr Met Leu Pro Phe Glu Glu
                405                 410                 415
Glu Ile Gly Gln His Pro Ser Leu Glu Glu Leu Gln Glu Val Val Val
            420                 425                 430
His Lys Lys Met Arg Pro Thr Ile Lys Asp His Trp Leu Lys His Pro
        435                 440                 445
Gly Leu Ala Gln Leu Cys Val Thr Ile Glu Glu Cys Trp Asp His Asp
    450                 455                 460
Ala Glu Ala Arg Leu Ser Ala Gly Cys Val Glu Glu Arg Val Ser Leu
465                 470                 475                 480
Ile Arg Arg Ser Val Asn Gly Thr Thr Ser Asp Cys Leu Val Ser Leu
                485                 490                 495
Val Thr Ser Val Thr Asn Val Asp Leu Pro Pro Lys Glu Ser Ser Ile
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500 505 510

<210> 17
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (amino acids 19-134 of SEQ ID NO:16)

<400> 17
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro
100 105 110
Thr Ala Pro Thr
115

<210> 18
<211> 101
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular) processed polypeptide with the C-terminal 15 aa deleted (aa 19-119 of SEQ ID NO:16)

<400> 18
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe

```
    50                  55                  60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65                  70                  75                  80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
                85                  90                  95
His Leu Pro Glu Ala
            100
```

<210> 19
<211> 1539
<212> DNA
<213> Homo sapiens

<220>
<223> nucleic acid sequence encoding a human ActRIIB (A64) precursor protein

<400> 19

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atgacggcgc cctgggtggc cctcgccctc ctctggggat cgctgtggcc cggctctggg 60
cgtggggagg ctgagacacg ggagtgcatc tactacaacg ccaactggga gctggagcgc 120
accaaccaga gcggcctgga gcgctgcgaa ggcgagcagg acaagcggct gcactgctac 180
gcctcctggg ccaacagctc tggcaccatc gagctcgtga agaagggctg ctggctagat 240
gacttcaact gctacgatag gcaggagtgt gtggccactg aggagaaccc ccaggtgtac 300
ttctgctgct gtgaaggcaa cttctgcaac gagcgcttca ctcatttgcc agaggctggg 360
ggcccggaag tcacgtacga gccacccccg acagccccca ccctgctcac ggtgctggcc 420
tactcactgc tgcccatcgg gggcctttcc ctcatcgtcc tgctggcctt ttggatgtac 480
cggcatcgca agccccccta cggtcatgtg gacatccatg aggaccctgg gcctccacca 540
ccatcccctc tggtgggcct gaagccactg cagctgctgg agatcaaggc tcgggggcgc 600
tttggctgtg tctggaaggc ccagctcatg aatgactttg tagctgtcaa gatcttccca 660
ctccaggaca agcagtcgtg gcagagtgaa cgggagatct tcagcacacc tggcatgaag 720
cacgagaacc tgctacagtt cattgctgcc gagaagcgag gctccaacct cgaagtagag 780
ctgtggctca tcacggcctt ccatgacaag ggctccctca cggattacct caaggggaac 840
atcatcacat ggaacgaact gtgtcatgta gcagagacga tgtcacgagg cctctcatac 900
ctgcatgagg atgtgccctg gtgccgtggc gagggccaca agccgtctat tgcccacagg 960
gactttaaaa gtaagaatgt attgctgaag agcgacctca cagccgtgct ggctgacttt 1020
ggcttggctg ttcgatttga gccagggaaa cctccagggg acacccacgg acaggtaggc 1080
acgagacggt acatggctcc tgaggtgctc gagggagcca tcaacttcca gagagatgcc 1140
ttcctgcgca ttgacatgta tgccatgggg ttggtgctgt gggagcttgt gtctcgctgc 1200
aaggctgcag acggacccgt ggatgagtac atgctgccct ttgaggaaga gattggccag 1260
cacccttcgt tggaggagct gcaggaggtg gtggtgcaca agaagatgag gcccaccatt 1320
aaagatcact ggttgaaaca cccgggcctg gcccagcttt gtgtgaccat cgaggagtgc 1380
tgggaccatg atgcagaggc tcgcttgtcc gcgggctgtg tggaggagcg ggtgtccctg 1440
attcggaggt cggtcaacgg cactacctcg gactgtctcg tttccctggt gacctctgtc 1500
accaatgtgg acctgccccc taaagagtca agcatctaa                        1539
```

<210> 20
<211> 344

<212> PRT
<213> Artificial Sequence

<220>
<223> fusion protein comprising a soluble extracellular domain of ActRIIB (A64; SEQ ID NO:17) fused to an Fc domain

<400> 20

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Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
 1               5                  10                  15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
            20                  25                  30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
        35                  40                  45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
    50                  55                  60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65                  70                  75                  80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
                85                  90                  95
His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro
            100                 105                 110
Thr Ala Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala
        115                 120                 125
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
    130                 135                 140
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
145                 150                 155                 160
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
                165                 170                 175
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
            180                 185                 190
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
        195                 200                 205
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
    210                 215                 220
Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
225                 230                 235                 240
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
                245                 250                 255
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
            260                 265                 270
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
        275                 280                 285
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
    290                 295                 300
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
305                 310                 315                 320
```

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
325 330 335
Ser Leu Ser Leu Ser Pro Gly Lys
340

<210> 21
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> fusion protein comprising a soluble extracellular domain of ActRIIB (A64) with the C-terminal 15 amino acids deleted (SEQ ID NO:18) fused to an Fc domain

<400> 21
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro
100 105 110
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205
Ala Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225 230 235 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro

```
                245                 250                 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            260                 265                 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        275                 280                 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    290                 295                 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305                 310                 315                 320
Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325
```

<210> 22
<211> 105
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular) processed polypeptide with the N-terminal 6 aa of the EC domain deleted and the C-terminal 5 aa of the EC domain deleted (aa 25-129 of SEQ ID NO:28) and with an L79D mutation

<400> 22

```
Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg
 1               5                  10                  15
Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg
            20                  25                  30
Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser Gly Thr Ile Glu Leu
        35                  40                  45
Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln
    50                  55                  60
Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys
65                  70                  75                  80
Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly
                85                  90                  95
Gly Pro Glu Val Thr Tyr Glu Pro Pro
            100                 105
```

<210> 23
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular) processed polypeptide

with the N-terminal 6 aa of the EC domain deleted and the C-terminal 3 aa of the EC domain deleted (aa 25-131 of SEQ ID NO:28) and with an L79D mutation

<400> 23
Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg
 1   5   10   15
Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg
            20   25   30
Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser Gly Thr Ile Glu Leu
        35   40   45
Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln
    50   55   60
Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys
65   70   75   80
Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly
                85   90   95
Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100   105

<210> 24
<211> 360
<212> PRT
<213> Artificial Sequence

<220>
<223> Unprocessed ActRIIB-Fc fusion protein with the N-terminal 6 aa of the EC domain deleted and the C-terminal 3 aa of the EC domain deleted (aa 25-131 of SEQ ID NO:28) and with an L79D mutation and with TPA leader sequence

<400> 24
Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
 1   5   10   15
Ala Val Phe Val Ser Pro Gly Ala Ala Glu Thr Arg Glu Cys Ile Tyr
            20   25   30
Tyr Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu
        35   40   45
Arg Cys Glu Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp
    50   55   60
Arg Asn Ser Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp
65   70   75   80
Asp Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu
                85   90   95
Asn Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu
            100   105   110
Arg Phe Thr His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu

```
        115                 120                 125
Pro Pro Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala
    130                 135                 140
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
145                 150                 155                 160
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
                165                 170                 175
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
            180                 185                 190
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
        195                 200                 205
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
    210                 215                 220
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
225                 230                 235                 240
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
                245                 250                 255
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
            260                 265                 270
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
        275                 280                 285
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
    290                 295                 300
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
305                 310                 315                 320
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
                325                 330                 335
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
            340                 345                 350
Ser Leu Ser Leu Ser Pro Gly Lys
        355                 360
```

<210> 25
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> Processed ActRIIB-Fc fusion protein with the N-terminal 6 aa of the EC domain deleted and the C-terminal 3 aa of the EC domain deleted (aa 25-131 of SEQ ID NO:28) and with an L79D mutation

<400> 25

```
Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg
 1               5                  10                  15
Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg
```

```
            20                  25                  30
Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser Gly Thr Ile Glu Leu
        35                  40                  45
Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln
    50                  55                  60
Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys
65                  70                  75                  80
Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly
                85                  90                  95
Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr Gly Gly Gly Thr His
            100                 105                 110
Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
        115                 120                 125
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
    130                 135                 140
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
145                 150                 155                 160
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
                165                 170                 175
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
            180                 185                 190
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
        195                 200                 205
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
    210                 215                 220
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
225                 230                 235                 240
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
                245                 250                 255
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
            260                 265                 270
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
        275                 280                 285
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
    290                 295                 300
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
305                 310                 315                 320
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330                 335
```

<210> 26
<211> 115
<212> PRT
<213> Homo sapiens

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide

sequence (amino acids 20-134 of SEQ ID NO:16)

<400> 26
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100   105   110
Ala Pro Thr
        115

<210> 27
<211> 100
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide
 sequence with the C-terminal 15 aa deleted (aa 20-119 of SEQ ID
NO:16)

<400> 27
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala
            100

<210> 28
<211> 512
<212> PRT
<213> Homo sapiens

<220>
<223> human ActRIIB precursor protein sequence (R64)

<400> 28

```
Met Thr Ala Pro Trp Val Ala Leu Ala Leu Leu Trp Gly Ser Leu Trp
 1               5                  10                  15
Pro Gly Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr
            20                  25                  30
Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg
        35                  40                  45
Cys Glu Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg
    50                  55                  60
Asn Ser Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp
65                  70                  75                  80
Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn
                85                  90                  95
Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg
            100                 105                 110
Phe Thr His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro
        115                 120                 125
Pro Pro Thr Ala Pro Thr Leu Leu Thr Val Leu Ala Tyr Ser Leu Leu
    130                 135                 140
Pro Ile Gly Gly Leu Ser Leu Ile Val Leu Leu Ala Phe Trp Met Tyr
145                 150                 155                 160
Arg His Arg Lys Pro Pro Tyr Gly His Val Asp Ile His Glu Asp Pro
                165                 170                 175
Gly Pro Pro Pro Pro Ser Pro Leu Val Gly Leu Lys Pro Leu Gln Leu
            180                 185                 190
Leu Glu Ile Lys Ala Arg Gly Arg Phe Gly Cys Val Trp Lys Ala Gln
        195                 200                 205
Leu Met Asn Asp Phe Val Ala Val Lys Ile Phe Pro Leu Gln Asp Lys
    210                 215                 220
Gln Ser Trp Gln Ser Glu Arg Glu Ile Phe Ser Thr Pro Gly Met Lys
225                 230                 235                 240
His Glu Asn Leu Leu Gln Phe Ile Ala Ala Glu Lys Arg Gly Ser Asn
                245                 250                 255
Leu Glu Val Glu Leu Trp Leu Ile Thr Ala Phe His Asp Lys Gly Ser
            260                 265                 270
Leu Thr Asp Tyr Leu Lys Gly Asn Ile Ile Thr Trp Asn Glu Leu Cys
        275                 280                 285
His Val Ala Glu Thr Met Ser Arg Gly Leu Ser Tyr Leu His Glu Asp
    290                 295                 300
Val Pro Trp Cys Arg Gly Glu Gly His Lys Pro Ser Ile Ala His Arg
```

```
305                 310                 315                 320
Asp Phe Lys Ser Lys Asn Val Leu Leu Lys Ser Asp Leu Thr Ala Val
                325                 330                 335
Leu Ala Asp Phe Gly Leu Ala Val Arg Phe Glu Pro Gly Lys Pro Pro
            340                 345                 350
Gly Asp Thr His Gly Gln Val Gly Thr Arg Arg Tyr Met Ala Pro Glu
        355                 360                 365
Val Leu Glu Gly Ala Ile Asn Phe Gln Arg Asp Ala Phe Leu Arg Ile
    370                 375                 380
Asp Met Tyr Ala Met Gly Leu Val Leu Trp Glu Leu Val Ser Arg Cys
385                 390                 395                 400
Lys Ala Ala Asp Gly Pro Val Asp Glu Tyr Met Leu Pro Phe Glu Glu
                405                 410                 415
Glu Ile Gly Gln His Pro Ser Leu Glu Glu Leu Gln Glu Val Val Val
            420                 425                 430
His Lys Lys Met Arg Pro Thr Ile Lys Asp His Trp Leu Lys His Pro
        435                 440                 445
Gly Leu Ala Gln Leu Cys Val Thr Ile Glu Glu Cys Trp Asp His Asp
    450                 455                 460
Ala Glu Ala Arg Leu Ser Ala Gly Cys Val Glu Glu Arg Val Ser Leu
465                 470                 475                 480
Ile Arg Arg Ser Val Asn Gly Thr Thr Ser Asp Cys Leu Val Ser Leu
                485                 490                 495
Val Thr Ser Val Thr Asn Val Asp Leu Pro Pro Lys Glu Ser Ser Ile
            500                 505                 510
```

<210> 29
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (amino acids 19-134 of SEQ ID NO:28)

<400> 29

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Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
 1               5                  10                  15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
            20                  25                  30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser
        35                  40                  45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
    50                  55                  60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65                  70                  75                  80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
```

85 90 95
His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro
100 105 110
Thr Ala Pro Thr
115

<210> 30
<211> 101
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence with the C-terminal 15 aa deleted (aa 19-119 of SEQ ID NO:28)

<400> 30
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala
100

<210> 31
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (amino acids 20-134 of SEQ ID NO:28)

<400> 31
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
1 5 10 15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
20 25 30

```
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35                  40                  45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe Asn
    50                  55                  60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85                  90                  95
Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100                 105                 110
Ala Pro Thr
        115
```

<210> 32
<211> 100
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide
sequence with the C-terminal 15 aa deleted (aa 20-119
of SEQ ID NO:28)

<400> 32

```
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1               5                  10                  15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20                  25                  30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35                  40                  45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe Asn
    50                  55                  60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85                  90                  95
Leu Pro Glu Ala
            100
```

<210> 33
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular) processed polypeptide

with the N-terminal 6 aa of the EC domain deleted and the C-terminal 3 aa of the EC domain deleted (aa 25-131 of SEQ ID NO:16) and with an L79D mutation

<400> 33
Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg
1 5 10 15
Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg
20 25 30
Leu His Cys Tyr Ala Ser Trp Ala Asn Ser Ser Gly Thr Ile Glu Leu
35 40 45
Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln
50 55 60
Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys
65 70 75 80
Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly
85 90 95
Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
100 105

<210> 34
<211> 360
<212> PRT
<213> Artificial Sequence

<220>
<223> Unprocessed ActRIIB-Fc fusion protein with the N-terminal 6 aa of the EC domain deleted and the C-terminal 3 aa of the EC domain deleted (aa 25-131 of SEQ ID NO:16) and with an L79D mutation and with TPA leader sequence

<400> 34
Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
1 5 10 15
Ala Val Phe Val Ser Pro Gly Ala Ala Glu Thr Arg Glu Cys Ile Tyr
20 25 30
Tyr Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu
35 40 45
Arg Cys Glu Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp
50 55 60
Ala Asn Ser Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp
65 70 75 80
Asp Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu
85 90 95
Asn Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu
100 105 110
Arg Phe Thr His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu

```
        115                 120                 125
Pro Pro Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala
    130                 135                 140
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
145                 150                 155                 160
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
                165                 170                 175
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
            180                 185                 190
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
        195                 200                 205
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
    210                 215                 220
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
225                 230                 235                 240
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
                245                 250                 255
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
            260                 265                 270
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
        275                 280                 285
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
    290                 295                 300
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
305                 310                 315                 320
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
                325                 330                 335
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
            340                 345                 350
Ser Leu Ser Leu Ser Pro Gly Lys
        355                 360
```

<210> 35
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> Processed ActRIIB-Fc fusion protein with the N-terminal 6 aa of the EC domain deleted and the C-terminal 3 aa of the EC domain deleted (aa 25-131 of SEQ ID NO:16) and with an L79D mutation

<400> 35

```
Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg
 1               5                  10                  15
Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg
            20                  25                  30
```

```
Leu His Cys Tyr Ala Ser Trp Ala Asn Ser Ser Gly Thr Ile Glu Leu
        35                  40                  45
Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln
    50                  55                  60
Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys
65                  70                  75                  80
Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly
                85                  90                  95
Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr Gly Gly Gly Thr His
            100                 105                 110
Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
        115                 120                 125
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
    130                 135                 140
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
145                 150                 155                 160
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
                165                 170                 175
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
            180                 185                 190
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
        195                 200                 205
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
    210                 215                 220
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
225                 230                 235                 240
Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
                245                 250                 255
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
            260                 265                 270
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
        275                 280                 285
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
    290                 295                 300
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
305                 310                 315                 320
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330                 335
```

<210> 36
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (amino acids 20-134 of SEQ ID NO:28) with L79D mutation

<400> 36
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100   105   110
Ala Pro Thr
        115

<210> 37
<211> 115
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide
 sequence (amino acids 20-134 of SEQ ID NO:16) with L79D mutation

<400> 37
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100   105   110
Ala Pro Thr
        115

<210> 38
<211> 343
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (aa 20-134 of SEQ ID NO:28) with L79D mutation fused to an Fc domain with a GGG linker

<400> 38

```
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1               5                  10                  15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20                  25                  30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35                  40                  45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn
    50                  55                  60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85                  90                  95
Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100                 105                 110
Ala Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala Pro
        115                 120                 125
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
    130                 135                 140
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
145                 150                 155                 160
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
                165                 170                 175
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
            180                 185                 190
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
        195                 200                 205
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
    210                 215                 220
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
225                 230                 235                 240
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
                245                 250                 255
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
            260                 265                 270
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
        275                 280                 285
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
```

```
    290                 295                 300
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
305                 310                 315                 320
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
                325                 330                 335
Leu Ser Leu Ser Pro Gly Lys
            340
```

<210> 39
<211> 343
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (aa 20-134 of SEQ ID NO:16) with L79D mutation fused to an Fc domain

<400> 39

```
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1               5                  10                  15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20                  25                  30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Ala Asn Ser Ser
        35                  40                  45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn
    50                  55                  60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65                  70                  75                  80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85                  90                  95
Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro Thr
            100                 105                 110
Ala Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala Pro
        115                 120                 125
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
    130                 135                 140
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
145                 150                 155                 160
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
                165                 170                 175
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
            180                 185                 190
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
        195                 200                 205
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
    210                 215                 220
```

```
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
225                 230                 235                 240
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
                245                 250                 255
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
            260                 265                 270
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
        275                 280                 285
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
    290                 295                 300
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
305                 310                 315                 320
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
                325                 330                 335
Leu Ser Leu Ser Pro Gly Lys
            340
```

<210> 40
<211> 368
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence (aa 20-134 of SEQ ID NO:28) with L79D mutation fused to an Fc domain and with TPA leader sequence

<400> 40

```
Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
 1               5                  10                  15
Ala Val Phe Val Ser Pro Gly Ala Ser Gly Arg Gly Glu Ala Glu Thr
            20                  25                  30
Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn
        35                  40                  45
Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg Leu His
    50                  55                  60
Cys Tyr Ala Ser Trp Arg Asn Ser Ser Gly Thr Ile Glu Leu Val Lys
65                  70                  75                  80
Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys
                85                  90                  95
Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly
            100                 105                 110
Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly Gly Pro
        115                 120                 125
Glu Val Thr Tyr Glu Pro Pro Pro Thr Ala Pro Thr Gly Gly Gly Thr
    130                 135                 140
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
```

```
145                 150                 155                 160
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                165                 170                 175
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            180                 185                 190
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        195                 200                 205
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    210                 215                 220
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
225                 230                 235                 240
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                245                 250                 255
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            260                 265                 270
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        275                 280                 285
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    290                 295                 300
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
305                 310                 315                 320
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                325                 330                 335
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            340                 345                 350
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        355                 360                 365
```

<210> 41
<211> 368
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide
sequence (aa 20-134 of SEQ ID NO:16) with L79D mutation fused
to an Fc domain and with TPA leader sequence

<400> 41

```
Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly
 1               5                  10                  15
Ala Val Phe Val Ser Pro Gly Ala Ser Gly Arg Gly Glu Ala Glu Thr
            20                  25                  30
Arg Glu Cys Ile Tyr Tyr Asn Ala Asn Trp Glu Leu Glu Arg Thr Asn
        35                  40                  45
Gln Ser Gly Leu Glu Arg Cys Glu Gly Glu Gln Asp Lys Arg Leu His
    50                  55                  60
```

```
Cys Tyr Ala Ser Trp Ala Asn Ser Ser Gly Thr Ile Glu Leu Val Lys
65                  70                  75                  80
Lys Gly Cys Trp Asp Asp Asp Phe Asn Cys Tyr Asp Arg Gln Glu Cys
                85                  90                  95
Val Ala Thr Glu Glu Asn Pro Gln Val Tyr Phe Cys Cys Cys Glu Gly
            100                 105                 110
Asn Phe Cys Asn Glu Arg Phe Thr His Leu Pro Glu Ala Gly Gly Pro
        115                 120                 125
Glu Val Thr Tyr Glu Pro Pro Pro Thr Ala Pro Thr Gly Gly Gly Thr
    130                 135                 140
His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
145                 150                 155                 160
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                165                 170                 175
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            180                 185                 190
Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        195                 200                 205
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    210                 215                 220
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
225                 230                 235                 240
Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                245                 250                 255
Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            260                 265                 270
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        275                 280                 285
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    290                 295                 300
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
305                 310                 315                 320
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                325                 330                 335
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            340                 345                 350
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        355                 360                 365
```

<210> 42
<211> 141
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide sequence having a variant C-terminal sequence (disclosed in

WO2007/053775)

<400> 42
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala Gly Gly Pro Glu Gly Pro Trp Ala Ser Thr Thr Ile
            100   105   110
Pro Ser Gly Gly Pro Glu Ala Thr Ala Ala Ala Gly Asp Gln Gly Ser
        115   120   125
Gly Ala Leu Trp Leu Cys Leu Glu Gly Pro Ala His Glu
    130   135   140

<210> 43
<211> 141
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide
 sequence having a variant C-terminal sequence (disclosed in
WO2007/053775) having an L79D mutation

<400> 43
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala Gly Gly Pro Glu Gly Pro Trp Ala Ser Thr Thr Ile
            100   105   110

Pro Ser Gly Gly Pro Glu Ala Thr Ala Ala Ala Gly Asp Gln Gly Ser
        115   120   125
Gly Ala Leu Trp Leu Cys Leu Glu Gly Pro Ala His Glu
    130   135   140

<210> 44
<211> 370
<212> PRT
<213> Artificial Sequence

<220>
<223> human ActRIIB soluble (extracellular), processed polypeptide
 sequence having a variant C-terminal sequence (disclosed in
WO2007/053775) having an L79D mutation fused to an Fc domain with
a TGGG linker

<400> 44
Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala Asn
 1   5   10   15
Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu Gly
            20   25   30
Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser Ser
        35   40   45
Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Asp Asp Asp Phe Asn
    50   55   60
Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln Val
65   70   75   80
Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr His
                85   90   95
Leu Pro Glu Ala Gly Gly Pro Glu Gly Pro Trp Ala Ser Thr Thr Ile
            100   105   110
Pro Ser Gly Gly Pro Glu Ala Thr Ala Ala Ala Gly Asp Gln Gly Ser
        115   120   125
Gly Ala Leu Trp Leu Cys Leu Glu Gly Pro Ala His Glu Thr Gly Gly
    130   135   140
Gly Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
145   150   155   160
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                165   170   175
Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            180   185   190
Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        195   200   205
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    210   215   220
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
225   230   235   240

```
Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                245                 250                 255
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            260                 265                 270
Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        275                 280                 285
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    290                 295                 300
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
305                 310                 315                 320
Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                325                 330                 335
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            340                 345                 350
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        355                 360                 365
Gly Lys
    370
```

<210> 45
<211> 1083
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding SEQ ID NO:24

<400> 45

```
atggatgcaa tgaagagagg gctctgctgt gtgctgctgc tgtgtggagc agtcttcgtt 60
tcgcccggcg ccgccgaaac ccgcgaatgt atttattaca atgctaattg ggaactcgaa 120
cggacgaacc aatccgggct cgaacggtgt gaggggggaac aggataaacg cctccattgc 180
tatgcgtcgt ggaggaactc ctccgggacg attgaactgg tcaagaaagg gtgctgggac 240
gacgatttca attgttatga ccgccaggaa tgtgtcgcga ccgaagagaa tccgcaggtc 300
tatttctgtt gttgcgaggg gaatttctgt aatgaacggt ttacccacct ccccgaagcc 360
ggcgggcccg aggtgaccta tgaacccccg cccaccggtg gtggaactca cacatgccca 420
ccgtgcccag cacctgaact cctgggggga ccgtcagtct tcctcttccc cccaaaaccc 480
aaggacaccc tcatgatctc ccggacccct gaggtcacat gcgtggtggt ggacgtgagc 540
cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 600
aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 660
gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 720
ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 780
gtgtacaccc tgcccccatc ccgggaggag atgaccaaga accaggtcag cctgacctgc 840
ctggtcaaag gcttctatcc cagcgacatc gccgtggagt gggagagcaa tgggcagccg 900
gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctat 960
agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1020
atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc cccgggtaaa 1080
tga                                                                 1083
```

<210> 46
<211> 344
<212> PRT
<213> Artificial Sequence

<220>
<223> fusion protein comprising a soluble extracellular domain
of ActRIIB (R64; SEQ ID NO:29) fused to an Fc domain

<400> 46
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
1 5 10 15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
20 25 30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser
35 40 45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
50 55 60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65 70 75 80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
85 90 95
His Leu Pro Glu Ala Gly Gly Pro Glu Val Thr Tyr Glu Pro Pro Pro
100 105 110
Thr Ala Pro Thr Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro Ala
115 120 125
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
130 135 140
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
145 150 155 160
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
165 170 175
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
180 185 190
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
195 200 205
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
210 215 220
Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
225 230 235 240
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
245 250 255
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
260 265 270
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
275 280 285
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr

```
    290                 295                 300
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
305                 310                 315                 320
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
                325                 330                 335
Ser Leu Ser Leu Ser Pro Gly Lys
            340
```

<210> 47
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> fusion protein comprising a soluble extracellular domain of ActRIIB (R64) with the C-terminal 15 aa deleted (SEQ ID NO:30) fused to an Fc domain

<400> 47

```
Ser Gly Arg Gly Glu Ala Glu Thr Arg Glu Cys Ile Tyr Tyr Asn Ala
 1               5                  10                  15
Asn Trp Glu Leu Glu Arg Thr Asn Gln Ser Gly Leu Glu Arg Cys Glu
            20                  25                  30
Gly Glu Gln Asp Lys Arg Leu His Cys Tyr Ala Ser Trp Arg Asn Ser
        35                  40                  45
Ser Gly Thr Ile Glu Leu Val Lys Lys Gly Cys Trp Leu Asp Asp Phe
    50                  55                  60
Asn Cys Tyr Asp Arg Gln Glu Cys Val Ala Thr Glu Glu Asn Pro Gln
65                  70                  75                  80
Val Tyr Phe Cys Cys Cys Glu Gly Asn Phe Cys Asn Glu Arg Phe Thr
                85                  90                  95
His Leu Pro Glu Ala Gly Gly Gly Thr His Thr Cys Pro Pro Cys Pro
            100                 105                 110
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        115                 120                 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
    130                 135                 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145                 150                 155                 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                165                 170                 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            180                 185                 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
        195                 200                 205
Ala Leu Pro Val Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
    210                 215                 220
```

```
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
225                 230                 235                 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
                245                 250                 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
            260                 265                 270
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
        275                 280                 285
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
    290                 295                 300
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
305                 310                 315                 320
Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325
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<210> 48
<211> 141
<212> PRT
<213> Artificial Sequence

<220>
<223> Exemplary human hemoglobin alpha subunit

<400> 48

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Val Leu Ser Pro Ala Asp Lys Thr Asn Val Lys Ala Ala Trp Gly Lys
 1               5                  10                  15
Val Gly Ala His Ala Gly Glu Tyr Gly Ala Glu Ala Leu Glu Arg Met
            20                  25                  30
Phe Leu Ser Phe Pro Thr Thr Lys Thr Tyr Phe Pro His Phe Asp Leu
        35                  40                  45
Ser His Gly Ser Ala Gln Val Lys Gly His Gly Lys Lys Val Ala Asp
    50                  55                  60
Ala Leu Thr Asn Ala Val Ala His Val Asp Asp Met Pro Asn Ala Leu
65                  70                  75                  80
Ser Ala Leu Ser Asp Leu His Ala His Lys Leu Arg Val Asp Pro Val
                85                  90                  95
Asn Phe Lys Leu Leu Ser His Cys Leu Leu Val Thr Leu Ala Ala His
            100                 105                 110
Leu Pro Ala Glu Phe Thr Pro Ala Val His Ala Ser Leu Asp Lys Phe
        115                 120                 125
Leu Ala Ser Val Ser Thr Val Leu Thr Ser Lys Tyr Arg
    130                 135                 140
```

<210> 49
<211> 146
<212> PRT

<213> Artificial Sequence

<220>
<223> Exemplary human hemoglobin beta subunit

<400> 49
Gly His Phe Thr Glu Glu Asp Lys Ala Thr Ile Thr Ser Leu Trp Gly
 1   5   10   15
Lys Val Asn Val Glu Asp Ala Gly Gly Glu Thr Leu Gly Arg Leu Leu
            20   25   30
Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Asp Ser Phe Gly Asn Leu
        35   40   45
Ser Ser Ala Ser Ala Ile Met Gly Asn Pro Lys Val Lys Ala His Gly
    50   55   60
Lys Lys Val Leu Thr Ser Leu Gly Asp Ala Thr Lys His Leu Asp Asp
65   70   75   80
Leu Lys Gly Thr Phe Ala Gln Leu Ser Glu Leu His Cys Asp Lys Leu
                85   90   95
His Val Asp Pro Glu Asn Phe Lys Leu Leu Gly Asn Val Leu Val Thr
            100   105   110
Val Leu Ala Ile His Phe Gly Lys Glu Phe Thr Pro Glu Val Gln Ala
        115   120   125
Ser Trp Gln Lys Met Val Thr Ala Val Ala Ser Ala Leu Ser Ser Arg
    130   135   140
Tyr His
145

<210> 50
<211> 146
<212> PRT
<213> Artificial Sequence

<220>
<223> Exemplary human hemoglobin gamma subunit

<400> 50
Val His Leu Thr Pro Glu Glu Lys Ser Ala Val Thr Ala Leu Trp Gly
 1   5   10   15
Lys Val Asn Val Asp Glu Val Gly Gly Glu Ala Leu Gly Arg Leu Leu
            20   25   30
Val Val Tyr Pro Trp Thr Gln Arg Phe Phe Glu Ser Phe Gly Asp Leu
        35   40   45
Ser Thr Pro Asp Ala Val Met Gly Asn Pro Lys Val Lys Ala His Gly
    50   55   60
Lys Lys Val Leu Gly Ala Phe Ser Asp Gly Leu Ala His Leu Asp Asn
65   70   75   80
Leu Lys Gly Thr Phe Ala Thr Leu Ser Glu Leu His Cys Asp Lys Leu

```
                85                  90                  95
His Val Asp Pro Glu Asn Phe Arg Leu Leu Gly Asn Val Leu Val Cys
            100                 105                 110
Val Leu Ala His His Phe Gly Lys Glu Phe Thr Pro Pro Val Gln Ala
        115                 120                 125
Ala Tyr Gln Lys Val Val Ala Gly Val Ala Asn Ala Leu Ala His Lys
    130                 135                 140
Tyr His
145
```