

pctib2010054908-seq1
SEQUENCE LISTING

<110> Pfizer Inc
Bagley, Scott W.
Griffith, David A.
Kung, Daniel W.-S.

<120> N1-Pyrazolospiroketone Acetyl-CoA Carboxylase Inhibitors

<130> PC33982

<150> 61/259,823
<151> 2009-11-10

<160> 2

<170> PatentIn version 3.5

<210> 1
<211> 2356
<212> PRT
<213> Homo sapiens

<400> 1

Met Ala His His His His His His Asp Glu Val Asp Asp Glu Pro Ser
1 5 10 15

Pro Leu Ala Gln Pro Leu Glu Leu Asn Gln His Ser Arg Phe Ile Ile
20 25 30

Gly Ser Val Ser Glu Asp Asn Ser Glu Asp Glu Ile Ser Asn Leu Val
35 40 45

Lys Leu Asp Leu Leu Glu Lys Glu Gly Ser Leu Ser Pro Ala Ser Val
50 55 60

Gly Ser Asp Thr Leu Ser Asp Leu Gly Ile Ser Ser Leu Gln Asp Gly
65 70 75 80

Leu Ala Leu His Ile Arg Ser Ser Met Ser Gly Leu His Leu Val Lys
85 90 95

Gln Gly Arg Asp Arg Lys Lys Ile Asp Ser Gln Arg Asp Phe Thr Val
100 105 110

Ala Ser Pro Ala Glu Phe Val Thr Arg Phe Gly Gly Asn Lys Val Ile
115 120 125

Glu Lys Val Leu Ile Ala Asn Asn Gly Ile Ala Ala Val Lys Cys Met
130 135 140

Arg Ser Ile Arg Arg Trp Ser Tyr Glu Met Phe Arg Asn Glu Arg Ala
145 150 155 160

Ile Arg Phe Val Val Met Val Thr Pro Glu Asp Leu Lys Ala Asn Ala
165 170 175

pctib2010054908-seq1

Glu Tyr Ile Lys Met Ala Asp His Tyr Val Pro Val Pro Gly Gly Pro
 180 185 190
 Asn Asn Asn Asn Tyr Ala Asn Val Glu Leu Ile Leu Asp Ile Ala Lys
 195 200 205
 Arg Ile Pro Val Gln Ala Val Trp Ala Gly Trp Gly His Ala Ser Glu
 210 215 220
 Asn Pro Lys Leu Pro Glu Leu Leu Leu Lys Asn Gly Ile Ala Phe Met
 225 230 235 240
 Gly Pro Pro Ser Gln Ala Met Trp Ala Leu Gly Asp Lys Ile Ala Ser
 245 250 255
 Ser Ile Val Ala Gln Thr Ala Gly Ile Pro Thr Leu Pro Trp Ser Gly
 260 265 270
 Ser Gly Leu Arg Val Asp Trp Gln Glu Asn Asp Phe Ser Lys Arg Ile
 275 280 285
 Leu Asn Val Pro Gln Glu Leu Tyr Glu Lys Gly Tyr Val Lys Asp Val
 290 295 300
 Asp Asp Gly Leu Gln Ala Ala Glu Glu Val Gly Tyr Pro Val Met Ile
 305 310 315 320
 Lys Ala Ser Glu Gly Gly Gly Lys Gly Ile Arg Lys Val Asn Asn
 325 330 335
 Ala Asp Asp Phe Pro Asn Leu Phe Arg Gln Val Gln Ala Glu Val Pro
 340 345 350
 Gly Ser Pro Ile Phe Val Met Arg Leu Ala Lys Gln Ser Arg His Leu
 355 360 365
 Glu Val Gln Ile Leu Ala Asp Gln Tyr Gly Asn Ala Ile Ser Leu Phe
 370 375 380
 Gly Arg Asp Cys Ser Val Gln Arg Arg His Gln Lys Ile Ile Glu Glu
 385 390 395 400
 Ala Pro Ala Thr Ile Ala Thr Pro Ala Val Phe Glu His Met Glu Gln
 405 410 415
 Cys Ala Val Lys Leu Ala Lys Met Val Gly Tyr Val Ser Ala Gly Thr
 420 425 430
 Val Glu Tyr Leu Tyr Ser Gln Asp Gly Ser Phe Tyr Phe Leu Glu Leu
 435 440 445

pctib2010054908-seq1

Asn Pro Arg Leu Gln Val Glu His Pro Cys Thr Glu Met Val Ala Asp
 450 455 460
 Val Asn Leu Pro Ala Ala Gln Leu Gln Ile Ala Met Gly Ile Pro Leu
 465 470 475 480
 Tyr Arg Ile Lys Asp Ile Arg Met Met Tyr Gly Val Ser Pro Trp Gly
 485 490 495
 Asp Ser Pro Ile Asp Phe Glu Asp Ser Ala His Val Pro Cys Pro Arg
 500 505 510
 Gly His Val Ile Ala Ala Arg Ile Thr Ser Glu Asn Pro Asp Glu Gly
 515 520 525
 Phe Lys Pro Ser Ser Gly Thr Val Gln Glu Leu Asn Phe Arg Ser Asn
 530 535 540
 Lys Asn Val Trp Gly Tyr Phe Ser Val Ala Ala Ala Gly Gly Leu His
 545 550 555 560
 Glu Phe Ala Asp Ser Gln Phe Gly His Cys Phe Ser Trp Gly Glu Asn
 565 570 575
 Arg Glu Glu Ala Ile Ser Asn Met Val Val Ala Leu Lys Glu Leu Ser
 580 585 590
 Ile Arg Gly Asp Phe Arg Thr Thr Val Glu Tyr Leu Ile Lys Leu Leu
 595 600 605
 Glu Thr Glu Ser Phe Gln Met Asn Arg Ile Asp Thr Gly Trp Leu Asp
 610 615 620
 Arg Leu Ile Ala Glu Lys Val Gln Ala Glu Arg Pro Asp Thr Met Leu
 625 630 635 640
 Gly Val Val Cys Gly Ala Leu His Val Ala Asp Val Ser Leu Arg Asn
 645 650 655
 Ser Val Ser Asn Phe Leu His Ser Leu Glu Arg Gly Gln Val Leu Pro
 660 665 670
 Ala His Thr Leu Leu Asn Thr Val Asp Val Glu Leu Ile Tyr Glu Gly
 675 680 685
 Val Lys Tyr Val Leu Lys Val Thr Arg Gln Ser Pro Asn Ser Tyr Val
 690 695 700
 Val Ile Met Asn Gly Ser Cys Val Glu Val Asp Val His Arg Leu Ser
 705 710 715 720

pctib2010054908-seq1

Asp Gly Gly Leu Leu₇₂₅ Leu Ser Tyr Asp Gly₇₃₀ Ser Ser Tyr Thr Thr₇₃₅ Tyr
 Met Lys Glu Glu₇₄₀ Val Asp Arg Tyr Arg₇₄₅ Ile Thr Ile Gly Asn₇₅₀ Lys Thr
 Cys Val Phe Glu Lys Glu Asn Asp₇₆₀ Pro Ser Val Met Arg₇₆₅ Ser Pro Ser
 Ala Gly Lys Leu Ile Gln Tyr₇₇₅ Ile Val Glu Asp Gly₇₈₀ Gly His Val Phe
 Ala Gly Gln Cys Tyr Ala₇₉₀ Glu Ile Glu Val Met₇₉₅ Lys Met Val Met Thr₈₀₀
 Leu Thr Ala Val Glu₈₀₅ Ser Gly Cys Ile His₈₁₀ Tyr Val Lys Arg Pro Gly₈₁₅
 Ala Ala Leu Asp₈₂₀ Pro Gly Cys Val Leu₈₂₅ Ala Lys Met Gln Leu₈₃₀ Asp Asn
 Pro Ser Lys Val Gln Gln Ala Glu₈₄₀ Leu His Thr Gly Ser₈₄₅ Leu Pro Arg
 Ile Gln Ser Thr Ala Leu Arg₈₅₅ Gly Glu Lys Leu His₈₆₀ Arg Val Phe His
 Tyr Val Leu Asp Asn Leu₈₇₀ Val Asn Val Met Asn₈₇₅ Gly Tyr Cys Leu Pro₈₈₀
 Asp Pro Phe Phe Ser₈₈₅ Ser Lys Val Lys Asp₈₉₀ Trp Val Glu Arg Leu Met₈₉₅
 Lys Thr Leu Arg₉₀₀ Asp Pro Ser Leu Pro₉₀₅ Leu Leu Glu Leu Gln₉₁₀ Asp Ile
 Met Thr Ser Val Ser Gly Arg Ile₉₂₀ Pro Pro Asn Val Glu₉₂₅ Lys Ser Ile
 Lys Lys Glu Met Ala Gln Tyr₉₃₅ Ala Ser Asn Ile Thr₉₄₀ Ser Val Leu Cys
 Gln Phe Pro Ser Gln Gln₉₅₀ Ile Ala Asn Ile Leu₉₅₅ Asp Ser His Ala Ala₉₆₀
 Thr Leu Asn Arg Lys₉₆₅ Ser Glu Arg Glu Val Phe Phe Met Asn Thr₉₇₅ Gln
 Ser Ile Val Gln Leu Val Gln Arg Tyr₉₈₅ Arg Ser Gly Ile Arg₉₉₀ Gly His

pctib2010054908-seq1

Met Lys Ala Val Val Met Asp Leu Leu Arg Gln Tyr Leu Arg Val Glu
995 1000 1005

Thr Gln Phe Gln Asn Gly His Tyr Asp Lys Cys Val Phe Ala Leu
1010 1015 1020

Arg Glu Glu Asn Lys Ser Asp Met Asn Thr Val Leu Asn Tyr Ile
1025 1030 1035

Phe Ser His Ala Gln Val Thr Lys Lys Asn Leu Leu Val Thr Met
1040 1045 1050

Leu Ile Asp Gln Leu Cys Gly Arg Asp Pro Thr Leu Thr Asp Glu
1055 1060 1065

Leu Leu Asn Ile Leu Thr Glu Leu Thr Gln Leu Ser Lys Thr Thr
1070 1075 1080

Asn Ala Lys Val Ala Leu Arg Ala Arg Gln Val Leu Ile Ala Ser
1085 1090 1095

His Leu Pro Ser Tyr Glu Leu Arg His Asn Gln Val Glu Ser Ile
1100 1105 1110

Phe Leu Ser Ala Ile Asp Met Tyr Gly His Gln Phe Cys Ile Glu
1115 1120 1125

Asn Leu Gln Lys Leu Ile Leu Ser Glu Thr Ser Ile Phe Asp Val
1130 1135 1140

Leu Pro Asn Phe Phe Tyr His Ser Asn Gln Val Val Arg Met Ala
1145 1150 1155

Ala Leu Glu Val Tyr Val Arg Arg Ala Tyr Ile Ala Tyr Glu Leu
1160 1165 1170

Asn Ser Val Gln His Arg Gln Leu Lys Asp Asn Thr Cys Val Val
1175 1180 1185

Glu Phe Gln Phe Met Leu Pro Thr Ser His Pro Asn Arg Gly Asn
1190 1195 1200

Ile Pro Thr Leu Asn Arg Met Ser Phe Ser Ser Asn Leu Asn His
1205 1210 1215

Tyr Gly Met Thr His Val Ala Ser Val Ser Asp Val Leu Leu Asp
1220 1225 1230

Asn Ser Phe Thr Pro Pro Cys Gln Arg Met Gly Gly Met Val Ser
1235 1240 1245

pctib2010054908-seq1

Phe	Arg	Thr	Phe	Glu	Asp	Phe	Val	Arg	Ile	Phe	Asp	Glu	Val	Met
	1250					1255					1260			
Gly	Cys	Phe	Ser	Asp	Ser	Pro	Pro	Gln	Ser	Pro	Thr	Phe	Pro	Glu
	1265					1270					1275			
Ala	Gly	His	Thr	Ser	Leu	Tyr	Asp	Glu	Asp	Lys	Val	Pro	Arg	Asp
	1280					1285					1290			
Glu	Pro	Ile	His	Ile	Leu	Asn	Val	Ala	Ile	Lys	Thr	Asp	Cys	Asp
	1295					1300					1305			
Ile	Glu	Asp	Asp	Arg	Leu	Ala	Ala	Met	Phe	Arg	Glu	Phe	Thr	Gln
	1310					1315					1320			
Gln	Asn	Lys	Ala	Thr	Leu	Val	Asp	His	Gly	Ile	Arg	Arg	Leu	Thr
	1325					1330					1335			
Phe	Leu	Val	Ala	Gln	Lys	Asp	Phe	Arg	Lys	Gln	Val	Asn	Tyr	Glu
	1340					1345					1350			
Val	Asp	Arg	Arg	Phe	His	Arg	Glu	Phe	Pro	Lys	Phe	Phe	Thr	Phe
	1355					1360					1365			
Arg	Ala	Arg	Asp	Lys	Phe	Glu	Glu	Asp	Arg	Ile	Tyr	Arg	His	Leu
	1370					1375					1380			
Glu	Pro	Ala	Leu	Ala	Phe	Gln	Leu	Glu	Leu	Asn	Arg	Met	Arg	Asn
	1385					1390					1395			
Phe	Asp	Leu	Thr	Ala	Ile	Pro	Cys	Ala	Asn	His	Lys	Met	His	Leu
	1400					1405					1410			
Tyr	Leu	Gly	Ala	Ala	Lys	Val	Glu	Val	Gly	Thr	Glu	Val	Thr	Asp
	1415					1420					1425			
Tyr	Arg	Phe	Phe	Val	Arg	Ala	Ile	Ile	Arg	His	Ser	Asp	Leu	Val
	1430					1435					1440			
Thr	Lys	Glu	Ala	Ser	Phe	Glu	Tyr	Leu	Gln	Asn	Glu	Gly	Glu	Arg
	1445					1450					1455			
Leu	Leu	Leu	Glu	Ala	Met	Asp	Glu	Leu	Glu	Val	Ala	Phe	Asn	Asn
	1460					1465					1470			
Thr	Asn	Val	Arg	Thr	Asp	Cys	Asn	His	Ile	Phe	Leu	Asn	Phe	Val
	1475					1480					1485			
Pro	Thr	Val	Ile	Met	Asp	Pro	Ser	Lys	Ile	Glu	Glu	Ser	Val	Arg
	1490					1495					1500			

pctib2010054908-seq1

Ser	Met	Val	Met	Arg	Tyr	Gly	Ser	Arg	Leu	Trp	Lys	Leu	Arg	Val
	1505					1510					1515			
Leu	Gln	Ala	Glu	Leu	Lys	Ile	Asn	Ile	Arg	Leu	Thr	Pro	Thr	Gly
	1520					1525					1530			
Lys	Ala	Ile	Pro	Ile	Arg	Leu	Phe	Leu	Thr	Asn	Glu	Ser	Gly	Tyr
	1535					1540					1545			
Tyr	Leu	Asp	Ile	Ser	Leu	Tyr	Lys	Glu	Val	Thr	Asp	Ser	Arg	Thr
	1550					1555					1560			
Ala	Gln	Ile	Met	Phe	Gln	Ala	Tyr	Gly	Asp	Lys	Gln	Gly	Pro	Leu
	1565					1570					1575			
His	Gly	Met	Leu	Ile	Asn	Thr	Pro	Tyr	Val	Thr	Lys	Asp	Leu	Leu
	1580					1585					1590			
Gln	Ser	Lys	Arg	Phe	Gln	Ala	Gln	Ser	Leu	Gly	Thr	Thr	Tyr	Ile
	1595					1600					1605			
Tyr	Asp	Ile	Pro	Glu	Met	Phe	Arg	Gln	Ser	Leu	Ile	Lys	Leu	Trp
	1610					1615					1620			
Glu	Ser	Met	Ser	Thr	Gln	Ala	Phe	Leu	Pro	Ser	Pro	Pro	Leu	Pro
	1625					1630					1635			
Ser	Asp	Met	Leu	Thr	Tyr	Thr	Glu	Leu	Val	Leu	Asp	Asp	Gln	Gly
	1640					1645					1650			
Gln	Leu	Val	His	Met	Asn	Arg	Leu	Pro	Gly	Gly	Asn	Glu	Ile	Gly
	1655					1660					1665			
Met	Val	Ala	Trp	Lys	Met	Thr	Phe	Lys	Ser	Pro	Glu	Tyr	Pro	Glu
	1670					1675					1680			
Gly	Arg	Asp	Ile	Ile	Val	Ile	Gly	Asn	Asp	Ile	Thr	Tyr	Arg	Ile
	1685					1690					1695			
Gly	Ser	Phe	Gly	Pro	Gln	Glu	Asp	Leu	Leu	Phe	Leu	Arg	Ala	Ser
	1700					1705					1710			
Glu	Leu	Ala	Arg	Ala	Glu	Gly	Ile	Pro	Arg	Ile	Tyr	Val	Ser	Ala
	1715					1720					1725			
Asn	Ser	Gly	Ala	Arg	Ile	Gly	Leu	Ala	Glu	Glu	Ile	Arg	His	Met
	1730					1735					1740			
Phe	His	Val	Ala	Trp	Val	Asp	Pro	Glu	Asp	Pro	Tyr	Lys	Gly	Tyr
	1745					1750					1755			

pctib2010054908-seq1

Arg	Tyr	Leu	Tyr	Leu	Thr	Pro	Gln	Asp	Tyr	Lys	Arg	Val	Ser	Ala
	1760					1765					1770			
Leu	Asn	Ser	Val	His	Cys	Glu	His	Val	Glu	Asp	Glu	Gly	Glu	Ser
	1775					1780					1785			
Arg	Tyr	Lys	Ile	Thr	Asp	Ile	Ile	Gly	Lys	Glu	Glu	Gly	Ile	Gly
	1790					1795					1800			
Pro	Glu	Asn	Leu	Arg	Gly	Ser	Gly	Met	Ile	Ala	Gly	Glu	Ser	Ser
	1805					1810					1815			
Leu	Ala	Tyr	Asn	Glu	Ile	Ile	Thr	Ile	Ser	Leu	Val	Thr	Cys	Arg
	1820					1825					1830			
Ala	Ile	Gly	Ile	Gly	Ala	Tyr	Leu	Val	Arg	Leu	Gly	Gln	Arg	Thr
	1835					1840					1845			
Ile	Gln	Val	Glu	Asn	Ser	His	Leu	Ile	Leu	Thr	Gly	Ala	Gly	Ala
	1850					1855					1860			
Leu	Asn	Lys	Val	Leu	Gly	Arg	Glu	Val	Tyr	Thr	Ser	Asn	Asn	Gln
	1865					1870					1875			
Leu	Gly	Gly	Ile	Gln	Ile	Met	His	Asn	Asn	Gly	Val	Thr	His	Cys
	1880					1885					1890			
Thr	Val	Cys	Asp	Asp	Phe	Glu	Gly	Val	Phe	Thr	Val	Leu	His	Trp
	1895					1900					1905			
Leu	Ser	Tyr	Met	Pro	Lys	Ser	Val	His	Ser	Ser	Val	Pro	Leu	Leu
	1910					1915					1920			
Asn	Ser	Lys	Asp	Pro	Ile	Asp	Arg	Ile	Ile	Glu	Phe	Val	Pro	Thr
	1925					1930					1935			
Lys	Thr	Pro	Tyr	Asp	Pro	Arg	Trp	Met	Leu	Ala	Gly	Arg	Pro	His
	1940					1945					1950			
Pro	Thr	Gln	Lys	Gly	Gln	Trp	Leu	Ser	Gly	Phe	Phe	Asp	Tyr	Gly
	1955					1960					1965			
Ser	Phe	Ser	Glu	Ile	Met	Gln	Pro	Trp	Ala	Gln	Thr	Val	Val	Val
	1970					1975					1980			
Gly	Arg	Ala	Arg	Leu	Gly	Gly	Ile	Pro	Val	Gly	Val	Val	Ala	Val
	1985					1990					1995			
Glu	Thr	Arg	Thr	Val	Glu	Leu	Ser	Ile	Pro	Ala	Asp	Pro	Ala	Asn
	2000					2005					2010			

pctib2010054908-seq1

Leu	Asp	Ser	Glu	Ala	Lys	Ile	Ile	Gln	Gln	Ala	Gly	Gln	Val	Trp
	2015					2020					2025			
Phe	Pro	Asp	Ser	Ala	Phe	Lys	Thr	Tyr	Gln	Ala	Ile	Lys	Asp	Phe
	2030					2035					2040			
Asn	Arg	Glu	Gly	Leu	Pro	Leu	Met	Val	Phe	Ala	Asn	Trp	Arg	Gly
	2045					2050					2055			
Phe	Ser	Gly	Gly	Met	Lys	Asp	Met	Tyr	Asp	Gln	Val	Leu	Lys	Phe
	2060					2065					2070			
Gly	Ala	Tyr	Ile	Val	Asp	Gly	Leu	Arg	Glu	Cys	Cys	Gln	Pro	Val
	2075					2080					2085			
Leu	Val	Tyr	Ile	Pro	Pro	Gln	Ala	Glu	Leu	Arg	Gly	Gly	Ser	Trp
	2090					2095					2100			
Val	Val	Ile	Asp	Ser	Ser	Ile	Asn	Pro	Arg	His	Met	Glu	Met	Tyr
	2105					2110					2115			
Ala	Asp	Arg	Glu	Ser	Arg	Gly	Ser	Val	Leu	Glu	Pro	Glu	Gly	Thr
	2120					2125					2130			
Val	Glu	Ile	Lys	Phe	Arg	Arg	Lys	Asp	Leu	Val	Lys	Thr	Met	Arg
	2135					2140					2145			
Arg	Val	Asp	Pro	Val	Tyr	Ile	His	Leu	Ala	Glu	Arg	Leu	Gly	Thr
	2150					2155					2160			
Pro	Glu	Leu	Ser	Thr	Ala	Glu	Arg	Lys	Glu	Leu	Glu	Asn	Lys	Leu
	2165					2170					2175			
Lys	Glu	Arg	Glu	Glu	Phe	Leu	Ile	Pro	Ile	Tyr	His	Gln	Val	Ala
	2180					2185					2190			
Val	Gln	Phe	Ala	Asp	Leu	His	Asp	Thr	Pro	Gly	Arg	Met	Gln	Glu
	2195					2200					2205			
Lys	Gly	Val	Ile	Ser	Asp	Ile	Leu	Asp	Trp	Lys	Thr	Ser	Arg	Thr
	2210					2215					2220			
Phe	Phe	Tyr	Trp	Arg	Leu	Arg	Arg	Leu	Leu	Leu	Glu	Asp	Leu	Val
	2225					2230					2235			
Lys	Lys	Lys	Ile	His	Asn	Ala	Asn	Pro	Glu	Leu	Thr	Asp	Gly	Gln
	2240					2245					2250			
Ile	Gln	Ala	Met	Leu	Arg	Arg	Trp	Phe	Val	Glu	Val	Glu	Gly	Thr
	2255					2260					2265			

pctib2010054908-seq1

Val Lys Ala Tyr Val Trp Asp Asn Asn Lys Asp Leu Ala Glu Trp
2270 2275 2280

Leu Glu Lys Gln Leu Thr Glu Glu Asp Gly Val His Ser Val Ile
2285 2290 2295

Glu Glu Asn Ile Lys Cys Ile Ser Arg Asp Tyr Val Leu Lys Gln
2300 2305 2310

Ile Arg Ser Leu Val Gln Ala Asn Pro Glu Val Ala Met Asp Ser
2315 2320 2325

Ile Ile His Met Thr Gln His Ile Ser Pro Thr Gln Arg Ala Glu
2330 2335 2340

Val Ile Arg Ile Leu Ser Thr Met Asp Ser Pro Ser Thr
2345 2350 2355

<210> 2
<211> 2458
<212> PRT
<213> Homo sapiens

<400> 2

Met Val Leu Leu Leu Cys Leu Ser Cys Leu Ile Phe Ser Cys Leu Thr
1 5 10 15

Phe Ser Trp Leu Lys Ile Trp Gly Lys Met Thr Asp Ser Lys Pro Ile
20 25 30

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

Pro Ala Ser Asp Asn Ser Gly Glu Thr Pro Gln Arg Asn Gly Glu Gly
50 55 60

His Thr Leu Pro Lys Thr Pro Ser Gln Ala Glu Pro Ala Ser His Lys
65 70 75 80

Gly Pro Lys Asp Ala Gly Arg Arg Arg Asn Ser Leu Pro Pro Ser His
85 90 95

Gln Lys Pro Pro Arg Asn Pro Leu Ser Ser Ser Asp Ala Ala Pro Ser
100 105 110

Pro Glu Leu Gln Ala Asn Gly Thr Gly Thr Gln Gly Leu Glu Ala Thr
115 120 125

Asp Thr Asn Gly Leu Ser Ser Ser Ala Arg Pro Gln Gly Gln Gln Ala
130 135 140

pctib2010054908-seq1

Gly Ser Pro Ser Lys Glu Asp Lys Lys Gln Ala Asn Ile Lys Arg Gln
 145 150 155 160
 Leu Met Thr Asn Phe Ile Leu Gly Ser Phe Asp Asp Tyr Ser Ser Asp
 165 170 175
 Glu Asp Ser Val Ala Gly Ser Ser Arg Glu Ser Thr Arg Lys Gly Ser
 180 185 190
 Arg Ala Ser Leu Gly Ala Leu Ser Leu Glu Ala Tyr Leu Thr Thr Gly
 195 200 205
 Glu Ala Glu Thr Arg Val Pro Thr Met Arg Pro Ser Met Ser Gly Leu
 210 215 220
 His Leu Val Lys Arg Gly Arg Glu His Lys Lys Leu Asp Leu His Arg
 225 230 235 240
 Asp Phe Thr Val Ala Ser Pro Ala Glu Phe Val Thr Arg Phe Gly Gly
 245 250 255
 Asp Arg Val Ile Glu Lys Val Leu Ile Ala Asn Asn Gly Ile Ala Ala
 260 265 270
 Val Lys Cys Met Arg Ser Ile Arg Arg Trp Ala Tyr Glu Met Phe Arg
 275 280 285
 Asn Glu Arg Ala Ile Arg Phe Val Val Met Val Thr Pro Glu Asp Leu
 290 295 300
 Lys Ala Asn Ala Glu Tyr Ile Lys Met Ala Asp His Tyr Val Pro Val
 305 310 315 320
 Pro Gly Gly Pro Asn Asn Asn Asn Tyr Ala Asn Val Glu Leu Ile Val
 325 330 335
 Asp Ile Ala Lys Arg Ile Pro Val Gln Ala Val Trp Ala Gly Trp Gly
 340 345 350
 His Ala Ser Glu Asn Pro Lys Leu Pro Glu Leu Leu Cys Lys Asn Gly
 355 360 365
 Val Ala Phe Leu Gly Pro Pro Ser Glu Ala Met Trp Ala Leu Gly Asp
 370 375 380
 Lys Ile Ala Ser Thr Val Val Ala Gln Thr Leu Gln Val Pro Thr Leu
 385 390 395 400
 Pro Trp Ser Gly Ser Gly Leu Thr Val Glu Trp Thr Glu Asp Asp Leu
 405 410 415

pctib2010054908-seq1

Gln Gln Gly Lys Arg Ile Ser Val Pro Glu Asp Val Tyr Asp Lys Gly
420 425 430

Cys Val Lys Asp Val Asp Glu Gly Leu Glu Ala Ala Glu Arg Ile Gly
435 440 445

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

Arg Lys Ala Glu Ser Ala Glu Asp Phe Pro Ile Leu Phe Arg Gln Val
465 470 475 480

Gln Ser Glu Ile Pro Gly Ser Pro Ile Phe Leu Met Lys Leu Ala Gln
485 490 495

His Ala Arg His Leu Glu Val Gln Ile Leu Ala Asp Gln Tyr Gly Asn
500 505 510

Ala Val Ser Leu Phe Gly Arg Asp Cys Ser Ile Gln Arg Arg His Gln
515 520 525

Lys Ile Val Glu Glu Ala Pro Ala Thr Ile Ala Pro Leu Ala Ile Phe
530 535 540

Glu Phe Met Glu Gln Cys Ala Ile Arg Leu Ala Lys Thr Val Gly Tyr
545 550 555 560

Val Ser Ala Gly Thr Val Glu Tyr Leu Tyr Ser Gln Asp Gly Ser Phe
565 570 575

His Phe Leu Glu Leu Asn Pro Arg Leu Gln Val Glu His Pro Cys Thr
580 585 590

Glu Met Ile Ala Asp Val Asn Leu Pro Ala Ala Gln Leu Gln Ile Ala
595 600 605

Met Gly Val Pro Leu His Arg Leu Lys Asp Ile Arg Leu Leu Tyr Gly
610 615 620

Glu Ser Pro Trp Gly Val Thr Pro Ile Ser Phe Glu Thr Pro Ser Asn
625 630 635 640

Pro Pro Leu Ala Arg Gly His Val Ile Ala Ala Arg Ile Thr Ser Glu
645 650 655

Asn Pro Asp Glu Gly Phe Lys Pro Ser Ser Gly Thr Val Gln Glu Leu
660 665 670

Asn Phe Arg Ser Ser Lys Asn Val Trp Gly Tyr Phe Ser Val Ala Ala
675 680 685

pctib2010054908-seq1

Thr Gly Gly Leu His Glu Phe Ala Asp Ser Gln Phe Gly His Cys Phe
 690 695 700

Ser Trp Gly Glu Asn Arg Glu Glu Ala Ile Ser Asn Met Val Val Ala
 705 710 715 720

Leu Lys Glu Leu Ser Ile Arg Gly Asp Phe Arg Thr Thr Val Glu Tyr
 725 730 735

Leu Ile Asn Leu Leu Glu Thr Glu Ser Phe Gln Asn Asn Asp Ile Asp
 740 745 750

Thr Gly Trp Leu Asp Tyr Leu Ile Ala Glu Lys Val Gln Ala Glu Lys
 755 760 765

Pro Asp Ile Met Leu Gly Val Val Cys Gly Ala Leu Asn Val Ala Asp
 770 775 780

Ala Met Phe Arg Thr Cys Met Thr Asp Phe Leu His Ser Leu Glu Arg
 785 790 795 800

Gly Gln Val Leu Pro Ala Asp Ser Leu Leu Asn Leu Val Asp Val Glu
 805 810 815

Leu Ile Tyr Gly Gly Val Lys Tyr Ile Leu Lys Val Ala Arg Gln Ser
 820 825 830

Leu Thr Met Phe Val Leu Ile Met Asn Gly Cys His Ile Glu Ile Asp
 835 840 845

Ala His Arg Leu Asn Asp Gly Gly Leu Leu Leu Ser Tyr Asn Gly Asn
 850 855 860

Ser Tyr Thr Thr Tyr Met Lys Glu Glu Val Asp Ser Tyr Arg Ile Thr
 865 870 875 880

Ile Gly Asn Lys Thr Cys Val Phe Glu Lys Glu Asn Asp Pro Thr Val
 885 890 895

Leu Arg Ser Pro Ser Ala Gly Lys Leu Thr Gln Tyr Thr Val Glu Asp
 900 905 910

Gly Gly His Val Glu Ala Gly Ser Ser Tyr Ala Glu Met Glu Val Met
 915 920 925

Lys Met Ile Met Thr Leu Asn Val Gln Glu Arg Gly Arg Val Lys Tyr
 930 935 940

Ile Lys Arg Pro Gly Ala Val Leu Glu Ala Gly Cys Val Val Ala Arg
 945 950 955 960

pctib2010054908-seq1

Leu Glu Leu Asp Asp Pro Ser Lys Val His Pro Ala Glu Pro Phe Thr
965 970 975

Gly Glu Leu Pro Ala Gln Gln Thr Leu Pro Ile Leu Gly Glu Lys Leu
980 985 990

His Gln Val Phe His Ser Val Leu Glu Asn Leu Thr Asn Val Met Ser
995 1000 1005

Gly Phe Cys Leu Pro Glu Pro Val Phe Ser Ile Lys Leu Lys Glu
1010 1015 1020

Trp Val Gln Lys Leu Met Met Thr Leu Arg His Pro Ser Leu Pro
1025 1030 1035

Leu Leu Glu Leu Gln Glu Ile Met Thr Ser Val Ala Gly Arg Ile
1040 1045 1050

Pro Ala Pro Val Glu Lys Ser Val Arg Arg Val Met Ala Gln Tyr
1055 1060 1065

Ala Ser Asn Ile Thr Ser Val Leu Cys Gln Phe Pro Ser Gln Gln
1070 1075 1080

Ile Ala Thr Ile Leu Asp Cys His Ala Ala Thr Leu Gln Arg Lys
1085 1090 1095

Ala Asp Arg Glu Val Phe Phe Ile Asn Thr Gln Ser Ile Val Gln
1100 1105 1110

Leu Val Gln Arg Tyr Arg Ser Gly Ile Arg Gly Tyr Met Lys Thr
1115 1120 1125

Val Val Leu Asp Leu Leu Arg Arg Tyr Leu Arg Val Glu His His
1130 1135 1140

Phe Gln Gln Ala His Tyr Asp Lys Cys Val Ile Asn Leu Arg Glu
1145 1150 1155

Gln Phe Lys Pro Asp Met Ser Gln Val Leu Asp Cys Ile Phe Ser
1160 1165 1170

His Ala Gln Val Ala Lys Lys Asn Gln Leu Val Ile Met Leu Ile
1175 1180 1185

Asp Glu Leu Cys Gly Pro Asp Pro Ser Leu Ser Asp Glu Leu Ile
1190 1195 1200

Ser Ile Leu Asn Glu Leu Thr Gln Leu Ser Lys Ser Glu His Cys
1205 1210 1215

pctib2010054908-seq1

Lys	Val	Ala	Leu	Arg	Ala	Arg	Gln	Ile	Leu	Ile	Ala	Ser	His	Leu
1220						1225					1230			
Pro	Ser	Tyr	Glu	Leu	Arg	His	Asn	Gln	Val	Glu	Ser	Ile	Phe	Leu
	1235					1240					1245			
Ser	Ala	Ile	Asp	Met	Tyr	Gly	His	Gln	Phe	Cys	Pro	Glu	Asn	Leu
	1250					1255					1260			
Lys	Lys	Leu	Ile	Leu	Ser	Glu	Thr	Thr	Ile	Phe	Asp	Val	Leu	Pro
	1265					1270					1275			
Thr	Phe	Phe	Tyr	His	Ala	Asn	Lys	Val	Val	Cys	Met	Ala	Ser	Leu
	1280					1285					1290			
Glu	Val	Tyr	Val	Arg	Arg	Gly	Tyr	Ile	Ala	Tyr	Glu	Leu	Asn	Ser
	1295					1300					1305			
Leu	Gln	His	Arg	Gln	Leu	Pro	Asp	Gly	Thr	Cys	Val	Val	Glu	Phe
	1310					1315					1320			
Gln	Phe	Met	Leu	Pro	Ser	Ser	His	Pro	Asn	Arg	Met	Thr	Val	Pro
	1325					1330					1335			
Ile	Ser	Ile	Thr	Asn	Pro	Asp	Leu	Leu	Arg	His	Ser	Thr	Glu	Leu
	1340					1345					1350			
Phe	Met	Asp	Ser	Gly	Phe	Ser	Pro	Leu	Cys	Gln	Arg	Met	Gly	Ala
	1355					1360					1365			
Met	Val	Ala	Phe	Arg	Arg	Phe	Glu	Asp	Phe	Thr	Arg	Asn	Phe	Asp
	1370					1375					1380			
Glu	Val	Ile	Ser	Cys	Phe	Ala	Asn	Val	Pro	Lys	Asp	Thr	Pro	Leu
	1385					1390					1395			
Phe	Ser	Glu	Ala	Arg	Thr	Ser	Leu	Tyr	Ser	Glu	Asp	Asp	Cys	Lys
	1400					1405					1410			
Ser	Leu	Arg	Glu	Glu	Pro	Ile	His	Ile	Leu	Asn	Val	Ser	Ile	Gln
	1415					1420					1425			
Cys	Ala	Asp	His	Leu	Glu	Asp	Glu	Ala	Leu	Val	Pro	Ile	Leu	Arg
	1430					1435					1440			
Thr	Phe	Val	Gln	Ser	Lys	Lys	Asn	Ile	Leu	Val	Asp	Tyr	Gly	Leu
	1445					1450					1455			
Arg	Arg	Ile	Thr	Phe	Leu	Ile	Ala	Gln	Glu	Lys	Glu	Phe	Pro	Lys
	1460					1465					1470			

pctib2010054908-seq1

Phe	Phe	Thr	Phe	Arg	Ala	Arg	Asp	Glu	Phe	Ala	Glu	Asp	Arg	Ile
	1475					1480					1485			
Tyr	Arg	His	Leu	Glu	Pro	Ala	Leu	Ala	Phe	Gln	Leu	Glu	Leu	Asn
	1490					1495					1500			
Arg	Met	Arg	Asn	Phe	Asp	Leu	Thr	Ala	Val	Pro	Cys	Ala	Asn	His
	1505					1510					1515			
Lys	Met	His	Leu	Tyr	Leu	Gly	Ala	Ala	Lys	Val	Lys	Glu	Gly	Val
	1520					1525					1530			
Glu	Val	Thr	Asp	His	Arg	Phe	Phe	Ile	Arg	Ala	Ile	Ile	Arg	His
	1535					1540					1545			
Ser	Asp	Leu	Ile	Thr	Lys	Glu	Ala	Ser	Phe	Glu	Tyr	Leu	Gln	Asn
	1550					1555					1560			
Glu	Gly	Glu	Arg	Leu	Leu	Leu	Glu	Ala	Met	Asp	Glu	Leu	Glu	Val
	1565					1570					1575			
Ala	Phe	Asn	Asn	Thr	Ser	Val	Arg	Thr	Asp	Cys	Asn	His	Ile	Phe
	1580					1585					1590			
Leu	Asn	Phe	Val	Pro	Thr	Val	Ile	Met	Asp	Pro	Phe	Lys	Ile	Glu
	1595					1600					1605			
Glu	Ser	Val	Arg	Tyr	Met	Val	Met	Arg	Tyr	Gly	Ser	Arg	Leu	Trp
	1610					1615					1620			
Lys	Leu	Arg	Val	Leu	Gln	Ala	Glu	Val	Lys	Ile	Asn	Ile	Arg	Gln
	1625					1630					1635			
Thr	Thr	Thr	Gly	Ser	Ala	Val	Pro	Ile	Arg	Leu	Phe	Ile	Thr	Asn
	1640					1645					1650			
Glu	Ser	Gly	Tyr	Tyr	Leu	Asp	Ile	Ser	Leu	Tyr	Lys	Glu	Val	Thr
	1655					1660					1665			
Asp	Ser	Arg	Ser	Gly	Asn	Ile	Met	Phe	His	Ser	Phe	Gly	Asn	Lys
	1670					1675					1680			
Gln	Gly	Pro	Gln	His	Gly	Met	Leu	Ile	Asn	Thr	Pro	Tyr	Val	Thr
	1685					1690					1695			
Lys	Asp	Leu	Leu	Gln	Ala	Lys	Arg	Phe	Gln	Ala	Gln	Thr	Leu	Gly
	1700					1705					1710			
Thr	Thr	Tyr	Ile	Tyr	Asp	Phe	Pro	Glu	Met	Phe	Arg	Gln	Ala	Leu
	1715					1720					1725			

pctib2010054908-seq1

Phe	Lys	Leu	Trp	Gly	Ser	Pro	Asp	Lys	Tyr	Pro	Lys	Asp	Ile	Leu
	1730					1735					1740			
Thr	Tyr	Thr	Glu	Leu	Val	Leu	Asp	Ser	Gln	Gly	Gln	Leu	Val	Glu
	1745					1750					1755			
Met	Asn	Arg	Leu	Pro	Gly	Gly	Asn	Glu	Val	Gly	Met	Val	Ala	Phe
	1760					1765					1770			
Lys	Met	Arg	Phe	Lys	Thr	Gln	Glu	Tyr	Pro	Glu	Gly	Arg	Asp	Val
	1775					1780					1785			
Ile	Val	Ile	Gly	Asn	Asp	Ile	Thr	Phe	Arg	Ile	Gly	Ser	Phe	Gly
	1790					1795					1800			
Pro	Gly	Glu	Asp	Leu	Leu	Tyr	Leu	Arg	Ala	Ser	Glu	Met	Ala	Arg
	1805					1810					1815			
Ala	Glu	Gly	Ile	Pro	Lys	Ile	Tyr	Val	Ala	Ala	Asn	Ser	Gly	Ala
	1820					1825					1830			
Arg	Ile	Gly	Met	Ala	Glu	Glu	Ile	Lys	His	Met	Phe	His	Val	Ala
	1835					1840					1845			
Trp	Val	Asp	Pro	Glu	Asp	Pro	His	Lys	Gly	Phe	Lys	Tyr	Leu	Tyr
	1850					1855					1860			
Leu	Thr	Pro	Gln	Asp	Tyr	Thr	Arg	Ile	Ser	Ser	Leu	Asn	Ser	Val
	1865					1870					1875			
His	Cys	Lys	His	Ile	Glu	Glu	Gly	Gly	Glu	Ser	Arg	Tyr	Met	Ile
	1880					1885					1890			
Thr	Asp	Ile	Ile	Gly	Lys	Asp	Asp	Gly	Leu	Gly	Val	Glu	Asn	Leu
	1895					1900					1905			
Arg	Gly	Ser	Gly	Met	Ile	Ala	Gly	Glu	Ser	Ser	Leu	Ala	Tyr	Glu
	1910					1915					1920			
Glu	Ile	Val	Thr	Ile	Ser	Leu	Val	Thr	Cys	Arg	Ala	Ile	Gly	Ile
	1925					1930					1935			
Gly	Ala	Tyr	Leu	Val	Arg	Leu	Gly	Gln	Arg	Val	Ile	Gln	Val	Glu
	1940					1945					1950			
Asn	Ser	His	Ile	Ile	Leu	Thr	Gly	Ala	Ser	Ala	Leu	Asn	Lys	Val
	1955					1960					1965			
Leu	Gly	Arg	Glu	Val	Tyr	Thr	Ser	Asn	Asn	Gln	Leu	Gly	Gly	Val
	1970					1975					1980			

pctib2010054908-seq1

Gln	Ile	Met	His	Tyr	Asn	Gly	Val	Ser	His	Ile	Thr	Val	Pro	Asp
1985						1990					1995			
Asp	Phe	Glu	Gly	Val	Tyr	Thr	Ile	Leu	Glu	Trp	Leu	Ser	Tyr	Met
2000						2005					2010			
Pro	Lys	Asp	Asn	His	Ser	Pro	Val	Pro	Ile	Ile	Thr	Pro	Thr	Asp
2015						2020					2025			
Pro	Ile	Asp	Arg	Glu	Ile	Glu	Phe	Leu	Pro	Ser	Arg	Ala	Pro	Tyr
2030						2035					2040			
Asp	Pro	Arg	Trp	Met	Leu	Ala	Gly	Arg	Pro	His	Pro	Thr	Leu	Lys
2045						2050					2055			
Gly	Thr	Trp	Gln	Ser	Gly	Phe	Phe	Asp	His	Gly	Ser	Phe	Lys	Glu
2060						2065					2070			
Ile	Met	Ala	Pro	Trp	Ala	Gln	Thr	Val	Val	Thr	Gly	Arg	Ala	Arg
2075						2080					2085			
Leu	Gly	Gly	Ile	Pro	Val	Gly	Val	Ile	Ala	Val	Glu	Thr	Arg	Thr
2090						2095					2100			
Val	Glu	Val	Ala	Val	Pro	Ala	Asp	Pro	Ala	Asn	Leu	Asp	Ser	Glu
2105						2110					2115			
Ala	Lys	Ile	Ile	Gln	Gln	Ala	Gly	Gln	Val	Trp	Phe	Pro	Asp	Ser
2120						2125					2130			
Ala	Tyr	Lys	Thr	Ala	Gln	Ala	Ile	Lys	Asp	Phe	Asn	Arg	Glu	Lys
2135						2140					2145			
Leu	Pro	Leu	Met	Ile	Phe	Ala	Asn	Trp	Arg	Gly	Phe	Ser	Gly	Gly
2150						2155					2160			
Met	Lys	Asp	Met	Tyr	Asp	Gln	Val	Leu	Lys	Phe	Gly	Ala	Tyr	Ile
2165						2170					2175			
Val	Asp	Gly	Leu	Arg	Gln	Tyr	Lys	Gln	Pro	Ile	Leu	Ile	Tyr	Ile
2180						2185					2190			
Pro	Pro	Tyr	Ala	Glu	Leu	Arg	Gly	Gly	Ser	Trp	Val	Val	Ile	Asp
2195						2200					2205			
Ala	Thr	Ile	Asn	Pro	Leu	Cys	Ile	Glu	Met	Tyr	Ala	Asp	Lys	Glu
2210						2215					2220			
Ser	Arg	Gly	Gly	Val	Leu	Glu	Pro	Glu	Gly	Thr	Val	Glu	Ile	Lys
2225						2230					2235			

pctib2010054908-seq1

Phe	Arg	Lys	Lys	Asp	Leu	Ile	Lys	Ser	Met	Arg	Arg	Ile	Asp	Pro
2240						2245					2250			
Ala	Tyr	Lys	Lys	Leu	Met	Glu	Gln	Leu	Gly	Glu	Pro	Asp	Leu	Ser
2255						2260					2265			
Asp	Lys	Asp	Arg	Lys	Asp	Leu	Glu	Gly	Arg	Leu	Lys	Ala	Arg	Glu
2270						2275					2280			
Asp	Leu	Leu	Leu	Pro	Ile	Tyr	His	Gln	Val	Ala	Val	Gln	Phe	Ala
2285						2290					2295			
Asp	Phe	His	Asp	Thr	Pro	Gly	Arg	Met	Leu	Glu	Lys	Gly	Val	Ile
2300						2305					2310			
Ser	Asp	Ile	Leu	Glu	Trp	Lys	Thr	Ala	Arg	Thr	Phe	Leu	Tyr	Trp
2315						2320					2325			
Arg	Leu	Arg	Arg	Leu	Leu	Leu	Glu	Asp	Gln	Val	Lys	Gln	Glu	Ile
2330						2335					2340			
Leu	Gln	Ala	Ser	Gly	Glu	Leu	Ser	His	Val	His	Ile	Gln	Ser	Met
2345						2350					2355			
Leu	Arg	Arg	Trp	Phe	Val	Glu	Thr	Glu	Gly	Ala	Val	Lys	Ala	Tyr
2360						2365					2370			
Leu	Trp	Asp	Asn	Asn	Gln	Val	Val	Val	Gln	Trp	Leu	Glu	Gln	His
2375						2380					2385			
Trp	Gln	Ala	Gly	Asp	Gly	Pro	Arg	Ser	Thr	Ile	Arg	Glu	Asn	Ile
2390						2395					2400			
Thr	Tyr	Leu	Lys	His	Asp	Ser	Val	Leu	Lys	Thr	Ile	Arg	Gly	Leu
2405						2410					2415			
Val	Glu	Glu	Asn	Pro	Glu	Val	Ala	Val	Asp	Cys	Val	Ile	Tyr	Leu
2420						2425					2430			
Ser	Gln	His	Ile	Ser	Pro	Ala	Glu	Arg	Ala	Gln	Val	Val	His	Leu
2435						2440					2445			
Leu	Ser	Thr	Met	Asp	Ser	Pro	Ala	Ser	Thr					
2450						2455								