

SEQUENCE LISTING

<110> GENENTECH, INC.

<120> SOLID FORMS OF 3-((1R,3R)-1-(2,6-DIFLUORO-4-((1-(3-FLUOROPROPYL) AZETIDIN-3-YL)AMINO)PHENYL)-3-METHYL-1,3,4,9-TETRAHYDRO -2H-PYRIDO[3,4-B]INDOL-2-YL)-2,2-DIFLUOROPROPAN-1-OL AND PROCESSES FOR PREPARING FUSED TRICYCLIC COMPOUNDS COMPRISING A SUBSTITUTED PHENYL OR PYRIDINYL MOIETY, INCLUDING METHODS OF THEIR USE

<130> P34807-WO

<140>

<141>

<150> 62/719,896

<151> 2018-08-20

<150> 62/687,930

<151> 2018-06-21

<160> 4

<170> PatentIn version 3.5

<210> 1

<211> 457

<212> PRT

<213> Artificial Sequence

<220>

<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1

Met Leu Lys Asn Asp Gln Leu Asp Gln Trp Asp Arg Asp Asn Phe Phe
1 5 10 15

His Pro Ser Thr His Leu Ala Gln His Ala Arg Gly Glu Ser Ala Asn
20 25 30

Arg Val Ile Lys Thr Ala Ser Gly Val Phe Ile Glu Asp Arg Asp Gly
35 40 45

Thr Lys Leu Leu Asp Ala Phe Ala Gly Leu Phe Cys Val Asn Val Gly
50 55 60

Tyr Gly Arg Gln Glu Ile Ala Glu Ala Ile Ala Asp Gln Ala Arg Glu
65 70 75 80

Leu Ala Tyr Tyr His Ser Phe Val Gly His Gly Thr Glu Ala Ser Ile
85 90 95

Thr Leu Ala Lys Met Ile Leu Asp Arg Ala Pro Lys Asn Met Ser Lys
100 105 110

Val Tyr Phe Gly Leu Gly Gly Ser Asp Ala Asn Glu Thr Asn Val Lys
115 120 125

Leu Ile Trp Tyr Tyr Asn Asn Ile Leu Gly Arg Pro Glu Lys Lys Lys
130 135 140

Ile Ile Ser Arg Trp Arg Gly Tyr His Gly Ser Gly Leu Val Thr Gly
145 150 155 160

Ser Leu Thr Gly Leu Glu Leu Phe His Lys Lys Phe Asp Leu Pro Val
165 170 175

Glu Gln Val Ile His Thr Glu Ala Pro Tyr Tyr Phe Arg Arg Glu Asp
180 185 190

Leu Asn Gln Thr Glu Glu Gln Phe Val Ala His Cys Val Ala Glu Leu
195 200 205

Glu Ala Leu Ile Glu Arg Glu Gly Ala Asp Thr Ile Ala Ala Phe Ile
210 215 220

Gly Glu Pro Ile Leu Gly Gly Gly Gly Ile Val Pro Pro Pro Ala Gly
225 230 235 240

Tyr Trp Glu Ala Ile Gln Thr Val Leu Asn Lys His Asp Ile Leu Leu
245 250 255

Val Ala Asp Glu Val Val Thr Gly Phe Gly Arg Leu Gly Thr Met Phe
260 265 270

Gly Ser Asp His Tyr Gly Leu Glu Pro Asp Ile Ile Thr Ile Ala Lys
275 280 285

Gly Leu Thr Ser Ala Tyr Ala Pro Leu Ser Gly Ser Ile Val Ser Asp

290 295 300

Lys Val Trp Lys Val Leu Glu Gln Gly Thr Asp Glu Asn Gly Pro Ile
305 310 315 320

Gly His Gly Trp Thr Tyr Ser Ala His Pro Ile Gly Ala Ala Ala Gly
 325 330 335

Val Ala Asn Leu Lys Leu Leu Asp Glu Leu Asn Leu Val Ser Asn Ala
 340 345 350

Gly Glu Val Gly Ala Tyr Leu Asn Ala Thr Met Ala Glu Ala Leu Ser
 355 360 365

Gln His Ala Asn Val Gly Asp Val Arg Gly Glu Gly Leu Leu Cys Ala
 370 375 380

Val Glu Phe Val Lys Asp Arg Asp Ser Arg Thr Phe Phe Asp Ala Ala
385 390 395 400

Asp Lys Ile Gly Pro Gln Ile Ser Ala Lys Leu Leu Glu Gln Asp Lys
 405 410 415

Ile Ile Ala Arg Ala Met Pro Gln Gly Asp Ile Leu Gly Phe Ala Pro
 420 425 430

Pro Phe Cys Leu Thr Arg Ala Glu Ala Asp Gln Val Val Glu Gly Thr
 435 440 445

Leu Arg Ala Val Lys Ala Val Leu Gly
 450 455

<210> 2

<211> 457

<212> PRT

<213> Artificial Sequence

<220>

<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 2

Met Leu Lys Asn Asp Gln Leu Asp Gln Trp Asp Arg Asp Asn Phe Phe

1 5 10 15

His Pro Ser Thr His Leu Ala Gln His Ala Arg Gly Glu Ser Ala Asn
20 25 30

Arg Val Ile Lys Thr Ala Ser Gly Val Phe Ile Glu Asp Arg Asp Gly
35 40 45

Thr Lys Leu Leu Asp Ala Phe Ala Gly Leu Trp Cys Val Asn Val Gly
50 55 60

Tyr Gly Arg Gln Glu Ile Ala Glu Ala Ile Ala Asp Gln Ala Arg Glu
65 70 75 80

Leu Ala Tyr Tyr His Ser Phe Val Gly His Gly Thr Glu Ala Ser Ile
85 90 95

Thr Leu Ala Lys Met Ile Leu Asp Arg Ala Pro Lys Asn Met Ser Lys
100 105 110

Val Tyr Phe Gly Leu Gly Gly Ser Asp Ala Asn Glu Thr Asn Val Lys
115 120 125

Leu Ile Trp Tyr Tyr Asn Asn Ile Leu Gly Arg Pro Glu Lys Lys Lys
130 135 140

Ile Ile Ser Arg Trp Arg Gly Tyr His Gly Ser Gly Leu Val Thr Gly
145 150 155 160

Ser Leu Thr Gly Leu Glu Leu Phe His Lys Lys Phe Asp Leu Pro Val
165 170 175

Glu Gln Val Ile His Thr Glu Ala Pro Tyr Tyr Phe Arg Arg Glu Asp
180 185 190

Leu Asn Gln Thr Glu Glu Gln Phe Val Ala His Cys Val Ala Glu Leu
195 200 205

Glu Ala Leu Ile Glu Arg Glu Gly Ala Asp Thr Ile Ala Ala Phe Ile
210 215 220

Gly Glu Pro Ile Leu Gly Ala Gly Gly Ile Val Pro Pro Pro Ala Gly
 225 230 235 240

Tyr Trp Glu Ala Ile Gln Thr Val Leu Asn Lys His Asp Ile Leu Leu
 245 250 255

Val Ala Asp Glu Val Val Thr Gly Phe Gly Arg Leu Gly Thr Met Phe
 260 265 270

Gly Ser Asp His Tyr Gly Leu Glu Pro Asp Ile Ile Thr Ile Ala Lys
 275 280 285

Gly Leu Thr Ser Ala Tyr Ala Pro Leu Ser Gly Ser Ile Val Ser Asp
 290 295 300

Lys Val Trp Lys Val Leu Glu Gln Gly Thr Asp Glu Asn Gly Pro Ile
 305 310 315 320

Gly His Gly Trp Thr Tyr Ser Ala His Pro Ile Gly Ala Ala Ala Gly
 325 330 335

Val Ala Asn Leu Lys Leu Leu Asp Glu Leu Asn Leu Val Ser Asn Ala
 340 345 350

Gly Glu Val Gly Ala Tyr Leu Asn Ala Thr Met Ala Glu Ala Leu Ser
 355 360 365

Gln His Ala Asn Val Gly Asp Val Arg Gly Glu Gly Leu Leu Cys Ala
 370 375 380

Val Glu Phe Val Lys Asp Arg Asp Ser Arg Thr Phe Phe Asp Ala Ala
 385 390 395 400

Asp Lys Ile Gly Pro Gln Ile Ser Ala Lys Leu Leu Glu Gln Asp Lys
 405 410 415

Ile Ile Ala Arg Ala Met Pro Gln Gly Asp Ile Leu Gly Phe Ala Pro
 420 425 430

Pro Phe Cys Leu Thr Arg Ala Glu Ala Asp Gln Val Val Glu Gly Thr
 435 440 445

Leu Arg Ala Val Lys Ala Val Leu Gly
 450 455

<210> 3

<211> 457

<212> PRT

<213> Artificial Sequence

<220>

<221> source

<223> /note="Description of Artificial Sequence: Synthetic
 polypeptide"

<400> 3

Met Leu Lys Asn Asp Gln Leu Asp Gln Trp Asp Arg Asp Asn Phe Phe
 1 5 10 15

His Pro Ser Thr His Leu Ala Gln His Ala Arg Gly Glu Ser Ala Asn
 20 25 30

Arg Val Ile Lys Thr Ala Ser Gly Val Phe Ile Glu Asp Arg Asp Gly
 35 40 45

Thr Lys Leu Leu Asp Ala Phe Ala Gly Leu Phe Cys Val Asn Val Gly
 50 55 60

Tyr Gly Arg Gln Glu Ile Ala Glu Ala Ile Ala Asp Gln Ala Arg Glu
 65 70 75 80

Leu Ala Tyr Tyr His Ala Phe Val Gly His Gly Thr Glu Ala Ser Ile
 85 90 95

Thr Leu Ala Lys Met Ile Leu Asp Arg Ala Pro Lys Asn Met Ser Lys
 100 105 110

Val Tyr Phe Gly Leu Gly Gly Ser Asp Ala Asn Glu Thr Asn Val Lys
 115 120 125

Leu Ile Trp Tyr Tyr Asn Asn Ile Leu Gly Arg Pro Glu Lys Lys Lys
 130 135 140

Ile Ile Ser Arg Trp Arg Gly Phe His Gly Ser Gly Leu Val Thr Gly
 145 150 155 160

Ser Leu Thr Gly Leu Glu Leu Phe His Lys Lys Phe Asp Leu Pro Val
 165 170 175

Glu Gln Val Ile His Thr Glu Ala Pro Tyr Tyr Phe Arg Arg Glu Asp
 180 185 190

Leu Asn Gln Thr Glu Glu Gln Phe Val Ala His Cys Val Ala Glu Leu
 195 200 205

Glu Ala Leu Ile Glu Arg Glu Gly Ala Asp Thr Ile Ala Ala Phe Ile
 210 215 220

Gly Glu Pro Ile Leu Gly Ala Gly Gly Met Val Pro Pro Pro Ala Gly
 225 230 235 240

Tyr Trp Glu Ala Ile Gln Thr Val Leu Asn Lys His Asp Ile Leu Leu
 245 250 255

Val Ala Asp Glu Val Val Thr Gly Phe Gly Arg Leu Gly Thr Met Phe
 260 265 270

Gly Ser Asp His Tyr Gly Leu Glu Pro Asp Ile Ile Thr Ile Ala Lys
 275 280 285

Gly Leu Thr Ser Ala Tyr Ala Pro Leu Ser Gly Ser Ile Val Ser Asp
 290 295 300

Lys Val Trp Lys Val Leu Glu Gln Gly Thr Asp Glu Asn Gly Pro Ile
 305 310 315 320

Gly His Gly Trp Thr Tyr Ser Ala His Pro Ile Gly Ala Ala Ala Gly
 325 330 335

Val Ala Asn Leu Lys Leu Leu Asp Glu Leu Asn Leu Val Ser Asn Ala
 340 345 350

Gly Glu Val Gly Ala Tyr Leu Asn Ala Thr Met Ala Glu Ala Leu Ser
 355 360 365

Gln His Ala Asn Val Gly Asp Val Arg Gly Glu Gly Leu Met Cys Ala
 370 375 380

Val Glu Phe Val Lys Asp Arg Asp Ser Arg Thr Phe Phe Asp Ala Ala
 385 390 395 400

Asp Lys Ile Gly Pro Gln Ile Ser Ala Lys Leu Leu Glu Gln Asp Lys
 405 410 415

Ile Ile Ala Arg Ala Met Pro Gln Gly Asp Ile Leu Gly Phe Ala Pro
 420 425 430

Pro Phe Cys Leu Thr Arg Ala Glu Ala Asp Gln Val Val Glu Gly Thr
 435 440 445

Leu Arg Ala Val Lys Ala Val Leu Gly
 450 455

<210> 4

<211> 464

<212> PRT

<213> Artificial Sequence

<220>

<221> source

<223> /note="Description of Artificial Sequence: Synthetic
 polypeptide"

<400> 4

Met Ala Thr Ile Thr Asn His Met Pro Thr Ala Glu Leu Gln Ala Leu
 1 5 10 15

Asp Ala Ala His His Leu His Pro Phe Ser Ala Asn Asn Ala Leu Gly
 20 25 30

Glu Glu Gly Thr Arg Val Ile Thr Arg Ala Arg Gly Val Trp Leu Asn
 35 40 45

Asp Ser Ala Leu Ala Gln Lys Leu Ala Glu Leu Ala Gly Leu Trp Cys
 50 55 60

Val Asn Ile Gly Tyr Gly Arg Asp Glu Leu Ala Glu Val Ala Ala Arg
 65 70 75 80

Gln Met Arg Glu Leu Pro Tyr Tyr Asn Thr Phe Phe Lys Thr Thr His
 85 90 95

Val Pro Ala Ile Ala Leu Ala Gln Lys Leu Ala Glu Leu Ala Pro Gly
 100 105 110

Asp Leu Asn His Val Phe Phe Ala Gly Gly Gly Ser Glu Ala Asn Asp
 115 120 125

Thr Asn Ile Arg Met Val Arg Thr Tyr Trp Gln Asn Lys Gly Gln Pro
 130 135 140

Glu Lys Thr Val Ile Ile Ser Arg Lys Asn Ala Tyr His Gly Ser Thr
 145 150 155 160

Val Ala Ser Ser Ala Leu Gly Gly Met Ala Gly Met His Ala Gln Ser
 165 170 175

Gly Leu Ile Pro Asp Val His His Ile Asn Gln Pro Asn Trp Trp Ala
 180 185 190

Glu Gly Gly Asp Met Asp Pro Glu Glu Phe Gly Leu Ala Arg Ala Arg
 195 200 205

Glu Leu Glu Glu Ala Ile Leu Glu Leu Gly Glu Asn Arg Val Ala Ala
 210 215 220

Phe Ile Ala Glu Pro Val Gln Gly Ala Gly Gly Val Ile Val Ala Pro
 225 230 235 240

Asp Ser Tyr Trp Pro Glu Ile Gln Arg Ile Cys Asp Lys Tyr Asp Ile
 245 250 255

Leu Leu Ile Ala Asp Glu Val Val Cys Gly Phe Gly Arg Thr Gly Asn
 260 265 270

Trp Phe Gly Thr Gln Thr Met Gly Ile Arg Pro His Ile Met Thr Ile
 275 280 285

Ala Lys Gly Leu Ser Ser Gly Tyr Ala Pro Ile Gly Gly Ser Ile Val
 290 295 300

Cys Asp Glu Val Ala His Val Ile Gly Lys Asp Glu Phe Asn His Gly

305 310 315 320

Tyr Thr Tyr Ser Gly His Pro Val Ala Ala Ala Val Ala Leu Glu Asn
 325 330 335

Leu Arg Ile Leu Glu Glu Glu Asn Ile Leu Asp His Val Arg Asn Val
 340 345 350

Ala Ala Pro Tyr Leu Lys Glu Lys Trp Glu Ala Leu Thr Asp His Pro
 355 360 365

Leu Val Gly Glu Ala Lys Ile Val Gly Met Met Ala Ser Ile Ala Leu
 370 375 380

Thr Pro Asn Lys Ala Ser Arg Ala Lys Phe Ala Ser Glu Pro Gly Thr
 385 390 395 400

Ile Gly Tyr Ile Cys Arg Glu Arg Cys Phe Ala Asn Asn Leu Ile Met
 405 410 415

Arg His Val Gly Asp Arg Met Ile Ile Ser Pro Pro Leu Val Ile Thr
 420 425 430

Pro Ala Glu Ile Asp Glu Met Phe Val Arg Ile Arg Lys Ser Leu Asp
 435 440 445

Glu Ala Gln Ala Glu Ile Glu Lys Gln Gly Leu Met Lys Ser Ala Ala
 450 455 460